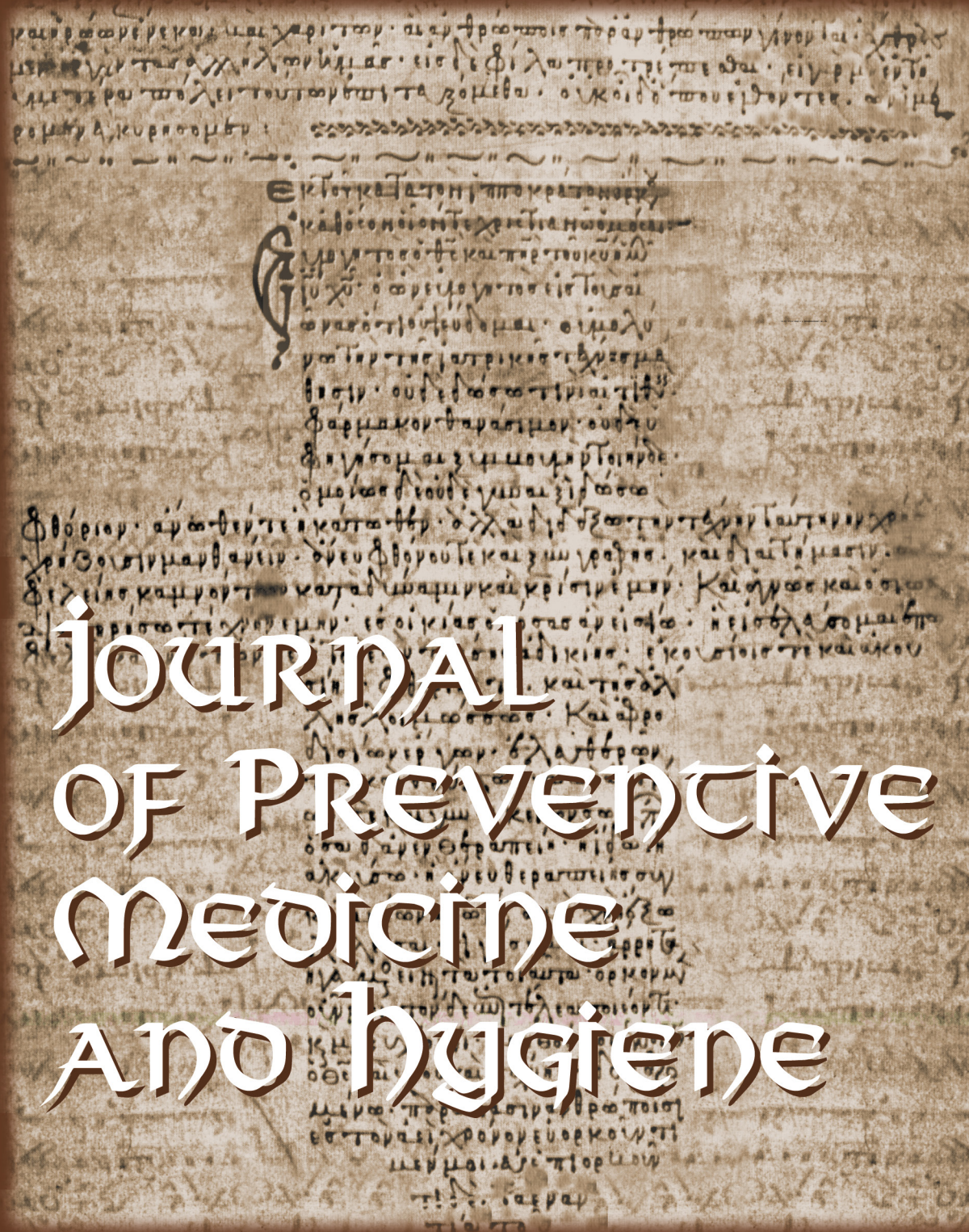


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LETTER TO THE EDITOR

Vaccines hesitancy in Africa: how COVID-19 pandemic may affect malaria vaccination campaigns

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According to the WHO Strategic Advisory Group of Experts on Immunization (SAGE), vaccine hesitancy (VH) refers to the delay in accepting or refusing vaccination despite the availability of vaccination services [1]. VH is complex and context-specific, varying across time, place and vaccines, and the term itself is debated, considering the variety of different and complex situations and determinants it implies [1].

Although VH was already considered a global health issue and it was therefore listed among the 10 global health threats identified by the WHO in 2019 [2], the COVID-19 pandemic and the management of the COVID-19 vaccination campaign, have contributed to making VH a contingent problem that might jeopardize future vaccination campaigns all over the world. In this context, waiving patents and recognizing vaccines as a global public good would have built a powerful trust engendering mechanism [3]. From this concept and by taking the recent approval of the antimalarial vaccine in areas of high endemicity as an example, we hereby discuss the possible influence that VH may have on the acceptance of new vaccines in the future.

Even in Africa, VH is becoming a major challenge despite the remarkable progress made by long-standing vaccination programmes through the improvement of routine childhood vaccination coverage [4], such as the rising in coverage of three doses of diphtheria-tetanus-pertussis containing vaccines (DTP3) from 57% to 74% in 15 years [5], or the decline of 85% in measles mortality between 2000 and 2015 [6] and the certification of the WHO African Region as free of wild poliovirus on August 25th 2020, after four years without a single case [7].

On 6th October 2021, the World Health Organization (WHO) recommended the widespread use of the RTS, S/AS01 (RTS,S) malaria vaccine among children in sub-Saharan Africa and in other regions with moderate to high *P. falciparum* malaria transmission [8]. Although results from the pilot programme represent a historical momentum in the fight against malaria, growing VH recently powered by issues related to the management of the response to the COVID-19 pandemic, may

hamper the real-world acceptance of RTS,S across the continent [9].

The rollout COVID-19 vaccines in Africa has been primarily halted by shortage and barriers to purchase, partially due to western countries hoarding. Driven by lack of corporate and institutional transparency, misinformation and misconceptions circulating on social media, VH threatens to further hamper the vaccination process [10]. Beliefs rooted in the history of unethical western medical practices in the African continent [11], and in the enduring legacy of colonial violence, fosters scepticism against vaccination [12]. A recent survey conducted across 15 African countries, showed a COVID-19 VH range going from 4 to 38% [13], while another study highlighted high rates (60%) in Benin, Liberia, Niger, Senegal, and Togo. The hesitancy was not confined to the general population only, but also among health workers in Ethiopia and Republic Democratic of Congo, frequently worried about safety, side effects and effectiveness of the vaccine against COVID-19 [14].

Generalized vaccine distrust boosted by the priority given to the economic benefits of the patent system, along with misinformation in mainstream media and social networks, and ineffective communication from some scientific and political representatives regarding COVID-19 vaccines [3], could compromise ongoing vaccination programs, also targeting other diseases. Consequently, it could also affect the introduction of new vaccines, such as the recent one approved by WHO against malaria in Africa. In fact, the pandemic has already altered parental health-seeking behaviour; a recent WHO global poll reported that 73% of countries have witnessed reduction in demand for immunization, higher for countries in the WHO Africa region (89%) [15].

The issue is not new, and the causes are numerous. For example, in 1990 the anti-tetanus vaccination campaign was halted in Cameroon because of the belief among the general population that vaccines would make young girls infertile [16]. In 2015, Ebola vaccine trials were suspended in Ghana in response to media accusations that researchers were infecting participants with Ebola

virus [17]. In 2003-2004, Nigeria saw a general polio vaccine boycott due to the belief that the vaccine contained a contraceptive that would render children infertile, resulting in a five-fold increase in the polio incidence between 2002 and 2006 [18]. Vaccine hesitancy was also at the root of the refusal of measles vaccination among Apostolic communities in Zimbabwe [19], the reticence towards vaccination in Benin [20], and in Nigeria, where in a recent survey 42% of respondents stated that they were immune to coronavirus, highlighting their belief in God as the reason, and more than a third of Nigerians were unwilling to get vaccinated [21].

A mix of myths and misinformation on the one side and lack of an effective communication policy by the authorities on the other, create distrust within communities, extending VH to consolidated vaccines and consequently to possible outbreaks and deaths by preventable diseases. Hence, it urges putting in place appropriate risk communication strategies to understand and tackle vaccine mistrust, specially at community level. Fact checking within communities is a great challenge. Once the misinformation is shared, it becomes almost impossible to have control over it. Community members, including local leaders and community health professionals, need to be mobilized and trained to understand the reasons of generalized mistrust, explain short term, as well as unknown long-term risks, and disseminate the benefits of routine vaccination, with decades long consolidated vaccine programs, to increase trust. It should be acknowledged that a dogmatic approach might not always be a suitable strategy to address persistent rumours that hamper vaccination programs.

Understanding the role of rumours in the collective identity of a community might facilitate the development and implementation of effective interventions targeting vaccine hesitancy [22]. Additionally, as evidence on VH from low-middle income countries is still emerging [23] little is known about the nature and causes of VH in Africa, considering its high variability, context-specificity, and multiplicity of contextual factors [24]. There is a need for conducting research, which i) integrates social science and the medical perspective; ii) builds transdisciplinary knowledge, integrating expertise and experiential knowledge from different academic and non-academic fields [25], including sociology, anthropology, psychology, and education; iii) implements interventions to address concerns rather than only describing them.

Vaccination against malaria should be introduced effectively, and trust toward regular immunization programmes would be regained only through transparent information on vaccines' risks and benefits at all levels, and according to age groups and health conditions. History shows that once people's confidence in vaccines is compromised, it is difficult to gain it back. Distrust in one vaccine can lead to distrust in other vaccines, and this is particularly dangerous for the African continent, where reaching the general population through health promotion and education programs can be challenging.

To conclude, the peculiar conditions in which the COVID-19 vaccines were developed could both hamper the COVID-19 vaccination campaigns and pose a risk for future vaccinations. Although the causes of VH are multiple and complex, authorities and politicians have a crucial role in building transparency and trust, particularly by ensuring access for all [3].

Finally, while global agendas are increasingly focusing on biomedical technical solutions to health issues, we urge reinforcing the importance of public policies and health interventions, and to address societal health determinants. Within this framework, commitments to health equity and social justice, and whole of society intersectoral policy action are required, targeting structural determinants of health and the social mechanisms at the roots of inequity and distrust.

Ethical approvals

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We have read and understood the Journal of Preventive Medicine and Hygiene policy on declaration of interests and have no relevant interests to declare.

Authors' contributions

NS conceptualised the viewpoint. NS, BA, BF, MV, SB and SU drafted the manuscript. LM, FC and EM contributed to reviewing and finalising the manuscript. All Authors approved the final version of the manuscript.

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Italian National Health Service immunized by COVID-19?

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Key words

COVID-19 • Italian national healthcare system • Litigation • Indemnity reparation

Dear Editor,

After lots of reforms the Italian healthcare system has changed on many levels from the inspirational idea of National Healthcare System (NHS) and its universality [1-3]. At the same time, recent Italian Legislation has expanded the perimeter of citizen's right of health, beyond psycho-physical well-being, but better as an extension of self-determination right. The aforementioned principle was also emphasized by a recent Italian Supreme Court pronouncement, that stated the right of compensation for injuries of the self-determination principle, putting the right of health within the sphere of the rights of freedom [4, 5]. Moreover, the Legislator with Laws no. 24/2017 and no. 219/2017 has strengthen the role of doctor in society, doctor-patient fiduciary relationship and citizens' accountability [6, 7]. In this legislative framework, COVID-19 emergency displayed the great strengths, but also the weaknesses of Italian NHS, always considered as one of the best in the world [8]. As professionals in healthcare, with a *forma mentis* more prone for the juridical aspects of medical art, and from these considerations, we draft emerging implications on the holding of our NHS after COVID emergency, mainly in a risk management way, proposing some solutions, especially as the state of emergency continues.

First of all, on the model of clinical risk prevention, Authors emphasize a deflationary approach, already well organized in many hospitals, but to be extended to the whole health sector, especially to protect general practitioners, who were unable in this emergency to handle all requests and are potentially exposed to litigation. In this horizon, the medico-legal causal assessment of any improper conduct and their eventual health consequences becomes pivotal, in order to quickly and effectively filter patients' claims, already growing, rose by COVID-19 patients but also by non-COVID-19 patients. For this purpose, medico-legal support is advocated for a better overall evaluation, in order to reduce judicial issues between *costumers* and professionals.

Secondly, and logically after the causal assessment of the health damage, it is to contemplate the introduction of an indemnity system opposed to current compensation method, considering both the contingent state of *force majeure*, subsequent to national emergency declaration by the Council of Ministers [9], and the impossibility of granting same health rights to people as in peace-time,

given the sudden *revolution* of Healthcare Service. In this sense, looking at European Legislation, there is already a tradition of indemnity-compensation, both in France and in Germany, for example regarding nosocomial infections, where liability system is characterized by the formula of no-fault or objective liability. In a healthcare system such as the French one, with the prevalence of a Bismarck mutualistic funding, the interest in better control of the health damage outlay was certainly greater. This would allow to plan ahead and better the disbursement from health damage, first of all by the structures. As for years and as stated by the Gelli-Bianco Law no. 24/2017, with this approach hospitals could have better knowledge of their budgets and consequently of their self-retention fund. The most important implication of this methodological approach, the no-fault liability, is not to blame medical conduct, since there is no purpose of *offense* repression in the medical activity as a whole, in particular during this extraordinary emergency. The French principle is so simple on the procedural front that effective on the deflationary and economical level: if the error could be attributed to the frailty of the Institutions, responsible for the public service, who failed to guarantee the right to health because unprepared to manage a irresistible situation -here pandemic-, health-workers' responsibility, but also healthcare managers' responsibility, must be excluded [10-14]. The patient then, such as in hospital infections or compulsory vaccination, has any *onus probandi* and receives an indemnity, financed by mutual insurance funds for illness. In this special condition of emergency and exception to the natural rule, in view of *factum principis*, planning an adverse event management method, prior to the lawsuit, could be fundamental. Fair compensation for damage is granted, with the incomparable advantage of knowing previously the relative value.

The question of liability in the COVID-19-era arose urgently. Authors do not consider possible and disagree to undo responsibility at all: responsibility is the fundamental element that guarantees the professional diligence in particular, and the care of mankind in general. Nor do Authors agreed, as professionals, on the amendments, withdrawn, of deleting *d'emblée* the liability of the structures towards damages to operators. The insurance companies, called into question already by the Gelli-Bianco Law, will also have to commit themselves to the protection of the health professionals and health system [7]. We conclude by discussing the very foundations of the current financing

and organization system of healthcare. The pure Beveridge model works with a general taxation system and with the instruction on the correct use of such a precious and expensive system, therefore Authors appeal to collective commitment, without forgetting that this model alone is no more sustainable. Rethinking healthcare architecture and taking the lesson from the emergency, we should clarify relations among stakeholders (State, Regions, Local Authorities) and strengthen the Regional primary care system. On this perspective, the synergic participation of all health players is needed in order to build a mechanism in which the State intervenes not only to compensate deficits, but also to encourage a more efficient Regional health organization, integrating both the territorial medicine and the hospital management. The pandemic forced all the players – stakeholders, clinicians and citizens – to rethink our precious healthcare system, particularly its resilience, to still ensure health right for all in the future.

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We dedicate this study to the memory of our Professor Antonio Osculati, our greatest instrument, rethinking to Quintilian, “that without which the matter cannot be shaped to achieve its purpose”.

Ethical approval

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Conflict of interest statement

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Authors' contributions

AR: conception or design of the work and drafting. VB: conception or design of the work and drafting. CC: drafting and final version approval. GB: drafting and final version approval. PB: drafting and final version approval. JQ: drafting and final version approval. LPT: supervision and final editing.

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ORIGINAL ARTICLE

Studying the factors associated with Premenstrual syndrome prevention among pre-university students in Tehran

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Key words

Premenstrual Syndrome • Preventive behavior • Female Students

Summary

Introduction. *Premenstrual syndrome is one of the common menstrual disorders in adolescents. Considering the destructive effects of this syndrome on adolescents' activity and performance and the importance of epidemiological studies in designing preventive interventions,*

Aim. *This study aimed to determine some of the factors associated with the prevention of premenstrual syndrome among adolescents.*

Settings and Design. *In a cross-sectional study, 255 female high school students in Tehran were selected using multistage random sampling method.*

Methods and Material. *The data were collected using a demographic and background questionnaire and a valid and reliable questionnaire to assess preventive behaviors of premenstrual syndrome.*

Statistical analysis used. *The collected data were analyzed using SPSS software version 16 and descriptive statistics and logistic regression.*

Results. *The mean (SD) score of adoption of preventive behaviors of premenstrual syndrome was 19.25 (0.63) out of 50, and it was low. Also, weekly physical activity, mother education level, and family income were the factors affecting the adoption of preventive behaviors of premenstrual syndrome ($P < 0.05$).*

Conclusion. *Due to the low adoption of preventive behaviors among students with lower income families, students with less physical activity and students with mothers with lower levels of education, it is suggested that more attention be paid to the above students in designing educational programs to promote the prevention of premenstrual syndrome.*

Introduction

Premenstrual syndrome is a set of the physical, psychological and emotional disorders affecting the quality of life of individuals, and it is important to control and cure it [1]. Many researchers consider premenstrual syndrome as one of the most common psychosomatic disorders that impairs the women's' life [2]. This syndrome causes communication disorders, disruption of normal activities, sedentary lifestyle, lack of motivation and reduced accuracy in doing things, and if the severity of the symptoms is high, it disrupts the person's lifestyle, comfort and health [3]. This syndrome is a mental, neurological and endocrine disorder that appears as a recurrent course of physical, psychological and behavioral symptoms after ovulation and during a few days of menstrual onset (first week of Luteal phase) [4, 5]. The etiology of PMS is multifactorial in which the effect of hormonal disorders, especially low levels of progesterone in luteal phase, autonomic dysfunction, hyperglycemia - induced secretion and environmental factors such as alcohol intake and stress seem to be important [5].

Moreover, more than 150 symptoms have been attributed to PMS. The Symptoms include breast tenderness, headache, back pain, fatigue, tension and anxiety, unexplained anger or irritability, depression, varying degrees of edema in hands and feet, changes in sexual desire, bloating, joint and muscle pain, lack of energy, change in appetite, thirst, periods of crying, difficulty in concentration, aggression and suicidal tendencies [5, 6]. It is not also possible to determine the prevalence of this syndrome due to the variety of the forms of its symptoms. However, the incidence of this syndrome in different communities is estimated between 5 and 95% [7]. The prevalence of this syndrome was estimated to be 48% worldwide in a meta-analysis study in 2013 [8]. Although it was well studied in adults, however, it was only recently recognized in adolescents [9]. The emotional and mood symptoms that are common in this syndrome, when accompanied by the stresses of adolescence, usually cause the person to quarrel with others, and due to the lack of knowledge about the cause of their behavior change, they are considered as negative behaviors which finally cause tension, physical and

behavioral conflicts [5]. Menstrual disorders, including PMS, are also common in young adults and women. These disorders are often sources of anxiety for these patients and their families [5]. In the study of Ahmadi et al, 37% [10] and in study of Bakhshani et al, 83.1% of female adolescents were affected by PMS [11].

However, preventive behaviors for premenstrual syndrome include behaviors such as eating calcium-rich foods such as milk and yogurt, taking multivitamin supplements, exercising, staying away from stressful situations, and so on [5]. Adolescence is one of the most important periods of life in which the lifestyle is formed and stabilized. Adolescents are the rich assets of the future and addressing adolescent health is one of the priority programs in health and prevention medicine in the world [12]. According to the studies conducted by the researchers of the present study, the adoption of preventive behaviors of premenstrual syndrome and the factors affecting them have not been studied so far in Iranian adolescents. According to experts, the first step in designing preventive interventions is epidemiological studies [13]. According to epidemiologists, the first step is to design preventive interventions for this disorder [13]. Also, because the woman's menstrual cycle begins in adolescence, and it is easier to internalize healthy behaviors at this age, and also because of the destructive effects of this syndrome on their performance in their life [5], this study aimed at determining the factors associated with the prevention of premenstrual syndrome among adolescents.

Methods

This was a descriptive-analytical cross-sectional study conducted with 255 students studying pre-university course in Tehran in 2016. The sampling method was multi-stage random, so that a list of all 19 education districts of Tehran was first prepared. Then, out of these 19 districts, 4 districts were randomly selected and one high school was randomly selected from each district. In the last stage, one class was randomly selected from each selected high school and their students were included in the study. Inclusion criteria were: having good health (no history or known disease), regular menstrual periods for at least one year, not using hormonal compounds, and willingness to take part in the study (by completing the informed consent form to participate in the study). Exclusion criteria were: incomplete completion of the questionnaires, lack of menstruation and irregular menstruation, and the use of hormonal compounds during the study.

Due to the results of a pilot study among 30 students and considering $P = 0.2$ for adoption of preventive behaviors of premenstrual syndrome, and also using Cochran's sample size formula and calculating $d = 0.05$, the sample size was estimated to be 245 Students, which according to statistical experts and taking into account the 5% probability of sample loss, 255 Students were included in the study.

The data collection tool in this study was a questionnaire that consisted of 2 parts:

1. Demographic and background information: included age, ethnicity, field of study, marital status, ethnicity, parental education level, parental employment status, monthly family income, physical activity per week, number of family members and the birth rank in the family;
2. Khalilipour Darestani and Panahi questionnaire was used to assess the behaviors associated with premenstrual syndrome prevention [5]. This questionnaire consisted of 10 items with a 5-level scale: always (5 points), often (4 points), sometimes (3 points), rarely (2 points) and never (1 point). The score range was between 10 and 50 [5]. This questionnaire has already been validated by the researchers; first, the questionnaire was sent to 10 professors to analyze its content and after getting their opinions, the necessary changes were made. Then it was resent to the professors to confirm the changes, and the final changes were made to the questionnaire. Finally, the questionnaire obtained an acceptable score in terms of CVR and CVI (CVR = 0.98, CVI = 0.89). Also, to make it reliable, it was given to 30 students in the same educational level and Cronbach's alpha coefficient was calculated to be 0.91 [5]. Also, according to the researchers, the rate of adoption of preventive behaviors was classified into two levels: poor (scoring less than 50% of the total score) and good (scoring 50-100%) [14, 15], and this classification was used for the logistic regression in the study.

After receiving ethical approval from Deputy Director of Research and Technology at the Islamic Azad University of Science and Research (IR.IAU.SRB.REC.1394.11), and informing the Department of Education in Tehran and school officials, questionnaires were completed by the students. Also, before starting the study, their written consent was obtained. The questionnaires were self administered and the students were assured that all requested information would be confidential. The collected data were analyzed using SPSS software version 16 and descriptive statistics and logistic regression. The variables entered simultaneously and the interaction method of independent variables classified as index (indicator) was used, and the first class of variables was selected as the reference class. Moreover, the preventive behaviors of premenstrual syndrome was dependent variable, whereas age, ethnicity, field of study, marital status, ethnicity, parental education level, parental employment status, monthly family income, physical activity per week, number of family members and the birth rank in the family were independent ones. The significant level was also considered less than 0.05.

Results

240 students were studied and 15 were excluded from the study due to incomplete completion of the questionnaires (participation rate: 94.2%). 50.8% (122 people) were in the age group of 18 years. Only 12.5% (30 people)

Tab. I. Demographic and background characteristics of the participating students.

| Variables | | Frequency | Percent |
|---------------------------|--|-----------|---------|
| Age | 17 | 64 | 26.7 |
| | 18 | 122 | 50.8 |
| | 19 | 54 | 22.5 |
| Field of study | Conservatory | 84 | 35 |
| | Experimental | 56 | 23.3 |
| | Math | 30 | 12.5 |
| | Human | 70 | 29.2 |
| Marital status | Single | 222 | 92.5 |
| | Married. | 18 | 7.5 |
| Ethnicity | Turk | 110 | 45.8 |
| | Turkmen | 78 | 32.5 |
| | Others | 52 | 21.7 |
| Mother's education status | Below-diploma | 78 | 32.5 |
| | Diploma and post-diploma | 78 | 32.5 |
| | Bachelor's and higher education levels | 84 | 35 |
| Father's Education Status | Below-diploma | 76 | 31.7 |
| | Diploma and post-diploma | 62 | 25.8 |
| | Bachelor's and higher education levels | 102 | 42.5 |
| Mother's Job Status | Housekeeper | 144 | 60 |
| | Employee | 40 | 16.7 |
| | Others | 56 | 23.3 |
| Father's Job Status | Freelance | 116 | 48.3 |
| | Employee | 36 | 15 |
| | Military | 24 | 10 |
| | Others | 64 | 26.7 |
| Monthly family income | less than 1 million | 74 | 30.8 |
| | 2-3 Million | 106 | 44.2 |
| | more than 3 million | 60 | 25 |
| Weekly physical activity | every day | 32 | 13.4 |
| | Sometimes | 92 | 38.3 |
| | Rarely | 116 | 48.3 |
| Number of family members | 3 | 56 | 23.3 |
| | 4 | 112 | 46.7 |
| | 5 or more | 72 | 30 |
| Birth rank in family | First | 98 | 40.8 |
| | Second | 80 | 33.4 |
| | Third or higher | 62 | 25.8 |

were studying mathematics, 97.5% (234 people) were single, and 12.5% (30 people) reported doing physical activity every day. Table I shows other demographic and background characteristics of the Participating students. Also, the mean (SD) score of adoption of preventive behaviors of premenstrual syndrome in participating students was 19.25 (0.63) out of 50. In other words, the participants received 38.5% of the score of adoption of preventive behaviors of premenstrual syndrome. Table II shows the results of logistic regression to determine the factors affecting the adoption of preventive behaviors in premenstrual syndrome among Participating students. The results showed that the variables used predicted a total of 72.8% of the adoption of preventive behaviors of premenstrual syndrome ($R^2 = 0.728$). Also the results showed that one of the effective factors in adopting such behaviors was the mothers' level of education ($P = 0.021$), so that the chance of adopting

these behaviors in students with mothers with diploma, post-diploma, bachelor's and higher education levels was 1.219 and 3.543 times higher than students with mothers with below-diploma degree, respectively. Another factor effective the adoption of premenstrual syndrome preventive behaviors was the amount of family income ($P = 0.041$), so that the chances of adopting such behaviors in students with their family income between 2 and 3 million and more than 3 million, were 1.129 and 2.869 times more than the students whose family income was less than 2 million in a month respectively. Another factor effective the adoption of premenstrual syndrome preventing behaviors was physical activity ($P = 0.008$), so that the chances of adopting these behaviors in students with occasional and rare physical activity were 0.758 and 0.451 times of those with a regular daily physical activity. Also, there was no significant relationship between age,

Tab. II. The factors affecting the preventive behaviors of premenstrual syndrome among participating students in logistic regression.

| Variable | Sig. | OR (95% CI) |
|--|-------|----------------------|
| Age | 0.541 | |
| 18 | 0.425 | 1.2222 (0.857-1.432) |
| 19 | 0.411 | 1.301 (0.841-1.475) |
| Field of study | 0.842 | |
| Experimental | 0.358 | 1.212 (0.974-1.359) |
| Math | 0.412 | 0.555 (0.456-1.136) |
| Human | 0.651 | 0.616 (0.543-1.712) |
| Marital status | 0.153 | |
| Married | 0.198 | 1.105 (0.711-1.981) |
| Ethnicity | 0.214 | |
| Turkmen | 0.325 | 4.189 (0.389-7.220) |
| Others | 0.648 | 1.526 (0.734-2.055) |
| Mother's education | 0.021 | |
| Diploma and post-diploma | 0.013 | 1.219 (1.107-1.654) |
| Bachelor's and higher education levels | 0.009 | 3.543 (2.916-6.005) |
| Father's education | 0.594 | |
| Diploma and post-diploma | 0.421 | 0.334 (0.212-1.340) |
| Bachelor's and higher education levels | 0.212 | 1.255 (0.830-2.971) |
| Mother's Job Status | 0.717 | |
| Employee | 0.592 | 0.554 (0.409-1.407) |
| Others | 0.645 | 1.333 (0.954, 2.210) |
| Father's Job Status | 0.453 | |
| Employee | 0.311 | 0.655 (0.550-1.077) |
| Military | 0.212 | 2.409 (0.713-6.017) |
| Others | 0.551 | 1.213 (0.879-1.999) |
| Monthly family income | 0.041 | |
| 2-3 million | 0.033 | 1.129 (1.033-1.906) |
| More than 3 million | 0.024 | 2.869 (1.769-4.662) |
| Weekly physical activity rate | 0.008 | |
| Sometimes | 0.025 | 0.758 (0.683-0.950) |
| Rarely | 0.036 | 0.451 (0.401-0.627) |
| Number of family members | 0.681 | |
| 4 | 0.753 | 0.469 (0.417-1.611) |
| 5 or more | 0.844 | 0.619 (0.313-1.213) |
| Birth rank in family | 0.551 | |
| Second | 0.489 | 1.333 (0.821-1.419) |
| Third or higher | 0.525 | 1.458 (0.712-1.286) |
| Constant | 1.000 | 7.541371 |

field of study, marital status, ethnicity, father's level of education, parental employment status, number of family members and birth rank in the family with premenstrual syndrome preventive behaviors ($P > 0.05$).

Discussion

This study aimed to determine some of the factors affecting the prevention of premenstrual syndrome among pre-university students in Tehran. The adoption of premenstrual syndrome preventing behaviors in these students was at a low level. This might be due to their insufficient knowledge and attitude about premenstrual syndrome, because there was a significant and direct relationship between these two variables and behavior [16, 17]. These results were in consistent

with the results of the studies of Panahi et al. [14], Gharlipour et al. [18] and Panahi et al. [19], but they were inconsistent with the results of the studies of Panahi et al. [15], Peyman et al. [20] and Farshbaf Khalili and Colleagues [21] which reported moderate preventive behaviors adoption. Possible reasons for this discrepancy could be differences in the age of the participants as well as differences in the type of preventive behaviors.

The results also showed that one of the effective factors in adopting preventive behaviors in premenstrual syndrome was physical activity. One of the possible reasons for this result might be the homogeneity of these two variables. In fact, physical activity is a kind of preventive behavior by itself. Similar to the present result, the results of a study by Ghaffari et al. showed that a regular exercise program reduced the severity of premenstrual syndrome [22]. Also, the results of the

study by Safavi Naeini showed that physical activity was effective in reducing the symptoms of premenstrual syndrome [23]. The results of this part of the present study were consistent with the results of Panahi et al. [15] and Masho et al. [24], but they were inconsistent with the results of Panahi et al. [19]. One of the possible reasons for this discrepancy might be the differences in factors such as the Prevention topic, gender and age of participants in both studies.

Moreover, the results showed that another factor influencing the adoption of preventive behaviors of premenstrual syndrome was the mother's level of education. Education is one of the most important socio-economic indicators that affects the knowledge, attitude and skills necessary to adopt health-related behaviors [25], and as the mothers' awareness, positive attitude and behaviors associated with preventing premenstrual syndrome increased, positive changes also occurred in the students' preventive behaviors because they had close relationship with their mothers. It also seemed that people with higher education had more resources to acquire knowledge and information, and accordingly, the level of education of mothers, which are a model for adopting health behaviors for their children, could improve their children's adoption of preventive behaviors of premenstrual syndrome. These results are consistent with the results of studies by Panahi et al. [26], Etehadnezhad et al. [27], Kumar et al. [28], Menshadi et al. [29], Rabiei et al. [30] and Khani Jeihooni et al. [31].

The results also showed that another factor influencing the adoption of preventive behaviors of premenstrual syndrome was family income. Prevention of premenstrual syndrome requires a combination of lifestyle modification, dietary and nutritional changes, physical activity, and drug therapy [7, 32, 33]. It is obvious that doing most of these requires sufficient income in the family. The results, here, were not consistent with the results of studies of Haji Karim Baba et al. [34], and Panahi et al. [19]. One of the possible reasons might be the differences between the factors such as prevention topic and age of participants in these studies and the present one. Also in the study of Panahi et al. [19], the participants were students of both sexes, while in the present study, only girls were present.

The limitations of this study included the limited sample size, lack of data analysis about the students excluded from the study, and also the self-report method in completing the questionnaires which made the comparison of the results with other studies difficult. Since the participants were only female undergraduate students in Tehran, the results cannot be generalized to students in other parts of the country as well as those peers who left school studies before. Therefore, it is recommended to do this study in different populations and groups of women (in terms of age, education and region of residence). Lack of accurate information about the studied topic was other limitation of the study.

Conclusion

The results of the present study showed that the adoption of preventive behaviors of premenstrual syndrome was poor among the Participating students. Due to the low adoption of preventive behaviors among the students with less physical activity, the students with mothers with lower levels of education, and the students with families with lower incomes, it is suggested that more attention be paid to the above students in designing educational programs to promote the prevention of premenstrual syndrome.

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Conflict of interest statement

No conflict of interest has been expressed by the authors.

Authors' contributions

MA, MA: implementation and collection of data, content collection, and writing the paper. RA, MKD, LD: collection of data and contributing to writing the paper. RP: content collection, writing the paper, supervisor, corresponding author.

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ORIGINAL ARTICLE

Addressing the COVID-19 Pandemic in an Iranian Sample: Health Beliefs and Respondent Characteristics Associated with Preventive Behaviors

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Key words

Coronavirus • COVID-19 • Preventive behavior • Health Belief Model

Summary

Background. The COVID-19 pandemic has become a grave threat to public health. Along with vaccination, preventive behaviors are still an important part in controlling the COVID-19 pandemic. The present study aimed to investigate health beliefs and sample characteristics associated with COVID-19 preventive health behaviors among an Iranian sample. Preventive behaviors are still an important part in controlling the COVID-19 pandemic.

Methods. This is a cross-sectional study, using a multi-stage randomized sampling method. Participants (N = 250 males and 236 females) were recruited from health centers in Saveh, Iran. Self-administered questionnaires included sociodemographic information, health behaviors, and constructs associated with the Health Beliefs Model (HBM). Data were analyzed using independent t-tests, analysis of variance, and multiple regression with significance level set at $\alpha \leq 0.05$.

Results. Perceived disease susceptibility ($\beta = 0.44$, $P < 0.001$), self-efficacy to enact preventative behaviors ($\beta = 0.24$, $P < 0.01$), education ($\beta = 0.20$, $P < 0.001$), non-smoking status ($\beta = 0.14$, $P < 0.01$), marital status ($\beta = 0.10$, $P < 0.03$), and perceived barriers to disease preventative behaviors ($\beta = -0.10$, $P < 0.04$) were important predictors of prevention practices for COVID-19, and accounted for 61.4% (adjusted R^2) of the variance associated with preventive behavior for COVID-19.

Conclusion. As there is accepted therapy for COVID-19, it is especially important to control COVID-19 through behavior change. Results indicate that two behavioral constructs that have the most impact on prevention are perceived disease susceptibility and self-efficacy. Therefore, public health initiatives are needed to enhance perceived susceptibility to the disease and improve self-efficacy to perform preventative behaviors in spite of perceived barriers.

Introduction

BACKGROUND

On December 29 of 2019, doctors from a hospital in Wuhan, China found non-normal cases of patients with pneumonia. On January 9, 2020, Chinese officials announced the cause as a new Coronavirus, called COVID-19 [1, 2], which stands for Corona Virus Disease-2019 [2]. The virus spread around the world, instilling fear and economic hardship. The World Health Organization announced world-wide public health warnings with the outbreak of the virus [3]. Infected persons can have mild or no symptoms, whereas others manifest severe respiratory illness resulting in shock, multi-organ dysfunction, and death [4, 5]. Complications of the disease are more severe in the elderly and those with chronic disease [6]. The virus, although perhaps less fatal than other emerging viruses in the Corona family, is very difficult to control and spreads rapidly, making it particularly dangerous [7]. Overall, the pandemic

has resulted in filled hospital beds, an exhausted health workforce, shortages of personal protective equipment, infected hospital staff, understaffing in care centers, and anxiety in various countries of the world [8, 9].

Along with vaccination, measures such as health education, increasing knowledge and information, and improving people's attitudes and perform preventive behaviors such as quarantining at home, using masks and gloves, washing hands and disinfecting surfaces play a very important role in controlling the COVID-19 pandemic [10, 11]. Despite the importance of these behaviors in the prevention and control of COVID-19, trending data in many areas of the world suggest such behaviors are not being utilized.. The results of a study in Iran showed that despite the positive attitude of women towards home quarantine, their performance was not reported as appropriate [12]. The results of another study in Australia showed that people (adults aged over 18 years) with inadequate health literacy had poor understanding of COVID-19 symptoms, were low able to identify behaviours to prevent infection,

and experienced high difficulty finding information and understanding government messaging about COVID-19 [13]. Therefore, it is necessary to identify factors affecting behavior change that will encourage use of preventive measures [14, 15].

Health behaviors are influenced by knowledge, attitudes, beliefs, values and habits [16-18]. A person's health beliefs can increase motivation to enact self-protective behaviors to mitigate disease risk and strengthen disease preventive behaviors [19]. The Health Beliefs Model (HBM) is a psychological model to describe the relationship between health beliefs and healthy behaviors [20]. HBM is one of the most effective models for identifying factors affecting preventive behaviors [16-18]. Based on this model, such factors include that a person believes: 1) s/he is susceptible to the disease (perceived sensitivity); 2) the effects of the disease are serious (perceived severity); 3) behaviors to reduce the risk of disease are useful (perceived benefits); 4) s/he can perform preventive tasks (self-efficacy); 5) and s/he can overcome inhibitory factors (perceived barriers) [12]. A meta-analysis showed that HBM can be used to understand many types of health behaviors among people [21]. The results of a study showed that the HBM is a good tool to predict COVID-19-preventive behaviors in Iranian population [22]. Although vaccination is considered a key strategy to end the COVID-19 pandemic [23], it is important to control this pandemic through preventive behaviors such as quarantining, use of masks and gloves, washing hands and disinfecting surfaces [24]. HBM can assist in identifying health beliefs that may enhance preventative behaviors for the spread of COVID-19. This study aimed to investigate health beliefs and respondent characteristics associated with preventive health behaviors for COVID-19 among a sample of Iranian people. We expect that constructs within the HBM model significantly predicted the protective behaviors of the disease, therefore, planning and implementation of health education programs can be done in accordance with the results of the present study.

Methods

DESIGN, PROCEDURE AND SAMPLE

A cross-sectional study design was utilized and data were collected in 2020. Sample size needed to obtain effects was estimated at $N = 400$ with precision of 5%, confidence level of 95%, and perceived susceptibility of 63% based on previous studies [25]. $N = 500$ were initially targeted for recruitment. Inclusion criteria were as follows: Resident of Saveh City; 18 years or older; and participation in written informed consent. The Research Ethics Committee of the Saveh University of Medical Sciences approved the study.

Multi-stage sampling was performed, where Saveh City was divided into northern, central and southern areas, in order to cover cultural characteristics of the population

in these regions. A healthcare center was selected from each region using simple random sampling. From the files of each healthcare center, 167 individuals meeting residence and age criteria were randomly selected for invitation to participate. Individuals were contacted by a researcher, who explained the study and consented participants. Following consent, data were collected in private using self-administered questionnaires, with private interviews used for illiterate persons.

MEASURES

Data were collected using questionnaires based on similar studies [14, 26-28] and that addressed constructs found in the HBM. There were three parts. 1) Demographics with 11 items (e.g., marital status). 2) HBM constructs (37 items) with responses rated using a Likert scale ranging from 1 (completely disagree) to 5 (completely agree): a) Perceived susceptibility with nine items such as, "If I do not follow health orders, I can get COVID-19." b) Perceived severity with six items such as, "I worry about dying and losing loved ones because of coronavirus." c) Perceived benefit with six items such as, "If I follow health and personal protection instructions, I have contributed to the control of the COVID-19 in the community." d) Perceived barriers with nine items such as, "I must work to avoid financial problems and I cannot quarantine in-home." e) Self-efficacy with six items such as, "I can follow the care advice even if it is time-consuming or expensive." f) Finally, a question was asked regarding the most important sources of information about COVID-19 to ascertain "cues to action," another important component of HBM. 3) Behaviors used to prevent COVID-19 were assessed via eight items such as, "I avoid shaking hands with others or kissing others." Preventive behaviors were assessed with a Likert scale ranging from, "I will definitely do this" (5) to "I will not do this at all" (1).

To develop the questionnaires, 10 experts, with knowledge of behavioral health models and with expertise in infectious disease and public health, were asked to generate and review items, using understandable language. Feedback was obtained and items were modified prior to deployment in the field. Cronbach's alpha was used to evaluate the internal consistency for scale. Cronbach alphas were as follows: Perceived susceptibility, $\alpha = .82$; perceived severity, $\alpha = .86$; perceived benefit, $\alpha = .79$; perceived barriers, $\alpha = .82$; self-efficacy, $\alpha = .81$; and COVID-19 preventive behaviors, $\alpha = .78$.

DATA ANALYSIS

The Kolmogorov-Smirnov test was used to determine the normal distribution of data. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) 21. A P-value of ≤ 0.05 was considered statistically significant. One-way analysis of variance (ANOVA) and *t*-tests were used to determine differences between the mean score of HBM constructs in two or more independent groups based on socio-demographic constructs (e.g., male vs female). Correlation among

variables was assessed with Pearson's *r*. To identify factors affecting COVID-19 preventive behaviors, multiple stepwise linear regression was used. The dependent variable was preventive behaviors and independent variables were demographics and HBM constructs. For analyses involving linear regression, the following were considered: Linear relationship among variables, multivariate normality, multicollinearity using a variance inflation factor < 5, and residual plot.

Results

SAMPLE

Of N = 500 questionnaires distributed, N = 486 were returned completed (250 males; 236 females; response rate = 97.2%). Mean (M) age of respondents was 32.8 years with standard deviation (SD) of 13. Table I presents descriptive data for the sample. Important sources for information about COVID-19 were radio and TV, cyberspace, friends and acquaintances, and health

system staff at 67%, 53%, 42% and 39%, respectively.

UNIVARIATE TESTS

The independent sample *t*-test showed that women and men had no significant difference in preventive behaviors for COVID-19 (Tab. I), but women had fewer perceived barriers and higher perceived susceptibility ($P < 0.05$). Married individuals had better preventive behaviors, fewer perceived barriers, and higher perceived benefit and susceptibility than widows and unmarried individuals ($P < 0.05$). University education was related to fewer perceived barriers, higher perceived susceptibility and more preventive behaviors as compared to illiterate persons or persons with only primary education ($P < 0.05$). No statistically significant differences were found among HBM constructs or preventive behaviors based on economic status. Job status was related to perceived susceptibility to COVID-19 ($P < 0.05$), with employees having the highest scores. Non-smokers had higher perceived benefits, self-efficacy, and better preventive behaviors compared to smokers ($P < 0.05$).

Tab. I. Differences in Health Belief Model Constructs by Socio-Demographics Variables.

| Preventive behavior | Perceived Self efficacy | Perceived Barriers | Perceived Benefits | Perceived Severity | Perceived Susceptibility | N | Variables |
|---------------------|-------------------------|--------------------|--------------------|--------------------|--------------------------|-----|----------------------|
| M (SD) | M (SD) | M (SD) | M (SD) | M (SD) | M (SD) | | |
| | | | | | | | Gender |
| 16.3 (5.5) | 13.9 (4.7) | 29.8 (7.7) | 12.3 (3.9) | 18.1 (5.2) | 21.3 (4.7) | 236 | Female |
| 14.7 (6.1) | 13.3 (5.1) | 34.8 (6.6) | 11.3 (4.6) | 17.9 (4.8) | 18.2 (5.6) | 250 | Male |
| 0.07 | 0.46 | 0.001 | 0.14 | 0.82 | 0.001 | | P value ^a |
| | | | | | | | Marital status |
| 16.2 (5.8) | 13.8 (4.8) | 30.6 (8.2) | 12.2 (4.3) | 17.7 (4.3) | 18.8 (5.3) | 189 | Single |
| 19.8 (3.1) | 16.2 (4.2) | 26.5 (10.2) | 16.8 (3.3) | 18.3 (5.6) | 20.3 (5.3) | 278 | Married |
| 15.0 (6.0) | 13.5 (4.9) | 34.2 (8.5) | 11.4 (4.0) | 16.2 (4.5) | 13.1 (2.2) | 19 | Divorced/ widow |
| 0.02 | 0.18 | 0.01 | 0.001 | 0.69 | 0.001 | | P value ^b |
| | | | | | | | Level of Education |
| 14.7 (5.4) | 12.9 (4.9) | 33.7 (7.1) | 11.2 (4.2) | 16.2 (3.7) | 16.9 (4.8) | 45 | Illiterate/ primary |
| 15.7 (5.3) | 13.6 (4.7) | 33.0 (8.2) | 12.0 (4.4) | 17.6 (4.0) | 17.6 (5.0) | 102 | Middle school |
| 16.6 (5.5) | 14.2 (5.9) | 28.3 (8.3) | 13.1 (4.3) | 19.6 (10.2) | 18.1 (5.8) | 250 | High school |
| 19.1 (5.6) | 14.9 (4.6) | 25.6 (9.7) | 13.8 (3.7) | 20.0 (3.0) | 20.5 (5.0) | 89 | University |
| 0.01 | 0.15 | 0.003 | 0.12 | 0.18 | 0.01 | | P value ^b |
| | | | | | | | Economic Status |
| 16.0 (5.7) | 13.1 (4.6) | 31.6 (8.6) | 11.8 (4.4) | 16.8 (3.6) | 18.8 (5.7) | 141 | good |
| 17.3 (6.8) | 13.4 (4.9) | 30.7 (7.1) | 11.6 (4.0) | 18.4 (5.1) | 19.4 (5.1) | 243 | medium |
| 15.1 (5.1) | 13.9 (4.8) | 32.0 (7.5) | 12.2 (4.3) | 18.6 (6.1) | 18.1 (5.9) | 102 | weak |
| 0.14 | 0.64 | 0.27 | 0.45 | 0.09 | 0.41 | | P value ^b |
| | | | | | | | Job |
| 14.2 (4.6) | 12.9 (5.1) | 33.2 (7.5) | 11.6 (4.4) | 17.1 (3.7) | 17.7 (5.2) | 159 | Housewife |
| 18.8 (7.7) | 14.8 (4.8) | 28.7 (8.0) | 13.8 (4.2) | 19.2 (7.8) | 20.3 (5.1) | 86 | Employee |
| 15.5 (5.1) | 12.8 (5.2) | 32.2 (5.7) | 11.3 (4.1) | 16.9 (5.2) | 15.7 (5.0) | 101 | worker |
| 16.9 (5.8) | 14.7 (5.0) | 31.3 (7.5) | 12.5 (5.0) | 18.7 (5.1) | 19.5 (5.3) | 92 | Free |
| 15.6 (6.1) | 13.5 (4.5) | 32.5 (8.9) | 12.2 (5.2) | 17.9 (4.5) | 17.8 (5.7) | 48 | Retired |
| 0.09 | 0.30 | 0.07 | 0.29 | 0.46 | 0.003 | | P value ^b |
| | | | | | | | Smoking |
| 14.2 (6.3) | 13.7 (5.0) | 32.6 (7.3) | 11.9 (4.3) | 16.8 (4.1) | 16.7 (5.4) | 73 | Yes |
| 18.9 (4.6) | 14.1 (4.5) | 29.6 (8.2) | 12.8 (4.2) | 18.5 (5.3) | 20.1 (5.2) | 413 | No |
| 0.04 | 0.01 | 0.12 | 0.01 | 0.21 | 0.17 | | P value ^a |

^a Independent Samples *t*-test. ^b Analysis of Variance (ANOVA). M: Mean; SD: Standard Deviation.

Tab. II. Final Model in a Step-Wise Regression Analysis Predicting Preventive Behaviors for COVID-19.

| Variables | Unstandardized Coefficients | | Standardized Coefficients | | 95.0% CI for B | | |
|--|-----------------------------|------|---------------------------|--------|----------------|-------------|---------|
| | B | SE | Beta (b) | t-test | Lower Bound | Upper Bound | P Value |
| (Constant) | 2.32 | 1.04 | | 2.21 | 0.25 | 4.39 | 0.02 |
| Marital status (Married = 1, Unmarried = 0) | 0.42 | 0.20 | 0.10 | 2.07 | 0.02 | 0.83 | 0.03 |
| Education (University = 1, Illiterate/ Primary = 0) | 0.76 | 0.22 | 0.20 | 3.47 | 0.33 | 1.20 | 0.001 |
| Non-Smoking (Yes = 1, No = 0) | 0.50 | 0.20 | 0.14 | 2.45 | 0.09 | 0.91 | 0.01 |
| Perceived Susceptibility | 1.95 | 0.25 | 0.44 | 7.79 | 1.45 | 2.44 | 0.001 |
| Perceived Self-Efficacy | 0.16 | 0.03 | 0.24 | 4.73 | 0.09 | 0.23 | 0.01 |
| Perceived Barriers | -0.31 | 0.15 | -0.10 | -2.01 | -0.62 | -0.006 | 0.04 |
| Model Adjusted R ² | 0.614 | | | | | | |

SE: Standard Error; CI: Confidence Interval.

The Pearson's correlation coefficient indicated that preventive behaviors had a statistically significant ($P < 0.05$) positive association with perceived susceptibility ($r = 0.43$), perceived severity ($r = 0.32$), perceived benefits ($r = 0.33$), and self-efficacy ($r = 0.41$), whereas perceived barriers had a negative association ($r = -0.36$).

MULTIVARIATE TESTS

Assumptions for regression were considered. Linearity was confirmed with an analysis of residuals; collinearity was checked and result was negative. Multiple stepwise linear regression (see Tab. II) showed that perceived susceptibility ($\beta = 0.44$, 95% CI: 1.45, 2.44), compared to other independent variables, had a greater impact on protective health behaviors for COVID-19. Self-efficacy ($\beta = 0.24$, 95% CI: 0.09, 0.23), education ($\beta = 0.20$, 95% CI: 0.33, 1.20), non-smoking ($\beta = 0.14$, 95% CI: 0.09, 0.91), marital status ($\beta = 0.10$, 95% CI: 0.02, 0.83), and perceived barriers ($\beta = -0.10$, 95% CI: -0.62, -0.006) were significant predictors of preventive behaviors. Together, these constructs accounted for 61.4% (adjusted R^2) of the variance in preventive behaviors.

Discussion

SUMMARY OF FINDINGS AND RELATION TO PRIOR STUDIES

The aim of this study was to assess the relationships between health beliefs, sample characteristics and COVID-19 preventive behaviors in an Iranian city. Sampling within the targeted region was robust with response rate of 97.2%. The most frequently endorsed sources of information on COVID-19 were radio and TV (67%) with relative less endorsement of healthcare staff (39%). The results of a study in another Iranian city showed that 37.5% of the population received most of their information about Coronavirus from TV and 53.9% received most of their information from social networks and the Internet [29]. In another study in Iran, internet and virtual social networks (49.8%), broadcast (33.5%),

and healthcare professionals (15.8%) were the main sources of people's information related to COVID-19, respectively [30]. Which are somewhat inconsistent with the results of the present study. Perhaps this difference is due to cultural and contextual differences.

Univariate tests indicated that HBM constructs (e.g., perceived disease severity) were significantly related to COVID-19 preventive behaviors (e.g., washing hands), and that being married, better educated and non-smoking related significantly to preventive behaviors. Further, being female, married, university-educated and non-smoking were significantly related to multiple constructs of the HBM, such as perceived barriers for health behaviors and perceived susceptibility. Results of univariate tests informed variable selection for multivariate analyses. Results of multivariate analyses are discussed below.

Perceived susceptibility was the most important construct for predicting behaviors in preventing COVID-19. This finding is consistent with a study by Kwok et al. [31] in Hong Kong and Lin et al. [32] in China that also found perceived susceptibility was an important factor in behavior. According to HBM, people must first perceive themselves to be at risk for a disease before acting to mitigate risk.

Self-efficacy was a significant factor in predicting preventive behavior. This finding was expected since self-efficacy is one of the most important factors explaining human behaviors and provides a good framework for understanding and predicting new behaviors [28]. Self-efficacy for preventive behaviors, or a belief that one can engage effectively in accomplishing goals, is critical in overcoming obstacles [28]. This result is consistent with a study by Karimy et al. [26], which showed that low self-efficacy is associated with reduced likelihood to change health behaviors. This is similar to a study by Elgzar et al. [20] that found self-efficacy was an important factor in overcoming perceived barriers to COVID-19 preventive behaviors. Similarly, a study in South Korea [33] found that perceived susceptibility and self-efficacy were important variables in determining preventive behaviors from COVID-19.

The current study found that perceived barriers significantly predicted preventive behaviors for COVID-19. Previous studies [26, 28] have documented that perceived barriers may act as a deterrent to performing recommended health behaviors, so health planners should consider ways to reduce perceived barriers. Understanding barriers to healthy behaviors is vital [34]. In particular, Maguire and colleagues [34] suggested identifying and overcoming perceived barriers are protective against COVID-19. Similarly, studies by Nowak et al. [35] and Elgzar et al. [20] found that individuals who perceived barriers as high were less likely to engage in COVID-19 preventive behavior.

In relation to socio-demographic factors, results showed that having a university degree significantly predicted preventive behaviors for COVID-19. Consistent with our findings, previous studies have highlighted the role of education as an important variable in health behaviors [36-38]. Our results showed that non-tobacco use was a significant predictor for preventive behavior; non-smokers may simply be more health-conscious. This finding is consistent with a study in Japan that also found smoking behavior appeared as a factor characterizing subjective prevention actions with non-smokers or less-frequent smokers more compliant to the protection behaviors [39].

Although previous studies have not shown a significant relationship between smoking and increased risk of severe COVID-19 [40], smoking can provide a favorable condition for virus transmission. Married individuals had better preventive behaviors than widows and unmarried individuals. This may be due to their higher perceived susceptibility for disease, greater perceived benefits of acting, and fewer perceived barriers to acting. At least one other study found a significant relationship between marital status and COVID-19 preventive behaviors [37].

Study Limitations and Strengths

The study has several limitations. This was a cross-sectional study and therefore does not allow causal inference. Second, data collection was based on self-report, not observation. Finally, the study was conducted in one city in Iran and hence cannot be generalized to the entire population; replication is recommended in other regions. However, the study has several strengths. Response rate was high. Procedures were designed to access a representative sample from the target city in terms of region (northern, central and southern). Although data were based on self-report, this method is often necessary to collect data on perceptions of risk, self-efficacy and other constructs of the HBM. Further, persons were not eliminated due to illiteracy, and trained interviewers gathered data in a private and confidential manner to enhance veridicality of self-report. Finally, the constructs under study were based on a well-validated model of health behaviors, namely the Health Beliefs Model. Results can inform interventions, and interventions based on well-validated

models may be more effective than models based on best-guess alone.

Conclusion

Results suggest targeting unmarried persons, those who smoke and those with less than a university degree may be important to enhance COVID-19 preventive behaviors. Disseminating public health messages regarding susceptibility to COVID-19, and enhancing efficacy to overcome common barriers to safety behaviors appears to be in order. The study identified several important avenues to provide such intervention including radio and TV, cyberspace, and health system staff.

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Ethics approval and consent to participate

The Research Ethics Committee of the Saveh University of Medical Sciences approved the study (Number: IR.SAVEHUMS.REC.1399.001). All participants provided written informed consent.

Conflict of interest statement

The authors declare that they have no competing interest.

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Availability of data and materials

Upon request, we can offer onsite access to external researchers to the data analyzed at Saveh University of Medical Sciences, Saveh, Iran. To do so, Dr. karimy should be contacted.

Authors' contributions

MK conceived the study. MA, HRK, LS, MRR and MM designed the study, collected the data, interpreted the results, contributed to writing the Article, and approved the final version for submission. MK supervised the study.

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ORIGINAL ARTICLE

A Comparative Study on Bacterial Co-Infections and Prevalence of Multidrug Resistant Organisms among Patients in COVID and Non-COVID Intensive Care Units

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Key words

Novel corona virus • Hospital acquired infections • SARS-CoV-2 • COVID-19 • Secondary bacterial infections • Multidrug resistance • Anti-microbial resistance • COVID ICU • Non-COVID ICU

Summary

Introduction. Secondary bacterial infections have been reported in majority of patients hospitalized with coronavirus disease 2019 (COVID-19). A study of the antimicrobial susceptibility profiles of these bacterial strains revealed that they were multidrug resistant, demonstrating their resistance to at least three classes of antimicrobial agents including beta-lactams, fluoroquinolones and aminoglycosides. Bacterial co-infection remains as an important cause for high mortality in patients hospitalized with COVID-19.

Methods. In our study, we conducted a retrospective comparative analysis of bacterial co-infections and the antimicrobial resistance profile of bacterial isolates obtained from inpatients admitted in COVID-19 and non-COVID-19 intensive care units. The goal was to obtain the etiology and antimicrobial resistance of these infections for more accurate use of antimicrobials in clinical settings.

This study involved a total of 648 samples collected from 356 COVID-19 positive patients and 292 COVID-19 negative patients admitted in the intensive care unit over a period of six months from May to October 2020.

Results. Among the co-infections found, maximum antimicrobial resistance was found in *Acinetobacter* species followed by *Klebsiella* species in both the ICU's. Incidence of bacterial co-infection was found to be higher in COVID-19 intensive care patients and most of these isolates were multidrug resistant strains.

Conclusion. Therefore, it is important that co-infections should not be underestimated and instead be made part of an integrated plan to limit the global burden of morbidity and mortality during the SARS-CoV-2 pandemic and beyond.

Introduction

The Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) first appeared in Wuhan, China in December 2019. It has now become a global pandemic affecting most of the countries round the world. Globally as on 3rd May 2021, the total confirmed cases and deaths due to COVID-19 disease reported to WHO include 152,387,917 and 3,195,624 respectively. India reported 19,925,604 confirmed cases of COVID-19 disease including 218,959 deaths to WHO [1]. Also, during the second wave, between 1st March and 3rd May, India has reported 8,813,363 confirmed cases and 61,802 deaths, thereby accounting for a total of 44.23% confirmed cases and 28.23% mortalities.

Antibiotics remain ineffective in treating COVID-19 but they are used to treat patients suspected of COVID-19. This is because of the difficulty in ruling out the Secondary bacterial infection and remains as a dangerous and common complication in hospitalized patients, especially with COVID-19 disease. They occur at an approximate incidence of 10-15% [2, 3]. Also, COVID-19 patients with secondary bacterial infections have a higher mortality rate of around 50% [4]. Therefore, early initiation of the appropriate antimicrobial therapy

can help to tackle the life threatening secondary bacterial infections. Current recommendations are extrapolated from the data available to treat other viral pneumonias as there are no proper controlled clinical trials available to support the use of empirical antimicrobial agents for the treatment of COVID-19 disease [5]. Studies have recommended empirical antimicrobial therapy like 3rd generation cephalosporins to treat all COVID-19 disease associated secondary bacterial infections [6, 7]. However, irrational use of broad-spectrum antibiotics to treat hospitalized patients can lead to the emergence of multidrug resistant isolates [8, 9]. Clear understanding of COVID-19 patients with secondary bacterial infection and the etiological agents will help to treat the COVID-19 patients promptly in order to assure the controlled use of antibiotics and to reduce the adverse effects of antibiotic overuse.

Therefore, based on the existing microbiological data, antibiotics ought to be judiciously used to treat COVID-19 patients with confirmed secondary bacterial infections. Currently there is no pre-existing data about the etiology or spectrum of secondary bacterial infections in patients with COVID-19 disease [10-12].

In the current study, a retrospective comparative analysis of secondary bacterial infections was made in critically ill patients with and without COVID-19 disease. The aim

was to obtain the etiology and antimicrobial resistance profile of bacterial isolates causing secondary bacterial infections in COVID-19 patients admitted in the ICU and also to compare the susceptibility profile of bacterial isolates obtained from critically ill COVID-19 negative patients. This can lead to a more accurate and effective antimicrobial use.

Materials and methods

This was a retrospective observational study carried out at Chettinad Hospital and Research Institute, a tertiary care hospital situated in Kelambakkam, Tamilnadu after obtaining due approval from the Institutional Human Ethics Committee.

Sample size: This study included a total of 648 patients which comprised of 356 COVID positive patients and 292 COVID negative patients admitted in other intensive care units (ICU). The study was conducted over a period of six months from May to October 2020.

The COVID-19 positive patients included in the study had tested positive for SARS CoV-2 infection by Real time RT-PCR (Reverse Transcriptase Polymerase Chain Reaction) as per Indian Council of Medical Research (ICMR) guidelines using SD-BIOSENSOR Real Time detection kit. SARS Cov2 RNA extraction for these samples was done using Qiacube, an automated nucleic acid extractor. The clinical samples from these patients, like blood, urine and sputum were obtained and processed for bacterial culture and sensitivity according to standard microbiological procedures [13]. The bacterial isolates were subjected to anti-microbial susceptibility testing (AST) by Kirby Bauer disc diffusion method as per Clinical and Laboratory Standards Institute (CLSI) Guidelines 2021. According to Centres for Disease Control and Prevention (CDC) definition the bacterial strains were identified as multidrug resistant if they were resistant to 1 drug each in at least 3 of the categories of drugs like extended spectrum cephalosporin, fluoroquinolones, aminoglycosides, carbapenems, and piperacillin tazobactam.

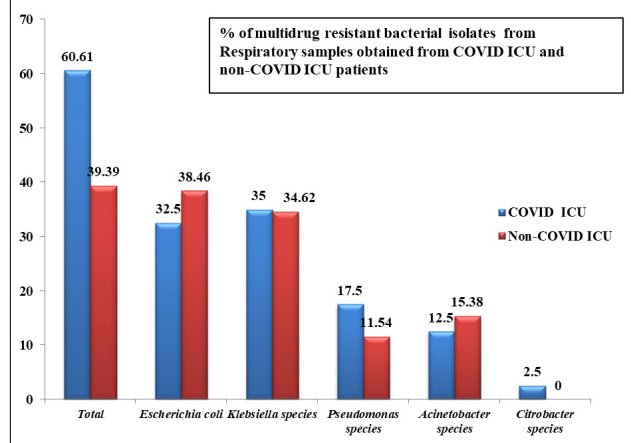
Results

Total of 648 patients were included in the study. Out of which 356 patients (54.94%) from the COVID ICU and 292 patients (45.06%) from the non-COVID ICUs.

Total respiratory samples processed was 316, out of which 178 (56.33%) samples were from COVID ICU and 138 (43.67%) samples were from other ICU's. Of the total 316 samples processed, 113 samples yielded pathogenic bacterial isolates, out of which 76 (67.26%) samples were from COVID ICU and 37 (32.74%) samples were from other ICU's.

Among the 113 samples that showed growth, 66 samples yielded multidrug resistant bacterial isolates. 40 (60.61%) samples were from COVID ICU and 26 (39.39%) samples were from other ICU's.

Fig. 1.



Bacteriological profile of the multidrug resistant isolates obtained from respiratory samples from COVID ICU and other ICU's includes *Escherichia coli*, *Klebsiella species*, *Pseudomonas species*, *Acinetobacter species* and *Citrobacter species* (Fig. 1). Multidrug resistant strains of *Escherichia coli* and *Klebsiella species* were found to be more prevalent in COVID ICU (32.5% & 35% respectively) and other ICU's (38.46% & 34.62% respectively).

A total of 320 urine samples were analyzed. Of the total 320 samples processed, 123 samples yielded growth, out of which 74 (60.16%) samples were from COVID ICU and 49 (39.84%) samples were from other ICU's. Among the 123 samples that yielded growth, 65 samples yielded multidrug resistant isolates. 40 (61.54%) Multidrug Resistant (MDR) isolates were from COVID ICU and 25 (38.46%) MDRO's were from other ICU's.

The bacteriological profile of the multidrug resistant bacterial urine isolates from COVID ICU and other ICU's includes *Escherichia coli*, *Klebsiella species*, *Pseudomonas species*, *Acinetobacter species* and *Proteus species* (Fig. 2) Multidrug resistant *Escherichia coli* and *Klebsiella species* were found to be more prevalent in COVID ICU (35% and 37.5% respectively) and other ICU's (40% each).

Total blood samples processed was 175, out of which 106 (60.57%) samples were from COVID ICU and 69 (39.43%) samples were from other ICU's. Of the total 175 samples processed, 76 samples yielded growth, out of which 53 (69.74%) samples were from COVID ICU and 23 (30.26%) samples were from other ICU's. Among the 76 samples that showed growth, 23 yielded multidrug resistant isolates. 14 (60.87%) samples were from COVID ICU and 9 (39.13%) samples from other ICU's.

The bacteriological profile of the MDRO's in blood samples obtained from COVID ICU and other ICU's included *Escherichia coli*, *Klebsiella species*, *Acinetobacter species* and *Candida albicans* (Fig. 3). MDR *Klebsiella species* were found to be more prevalent in COVID ICU (35.71%) and other ICU's (44.44%).

An overview on the total profile of various bacterial

Fig. 2.

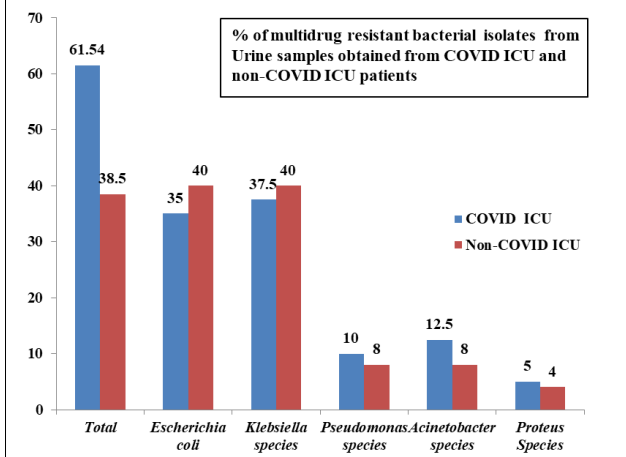
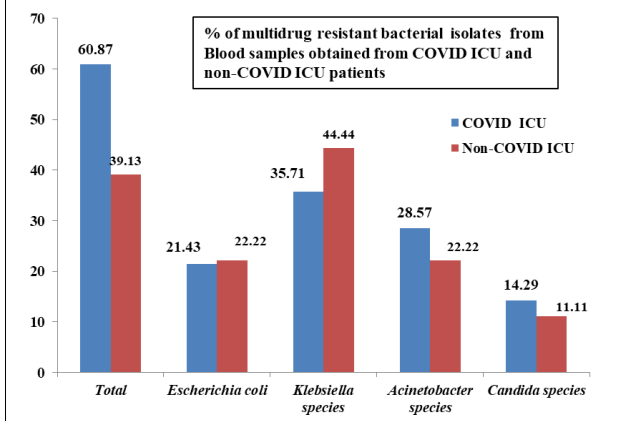


Fig. 3.



isolates and multidrug resistant isolates isolated from respiratory, urine and blood samples of COVID ICU and other ICU patients are demonstrated (Tab. I).

In our study highest resistance was demonstrated among *Acinetobacter species* (n = 22) (Fig. 4). Of these, 14 (63.6 %) were from COVID ICU and 8 (36.3%) were from other ICU patients.

Among the 14 strains from COVID ICU, 11 (78.6%) strains were resistant to cefotaxime, 9 (64.3%) resistant to cefepime, 7 each (50%) were resistant to piperacillin tazobactam, ciprofloxacin and amikacin, 6 (42.9%) to gentamicin and 3 each (21.4%) to imipenem and meropenem.

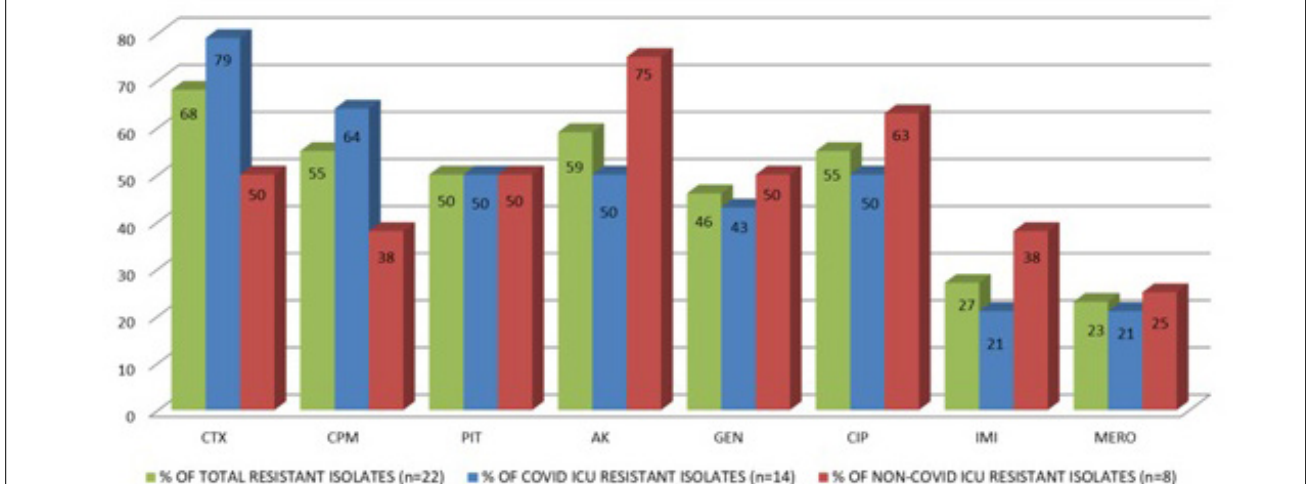
Of the 8 *Acinetobacter* strains from other ICUs, 4 each (50%) showed resistance to gentamicin, cefotaxime and to piperacillin tazobactam, 3 each (37.5%) to cefepime and imipenem, 6 (75%) to amikacin, 5 (62.5%) to ciprofloxacin and 2 (25%) to meropenem.

The total resistance pattern of *Acinetobacter* isolates from both the ICU's (COVID and non- COVID) is as follows: 68.2% (n = 15/22) to cefotaxime, 54.5% (n = 12/22) to cefepime, 50% (11/22) to piperacillin tazobactam, 59.1% (13/22) to amikacin, 45.5% (n = 10/22) to gentamicin, 54.5% (n = 12/22) to ciprofloxacin, 27.3% (6/22) to imipenem and 22.7% (n = 5/22) to meropenem.

In our study next highest resistance was demonstrated among *Klebsiella species* (n = 57) (Fig. 5). Of the total 57 isolates of *Klebsiella species*, 34 were (59.6%) were isolated from COVID ICU and 23 (40.3%) were from other ICU patients.

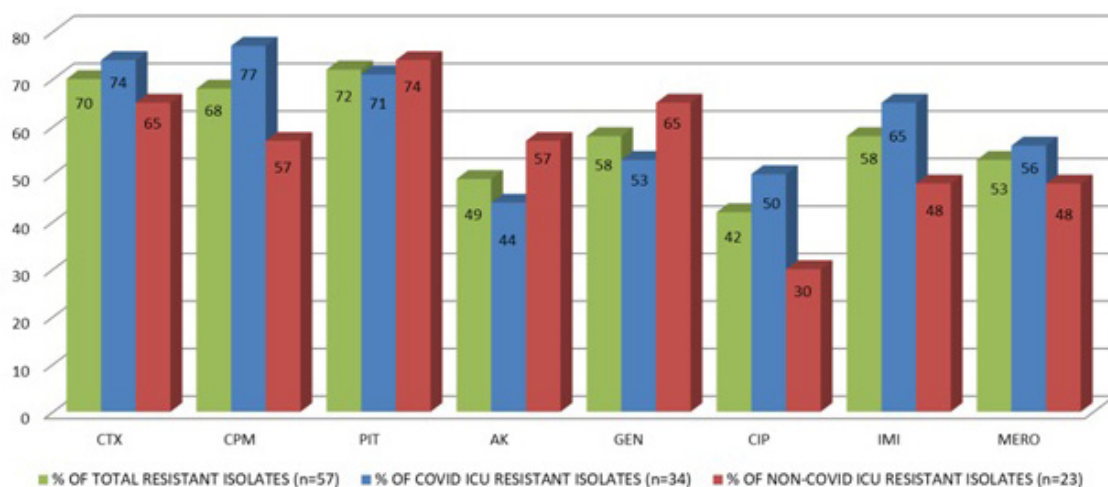
Among the 34 strains from COVID ICU, 25 (73.5%) were resistant to cefotaxime, 26 (76.5%) to cefepime, 24 (70.6%) to piperacillin tazobactam, 15 (44.1%) to amikacin, 18 (52.9%) to gentamicin, 17 (50%) to ciprofloxacin, 22 (64.7%) to imipenem and 19 (55.9%) to meropenem.

Of the 23 strains from other ICUs, 15 (65.2%) were resistant to cefotaxime, 13 (56.5%) to cefepime, 17 (73.9%) to piperacillin tazobactam, 13 (56.5%) to amikacin, 15 (65.2%) to gentamicin, 7 (30.4%) to ciprofloxacin, 11 (47.8%) to imipenem and meropenem. Therefore, the total resistance pattern of *Klebsiella species* from COVID and non-COVID ICU is as follows:

Fig. 4. *Acinetobacter* Species - Antibiotic resistance profile.

Tab. I. An overview on the total profile of various bacterial isolates and drug resistant isolates isolated from various clinical samples.

| Sample type | No of Organisms | Urine | | Blood | | Respiratory | |
|--|-----------------|-----------|-----------|-----------|-----------|-------------|-----------|
| Type of ICU | | COVID ICU | Other ICU | COVID ICU | Other ICU | COVID ICU | Other ICU |
| <i>Escherichia coli</i> | TOTAL | 28 | 22 | 9 | 7 | 23 | 17 |
| | MDR | 14 | 10 | 3 | 2 | 13 | 10 |
| | % MDR | 50 | 45.45 | 33.33 | 28.57 | 56.52 | 58.82 |
| <i>Klebsiella species</i> | TOTAL | 21 | 17 | 9 | 11 | 21 | 16 |
| | MDR | 15 | 10 | 5 | 4 | 14 | 9 |
| | % MDR | 71.42 | 58.82 | 55.55 | 36.36 | 66.66 | 56.25 |
| <i>Pseudomonas species</i> | TOTAL | 9 | 7 | 0 | 0 | 14 | 9 |
| | MDR | 4 | 2 | 0 | 0 | 7 | 3 |
| | % MDR | 44.44 | 28.57 | 0 | 0 | 50.00 | 33.33 |
| <i>Acinetobacter species</i> | TOTAL | 5 | 3 | 5 | 2 | 7 | 5 |
| | MDR | 5 | 2 | 4 | 2 | 5 | 4 |
| | % MDR | 100.00 | 66.67 | 80.00 | 100.00 | 71.43 | 80.00 |
| <i>Citrobacter species</i> | TOTAL | 0 | 0 | 0 | 0 | 1 | 0 |
| | MDR | 0 | 0 | 0 | 0 | 1 | 0 |
| | % MDR | 0 | 0 | 0 | 0 | 100 | 0 |
| <i>Proteus species</i> | TOTAL | 4 | 3 | 0 | 0 | 0 | 0 |
| | MDR | 2 | 1 | 0 | 0 | 0 | 0 |
| | % MDR | 50 | 33.33 | 0 | 0 | 0 | 0 |
| <i>Coagulase Negative Staphylococcus species</i> | TOTAL | 0 | 0 | 13 | 5 | 0 | 0 |
| | MDR | 0 | 0 | 0 | 0 | 0 | 0 |
| | % MDR | 0 | 0 | 0 | 0 | 0 | 0 |
| <i>Candida albicans</i> | TOTAL | 0 | 0 | 7 | 4 | 0 | 0 |
| | MDR | 0 | 0 | 2 | 1 | 0 | 0 |
| | % MDR | 0 | 0 | 28.57 | 25 | 0 | 0 |
| <i>Candida species (non-albicans)</i> | TOTAL | 2 | 2 | 0 | 0 | 0 | 0 |
| | MDR | 0 | 0 | 0 | 0 | 0 | 0 |
| | % MDR | 0 | 0 | 0 | 0 | 0 | 0 |
| <i>Staphylococcus aureus</i> | TOTAL | 0 | 0 | 2 | 2 | 0 | 0 |
| | MDR | 0 | 0 | 0 | 0 | 0 | 0 |
| | % MDR | 0 | 0 | 0 | 0 | 0 | 0 |

Fig. 5. *Klebsiella species* - Antibiotic resistance profile.

70.2% (n = 40/57) to cefotaxime, 68.4% (n = 39/57) to cefepime, 71.9% (n = 41/57) to piperacillin tazobactam, 49.1% (n=28/57) to amikacin, 57.9% (n = 33/57) to

gentamicin, 42.1% (n = 24/57) to ciprofloxacin, 57.9% (n = 33/57) to imipenem and 52.6% (n = 30/57) to meropenem.

Next highest resistance was demonstrated among *Escherichia coli* (n = 52). Of these, n = 30/52 isolates were from COVID ICU and n = 22/52 were from other ICU patients. (Fig. 6)

Among the 30 strains from COVID ICU, 23 (76.7%) showed resistance to cefotaxime, 18 (60%) to ceftazidime, 21 (70%) to piperacillin tazobactam, 19 (63.3%) to amikacin, 17 (56.7%) to imipenem, 14 (46.7%) to gentamicin and meropenem, 16 (53.3%) to ciprofloxacin. Of the 22 strains from other ICUs, 17 (77.3%) showed resistance to cefotaxime, 11 (50%) to ceftazidime, 17 (77.3%) to piperacillin tazobactam, 20 (90.9%) to amikacin, 15 (68.2%) gentamicin, 10 (45.5%) to ciprofloxacin, 9 (40.9%) to imipenem and 7(31.8%) to meropenem.

Therefore, the total resistance pattern of *Escherichia coli* from both the ICUs is as follows: 76.9% (n = 40/52) of the strains showed resistance to cefotaxime, 55.8% (n = 29/52) to ceftazidime, 73.1% (n = 38/52) to piperacillin tazobactam, 75% (n = 39/52) to amikacin, 55.8% (n = 29/52) to gentamicin, 50% (n = 26/52) to ciprofloxacin, 50% (n = 26/52) to imipenem and 40.4%(n = 21/52) to meropenem.

Also the resistance profile of *Pseudomonas species*, (n = 16) was analyzed. Of these, n = 11/16 isolates were from COVID ICU and n = 5/16 were from other ICU patients. (Fig. 7)

Among the 11 strains from COVID ICU, 7 (63.6%) showed resistance to ceftazidime and piperacillin tazobactam, 6 (54.5%) to imipenem, ceftazidime and amikacin, 5 (45.5%) to gentamicin and meropenem, 4 (36.4%) to ofloxacin.

Of the 5 strains from other ICU's, 2 (40%) strains showed resistance to ofloxacin and ceftazidime, 1 (20%) to ceftazidime, 3 (60%) to piperacillin tazobactam, amikacin and gentamicin, 4 (80%) each to imipenem and meropenem.

Therefore, the total resistance pattern of *Pseudomonas* from both the ICUs is as follows: 56.3% (n = 9/16)

to ceftazidime, 43.8% (n = 7/16) to ceftazidime, 62.5% (n = 10/16) to piperacillin tazobactam, 56.3% (n = 9/16) to amikacin, 50% (n = 8/16) to gentamicin, 37.5% (n = 6/16) to ofloxacin, 62.5% (n = 10/16) to imipenem and 56.3% (n = 9/16) to meropenem.

In this study, 3 out of 11 *Candida albicans* isolates demonstrated 27.27% resistance, out of which 2 (66.66%) of the isolates were from COVID ICU patients and 1(33.33%) was from patients admitted in other ICUs. All the three resistant strains were blood isolates. Among the 2 strains isolated from COVID ICU, no strains (0%) showed resistance to amphotericin-B and nystatin, 1 strain (50%) showed resistance to ketoconazole and both strains (100%) showed resistance to clotrimazole, fluconazole and itraconazole. The single strain isolated from other ICU's, showed no resistance to amphotericin-B, fluconazole and itraconazole, and showed resistance to clotrimazole, ketoconazole and nystatin.

The total resistance pattern of *Candida albicans* from both the ICUs is as follows: 0% (n = 0/3) to amphotericin-B, 100% (n = 3/3) to clotrimazole, 66.67% (n = 2/3) to fluconazole, itraconazole and ketoconazole and 33.33% (n = 1/3) to nystatin.

In our study we also isolated other *Candida species* which include three strains of *Candida tropicalis* and one strain of *Candida parapsilosis* obtained from urine samples and these isolates did not demonstrate any antifungal resistance.

Discussion

Bacterial co-infections occurring in patients hospitalized with COVID-19 are a leading cause of mortality. A meta-analysis done by Langford BJ *et.al* states that bacterial co-infection remains very common among COVID-19 infected ICU patients than critically ill patients belonging to other ICU settings [14].

Fig. 6. *Escherichia coli* - Antibiotic resistance profile.

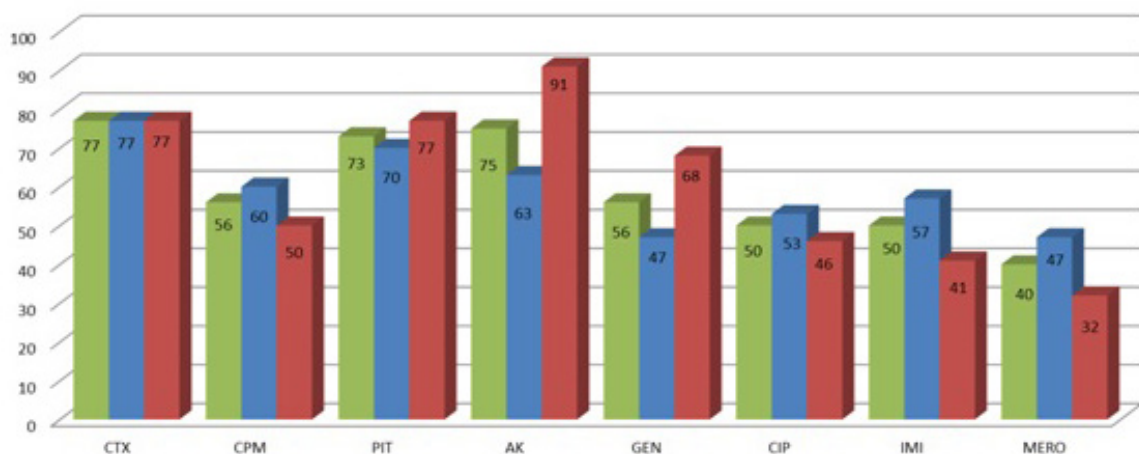
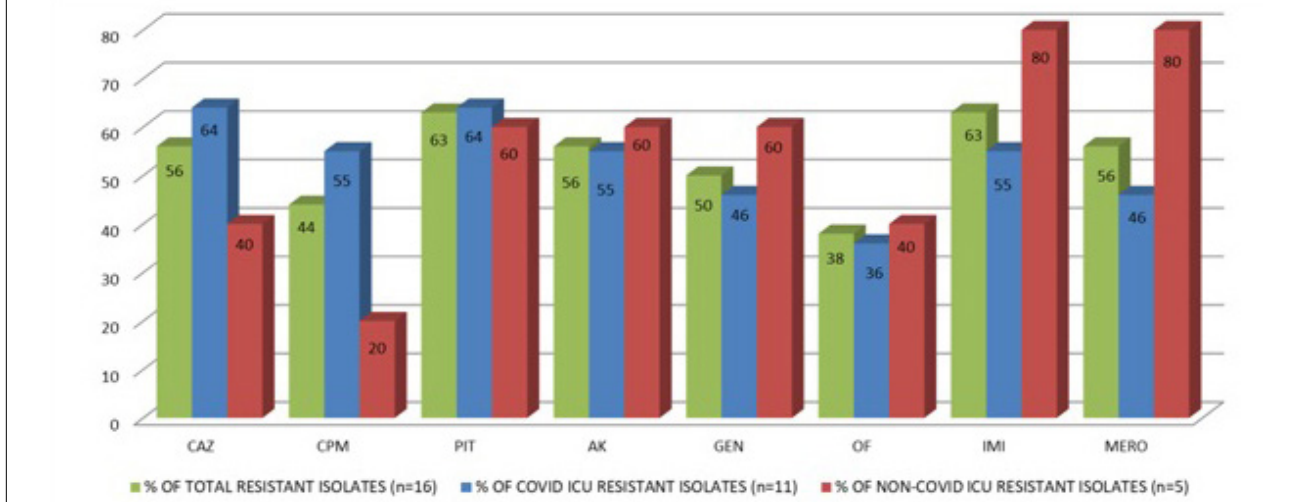


Fig. 7. *Pseudomonas* species - Antibiotic resistance profile.

Among the Gram-negative bacteria, *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter baumannii* are the most prevalent bacterial isolates and the antimicrobial resistance rates among these bacteria were found to be very high.

A study conducted by Russell et al., showed that among the Gram negative bacteria, members belonging to the family *Enterobacteriaceae*, like *Escherichia coli* commonly are associated blood stream infections [15]. In our study *Escherichia coli* and *Klebsiella species* are the predominant isolates causing blood stream infections affected with COVID-19.

In our study, we included 356 COVID positive patients admitted in the intensive care unit and 292 COVID negative patients admitted in other non-COVID intensive care units. We found that COVID patients admitted in the ICU were more prone to bacterial co-infections and also the resistant bacterial strains were found to be more prevalent in COVID patients admitted in the ICU (Fig. 1-3).

Higher resistance was found in *Acinetobacter spp* 81.48% (n = 22/27), out of which 63.63% (n = 14/22) of the bacterial strains were isolated from COVID ICU and 36.26% (n = 8/22) were from other ICU patients.

This finding is similar to the study done by Jie Le et al. [9]. However, the study conducted by Mahmoudi and another study conducted by Surbhi Khurana et al. [16, 17] showed higher resistance among *Klebsiella species*, followed by *Acinetobacter species*. In our study, *Acinetobacter species* showed higher resistance followed by *Klebsiella species*. A study by Ehsan Sharifipour et al. also showed that a wide spread resistance was contributed by *Acinetobacter species* [18]. Another study conducted by Sama Rezasoltani et al. showed more resistance among *Staphylococcus aureus* (MRSA) strains [19].

Klebsiella species was the next most resistant organism isolated (60%), out of which 59.64% (n = 34/57) were from COVID ICU patients and 40.35% (n = 23/57) were

from other ICU patients. A study by Sreenath K et al. states that *Klebsiella species* is the common organism that usually complicates treatment options in COVID-19 affected patients admitted in ICU setting [20]. Another study by Arcari et al. shows that multidrug resistant *Klebsiella species* remain as a common pathogen in critically ill COVID-19 patients [21].

Other bacterial isolates like *Escherichia coli* showed 49.05% resistance (n = 52/106), out of which 57.69% (n = 30/52) were obtained from COVID ICU patients 42.31% (n = 22/52) were from non-COVID ICU patients. A study by Mahmoudi et al. shows that *Escherichia coli* obtained by COVID-19 patients showed greater resistance to cephalosporins, co-trimoxazole and piperacillin-tazobactam [16]. However, in our study many isolates were resistant to cephalosporins and few were also resistant to imipenem and meropenem.

Drug resistance was found to be 42.85% (n = 3/7) in *Proteus spp* isolates, out of which 66.66% (n = 2/3) were from COVID ICU patients and 33.33% (n = 1/3) were from non-COVID ICU patients.

Pseudomonas spp showed 41.02% resistance (n = 16/39), out of which 68.75% (n = 11/16) were obtained from COVID ICU patients and 31.25% (n = 5/16) were obtained from patients admitted in non-COVID ICU's. A study by Qu et al. states that *Pseudomonas aeruginosa* can remain as an important co-infecting pathogen in critically ill COVID-19 patients with a greater capacity of producing biofilm and thereby conferring antibiotic resistance [22].

In our study we isolated a single strain of *Citrobacter spp* (n = 1/1) that was found to be multidrug resistant. That strain was isolated from a respiratory sample in COVID ICU.

Other gram-positive bacterial isolates like *Coagulase negative staphylococci* (n = 18) and *Staphylococcus aureus* (n = 4) obtained from blood culture did not show any multi drug resistance.

In our study we respiratory samples from COVID-19

patients remain predominant as lower respiratory tract bacterial co-infections remain common in these patients. The underlying pathogenesis of bacterial co-infection in severe and critical COVID-19 cases is due to the host-pathogen interactions, which include the virulence factors of the pathogens, dysregulations of immune responses and disturbed microbial flora during viral pneumonia [23, 24].

Viral pneumonia and bacterial co-infection act as mutual reinforcing factor to promote the progression of COVID-19 disease. Severe cases of COVID-19 cause multiple damages in the lungs, thereby decreasing the oxygen and carbon dioxide diffusion capacities. Surfactant disruption and sloughing of cells into the airways provide access and rich source of nutrients, thereby leading to rapid bacterial invasion. Both the factors like changes in microbial flora and bacterial virulence can alter the immune responses to SARS-CoV-2, resulting in the rebound of viral titres and high mortality in severe and critically ill patients [25].

The strengths of the present study include, we analysed significant number of samples from critically ill COVID-19 patients and we were able to present an appropriate microbiological and antibiotic resistance profile. However, the study also has weakness that has to be addressed in the future. This study is a retrospective study and therefore systemic patient review was not performed. Also this study was conducted in a single centre and not a multicentric study because the microbiological and antibiotic profile can vary with respect to the different geographical location.

Conclusion

An effective antimicrobial regimen remains the key step for the successful treatment of COVID-19. Also, due to the scarcity of data available on the empirical use of antimicrobials to treat COVID-19 secondary infections and the irrational use of antimicrobials to treat these patients, has led to the emergence of multidrug resistance [25].

Therefore, molecular approaches like meta genomic next-generation sequencing can help in the detection of a broad range of pathogens and their antimicrobial resistance which further contribute to the appropriate antibiotic stewardship programmes. In addition, molecular understanding of the causes and consequences of bacterial co-infections in COVID-19 patients aid the development of novel therapeutic interventions influencing targets with high efficacy and safety during co-infections [26].

To conclude, it is important that the bacterial co-infections in critically ill patients should not be underestimated. It should be taken as a key factor in order to reduce the morbidity and mortality rate in COVID-19 patients globally. Investigation of bacterial co-infections and antibiotic profile can further help in improved health of COVID-19 patients and also will help us understand the viral and bacterial pathogen interaction within the

host [26]. Ethical and rational use of antibiotics is highly recommended.

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Conflict of interest statement

No conflicts of interest.

Authors' contributions

PS and SR designed the study. SR collected and analysed the data. SR, PS and APSR participated in the manuscript revision. All authors of the manuscript gave their complete approval.

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ORIGINAL ARTICLE

An assessment of nurses' participation in Health Promotion: a knowledge, perception, and practice perspective

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Key words

Nurses • Health promotion • Practice

Summary

Background. Health promotion (HP) at the population level serves to improve health inequalities, enhance the quality of life, and ensures the provision of healthcare and related services. Nurses at all levels are charged with the task of ensuring that patients receive HP services. However, their competence in addressing this challenge needs further exploration. This study assessed the influence of HP knowledge and perceptions in nurses' HP practice.

Methods. The study was conducted using a self-administered questionnaire among 184 nurses randomly sampled from a tertiary hospital. Questions bordered on respondents' demographics, knowledge, perception, and practice of HP. Responses were retrieved and analysed using IBM SPSS Statistics, Version 26.0. Armonk, NY: IBM Corp, 2019.

Results. Analysis showed a statistically significant relationship between participants demographics and possessing adequate

knowledge to provide HP services. Statistically significant relationships were found amongst the following variables: 'A holistic knowledge of disease pathology and processes are vital for effective care of patients' and 'education of patients on medication' $p = 0.001$, 'awareness of importance of educating patients about their condition' and 'patients encouraged to engage in healthy lifestyle' $p < 0.001$.

Conclusion. Data showed that nurses' knowledge regarding HP had a strong influence on their perception of HP. Their perception of HP in turn strongly influenced their practice of the same. Therefore, rigorous efforts must be made by governmental agencies, and organizations involved in healthcare worker training and nursing accreditation, to ensure the HP curriculum is well incorporated in nursing undergraduate training and sustained in service.

Introduction

Health Promotion involves a variety of approaches aimed at preserving the wellbeing and quality of life of people by addressing the fundamental causes of certain diseases as opposed to purely focusing on biomedical care [1]. Previously, health was seen as the very opposite of illness and diseases. With the Ottawa charter for HP in 1986, the World Health Organization effected a major change to the global view of health, not as a goal but a means to a full life [2]. As a result, HP emerged as a prime and essential activity for contemporary society with diverse initiatives and interventions designed by the World Health Organization aimed at translating the numerous concepts of HP towards practical reality [3]. Amongst the initiatives are the health-promoting hospitals (HPH) [4], health-promoting schools [5], health promotion in the sustainable development goals (SDGs) [6] and workplace-related HP [7]. These programmes have thrived due to the beneficial health outcomes emanating from them.

Today more than ever, nurses play a crucial role in HP. In addition to routine consultations and clinical duties,

nurses are also involved in check-up care, patients education as well as disease prevention (DP) services [8]. In addition, nurses meaningfully contribute to several beneficial health outcomes such as educating patients on how prescribed medication works, therapeutic compliance [9], quality of life [8], and overall patient support and empowerment. To further uncover the importance of the nursing role in health promotion, Whitehead explored the current position of nursing concerning its practice, associated concept, and policy [10]. The questions raised included how much nurses know about HP and their views towards the subject of HP. Literature confirms that nurses utilize a range of expertise in delivering HP which may be generalized, patient-centered, or project management-related HP [8]. Despite the vital role nurses play in promoting population health, the prevalence of several preventable diseases continue to pose a major public health concern. In 2017, about 60% of patients presenting at all hospital emergency departments in the United States presented with preventable chronic conditions amounting to \$8.3 billion in costs [11]. Relating to hospitalization, patients with chronic preventable diseases feature more

frequently and stayed longer in hospital [12]. Similarly, in 2017 in India, more than 9.5 million deaths and nearly half a billion disability-adjusted life-years (DALY) were recorded [13]. Of the recorded deaths, more than 33% were considered to be preventable [13]. Within the low- and middle-income countries (LMIC), the adverse impact of the global burden of non-communicable disease (NCD) remains dire [14]. Despite widespread access to information regarding adjustable lifestyle behaviours, such knowledge does not necessarily translate to lifestyle changes [15].

South Africa is faced with a quadruple burden of disease comprising a mélange of four colliding epidemics [16]. These include communicable diseases such as HIV/AIDS and TB; maternal and child mortality; NCDs such as hypertension and cardiovascular diseases, diabetes, cancer, mental illnesses, and chronic lung diseases like asthma (mainly related to preventable lifestyle behaviour); as well as trauma and injury [16]. The quadruple burden of disease has led to the country's adoption, in February 2013, of the 17-year visionary health plan for 2030 referred to as the national development plan (NDP) [16].

Nurses working at the various levels of healthcare delivery have a significant responsibility in HP, DP, and wellness. Due to the nursing profession's ability to navigate the entire healthcare system worldwide, plus their role as patients' advocates, nurses are in a position to achieve the comprehensive goal of universal health coverage (UHC) through HP. However, some reports have questioned nurses effectiveness in the discipline and practice of HP. In this study, we assessed the health promotion knowledge, perceptions, and practice of nurses in a South African tertiary hospital.

Methods

DESIGN, SAMPLE, AND RESPONDENTS

A descriptive cross-sectional design was used for this study. The population comprised of registered nurses working in a tertiary hospital in the Eastern Cape province of South Africa. The respondents were randomly selected from the overall population. Student nurses, and nurses on exchange training programs from different countries and auxiliary nurses were excluded from the study.

DATA COLLECTION

Data were collected using a self-administered structured questionnaire. Retrieved information was anonymised and only the principal researcher had access to the data. The questionnaire was adapted from a previous study [17] which had similar objectives. The questionnaire was administered over a three-month time frame between February and April 2017. Using a 95% confidence interval and a 5% error margin, a sample size of 184 was calculated. Data collection was stopped when the target sample size was achieved. Data collection was carried out by the principal investigator and a trained fieldworker.

SURVEY INSTRUMENT

The questionnaire (supplementary file 1) comprised of 22 closed-ended questions divided into four sections. Section A comprised of seven questions focused on demographics including sex, age group, registration status as a nurse, and duration of registration as a nurse. Section B (questions 8-9) elicited information on knowledge; Section C (questions 10-15) concentrated on nurses' perceptions towards health promotion, while section D (questions 16-22) centered on nurses' practice of health promotion.

DATA ANALYSIS

Data was analyzed using IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp, 2019. Simple descriptive analysis was conducted on all four sections (demographics, knowledge, perception, and practice) for which data were retrieved. Bivariate analysis was conducted to establish the relationship between demographics and knowledge, perception, and practice. A similar analysis was conducted to assess the relationship between perception and practice, knowledge, and practice, as well as knowledge and perceptions.

ETHICS

The study protocol received ethics approval from both the University of Roehampton, London, and the Research Ethics Committee (Human) (REC-H) of the Nelson Mandela University (NMU), Ref: H16-HEA-NUR-EXT-003. Every respondent signed an informed, written consent form prior to participation. The study comprised of a survey of non-vulnerable adults, and there was no potential for coercion of respondents, distress, loss of work time, or damage to professional reputation.

Results

BASELINE CHARACTERISTICS

A total of 184 nurses responded to the questionnaire. Female nurses comprised 82.6% (n = 152), while males comprised 7.6% (n = 14) of the respondents. Genders for 9.8% (n = 18) were not specified. Most nurses, 72% (n = 133) were 40 years or above. Of the respondents, 35.9% (n = 66) have been registered for 10 years or less as nurses. Analysis on each variable is relative to the total responses received on that variable. A descriptive summary of the variables has been presented in Tables I-IV.

KNOWLEDGE, PERCEPTION AND PRACTICE OF HEALTH PROMOTION

Of the participating 184 nurses, 56.0% (n = 103) agreed to having adequate knowledge regarding the conditions patients present within their units and their ability to provide health promotion services. A total of 63.6% (n = 117) respondents strongly held the perception that health education and counselling from nurses could

Tab. I. Knowledge, perception and practice of health promotion.

| Variables | Responses | | | | |
|---|--------------------------|-----------------|----------------|--------------|-----------------------|
| | Strongly Disagree n. (%) | Disagree n. (%) | Neutral n. (%) | Agree n. (%) | Strongly Agree n. (%) |
| Knowledge Variables | | | | | |
| I have adequate knowledge necessary for HP provision | 3 (1.6) | 7 (3.8) | 12 (6.5) | 103 (56.0) | 55 (29.9) |
| I am aware of the importance of providing HE to patients | 0 | 0 | 2 (1.1) | 57 (31) | 121 (65.8) |
| Perception Variables | | | | | |
| A holistic knowledge of disease processes is a pre-requisite for patient care | 0 | 0 | 2 (1.1) | 70 (38) | 112 (60.9) |
| Hospital is an ideal place for HP | 1 (0.5) | 15 (8.2) | 11 (6.0) | 70 (38.0) | 83 (45.1) |
| Health promotion is a waste of time | 129 (70.1) | 41 (22.3) | 5 (2.2) | 2 (1.1) | 2 (1.1) |
| Patients who engage in an unhealthy lifestyle will not benefit from HP | 60 (32.6) | 45 (24.5) | 13 (7.1) | 29 (15.8) | 31 (16.8) |
| Health education and counseling from nurses could enhance patients' health | 1 (0.5) | 3 (1.6) | 1 (0.5) | 59 (32.1) | 117 (63.6) |
| Patients do not want health education from nurses | 71 (38.6) | 78 (42.4) | 17 (9.2) | 7 (3.8) | 6 (3.3) |
| Practice Variables | | | | | |
| I educate my patients on medication and how it works | 0 | 2 (1.1) | 6 (3.3) | 74 (40.2) | 98 (53.3) |
| I educate my patients about their disease conditions | 0 | 2 (1.1) | 14 (7.6) | 84 (45.7) | 80 (43.5) |
| I provide my patients with necessary guidance about diet and lifestyle | 2 (1.1) | 2 (1.1) | 15 (8.2) | 76 (41.3) | 86 (46.7) |
| I educate my patients on the need for a routine checkup | 1 (0.5) | 4 (2.2) | 13 (7.1) | 73 (39.2) | 89 (48.4) |
| I use my smart phone/devices to search for key information for my patients | 10 (5.4) | 16 (8.7) | 36 (19.6) | 74 (40.2) | 43 (23.4) |
| I encourage my patients to engage in the healthiest lifestyle they can attain | 0 | 1 (0.5) | 12 (6.5) | 94 (51.1) | 74 (40.2) |
| I encourage my patients to observe fitness assessments and health screening | 0 | 3 (1.6) | 26 (14.1) | 95 (51.6) | 57 (31.0) |

enhance patients' health, while 51.6% (n = 95) encourage their patients to observe fitness assessments and health screening. A descriptive summary of the respondents has been presented (Tab. I).

BIVARIATE ANALYSIS OF RELATIONSHIPS AMONG OUTCOMES

Results show that at a 5% significance level, there is a significant association between the professional registration duration of a nurse and them having adequate knowledge to provide HP services regarding the conditions patients present with in their unit ($p = 0.015$). Similarly, the demographic variable 'age range' has a statistically significant relationship with the perception that the hospital is an ideal place for HP to occur ($p = 0.006$). No statistical association was identified between nurses' demography and practice.

In a comparative assessment of nurses' perceptions and their HP practices as outcome variables, 21 variables were statistically significant (Tab. II). Of the 21 emerging factors, four emerged between the perception that a holistic knowledge of disease processes is a pre-requisite for patient care when compared with HP practice; four from the perception that a hospital is an

ideal place for HP when compared with practices; four factors were observed from the perception that patients who engage in an unhealthy lifestyle will not benefit from HP when compared with HP practice; two from the perception that health education and counselling from nurses could enhance patients' health when compared with HP practice; and seven factors from the perception that patients do not want health education from nurses when compared with HP practice. No statistically significant factor emerged from the perception that health promotion is a waste of time when compared with HP practice.

Comparison of the relationship between Knowledge and Practice yielded 11 statistically significant relationships (Tab. III). A breakdown of the 11 factors shows that nurses having adequate knowledge necessary for HP provision and practice had six significant factors, while the relationship between nurses being aware of the importance of providing health education (HE) to patients with HP practice produced five statistically significant relationships. The results showed that there were significant associations between 'having adequate knowledge regarding the conditions patients present with in this unit to provide HP services' and educating

Tab. II. Relationship between responses on health promotion perception and practices by nurses

| Perception | Practice | SDA | DA | N | A | SA | p-value |
|---|---|-----|----|----|----|-----|---------|
| A holistic knowledge of disease pathology and processes are vital for effective care of patients | I educate my patients on medication | 0 | 0 | 2 | 69 | 109 | 0.001 |
| | I educate my patients on need for checkup | 0 | 0 | 2 | 69 | 109 | 0.008 |
| | patients encouraged to engage in healthy lifestyle | 0 | 0 | 2 | 68 | 111 | 0.004 |
| | I encourage my patients to observe fitness assessments and health screening | 0 | 0 | 2 | 68 | 111 | 0.049 |
| Hospital is an ideal place for HP | I educate my patients on medication | 1 | 5 | 10 | 67 | 83 | 0.010 |
| | I educate my patients on need for checkup | 1 | 15 | 10 | 67 | 83 | 0.044 |
| | I use my smart phone/ devices for supportive information on HP | 1 | 14 | 10 | 68 | 82 | 0.004 |
| Patients who deliberately engage in an unhealthy lifestyle will not benefit from health promotion | I educate my patients about their disease condition | 60 | 45 | 13 | 28 | 31 | < 0.001 |
| | I provide necessary guidance about diet and lifestyle | 60 | 45 | 13 | 29 | 31 | 0.007 |
| | patients encouraged to engage in healthy lifestyle | 60 | 44 | 12 | 29 | 31 | 0.026 |
| | I encourage my patients to observe fitness assessments and health screening | 60 | 44 | 13 | 29 | 30 | 0.031 |
| | patients encouraged to engage in healthy lifestyle | 1 | 15 | 10 | 69 | 82 | < 0.001 |
| Health education, advise and counseling from nurses could positively enhance patients' health | I educate my patients on medication | 1 | 3 | 1 | 58 | 117 | 0.007 |
| | I educate my patients about their disease condition | 1 | 3 | 1 | 59 | 116 | 0.048 |
| Patients do not want health education from nurses | I educate my patients on medication | 71 | 77 | 17 | 7 | 6 | 0.049 |
| | I educate my patients about their disease condition | 70 | 78 | 17 | 7 | 6 | 0.016 |
| | I provide necessary guidance about diet and lifestyle | 71 | 78 | 17 | 7 | 6 | 0.012 |
| | I educate my patients on need for checkup | 70 | 78 | 17 | 7 | 6 | 0.011 |
| | I use my smart phone/devices for supportive information on HP | 70 | 77 | 17 | 7 | 6 | 0.037 |
| | patients encouraged to engage in healthy lifestyle | 71 | 76 | 17 | 7 | 6 | < 0.001 |
| | I encourage my patients to observe fitness assessments and health screening | 70 | 77 | 17 | 7 | 6 | 0.001 |

SA: Strongly Agree; A: Agree; N: Neutral; DA: Disagree; SDA: Strongly disagree.

patients about their disease condition', $p < 0.001$; 'awareness of the importance of educating patients about their condition' and 'patients encouraged to engage in healthy lifestyle' $p < 0.001$.

Table IV shows the relationship between nurses' knowledge and perception towards HP. The analysis showed nine significant associations emerging including: 'having adequate knowledge regarding the conditions patients present with in this unit to provide HP services' and 'HE, advise and counseling from nurses could positively enhance patients health', $p < 0.001$; 'awareness of the important of educating patients about their condition' and 'patients do not want HE from nurses', $p < 0.001$.

Discussion

This study provides an assessment of nurses' views regarding their knowledge, perception, and practice towards health promotion in a South African tertiary hospital. The data analysis revealed that nurses agreed to having adequate knowledge regarding their patients' disease condition to provide adequate health promotion; that hospital is an ideal place to provide health promotion; and that they do encourage their patients to engage in the healthiest lifestyle they can attain. They therefore deserve a strong support system to enable them to sustain and improve their role in HP.

Findings from this study show that the duration of

Tab. III. Relationship between Knowledge and Practice

| Knowledge variables | Practice variables | SDA | DA | N | A | SA | p-value |
|--|---|-----|----|----|-----|-----|---------|
| I have adequate knowledge regarding the conditions patients present with in this unit to provide health promotion services | I educate my patients on medication | 3 | 7 | 12 | 102 | 55 | 0.014 |
| | I educate my patients about their disease condition | 3 | 7 | 12 | 103 | 54 | < 0.001 |
| | I provide necessary guidance about diet and lifestyle | 3 | 7 | 12 | 103 | 55 | < 0.001 |
| | I educate my patients on need for checkup | 3 | 7 | 12 | 103 | 54 | < 0.001 |
| | I use my smart phone/devices for supportive information on HP | 3 | 7 | 12 | 103 | 53 | 0.149 |
| | patients encouraged to engage in healthy lifestyle | 3 | 7 | 11 | 103 | 54 | < 0.001 |
| | I encourage my patients to observe fitness assessments and health screening | 3 | 7 | 12 | 101 | 55 | < 0.001 |
| I am aware of how important it is to educate my patients about their condition | I educate my patients on medication | 0 | 0 | 2 | 57 | 120 | 0.005 |
| | I educate my patients about their disease condition | 0 | 0 | 2 | 57 | 120 | < 0.001 |
| | I provide necessary guidance about diet and lifestyle | 0 | 0 | 2 | 57 | 121 | < 0.001 |
| | I educate my patients on need for checkup | 0 | 0 | 2 | 57 | 120 | < 0.001 |
| | I use my smart phone/ devices for supportive information on HP | 0 | 0 | 2 | 57 | 119 | 0.146 |
| | patients encouraged to engage in healthy lifestyle | 0 | 0 | 2 | 56 | 120 | < 0.001 |
| | I encourage my patients to observe fitness assessments and health screening | 0 | 0 | 2 | 56 | 120 | < 0.001 |

SA: Strongly Agree; A: Agree; N: Neutral; DA: Disagree; SDA: Strongly disagree.

registration as a nurse was associated with adequate knowledge, indicating that experience adds to the nurses know-how and expertise [18]. Lartey et al. reported on the wealth of knowledge and wisdom associated with experienced nurses as being critical in the provision of high quality care to patients and their family [19]. Though this benefit of experience and adequate knowledge resulting from experience could be generalized in some cases, it is mostly discipline-specific. For example, it has been observed that nurses without exposure to health promotion and health literacy, regardless of their nursing experience, lack requisite knowledge in these disciplines [20].

The present study revealed the influence of nurses HP perception on their practice of HP. For example, the nurses who had the perception that holistic knowledge of disease pathology and processes are vital for effective care of patients were more inclined to educate their patients about adherence to medication, the importance of check-ups, and engagement in a healthy lifestyle. In a similar study by Al-Noumani et al., (2019), the authors demonstrated that adherence to medication was greater among those that believed in the importance of medication [21]. In the study of Ojong, Nsemo and Aji, (2020) conducted in Nigeria, it was observed that despite good knowledge and perception towards routine check-ups, there was still a poor practice of check-up care [22], which is an essential component of HP.

The finding of good check-up practice in the current study may be related to the study context, in our case, a public tertiary hospital in South Africa where the public healthcare is solely funded by the state [23, 24], and free transport services to and from hospitals are provided to indigent patients living in the rural areas [25]. A major fact regarding perception is its ability to become reality and guide people's behavior [26]. In this study, the perception of the respondents is that holistic knowledge of disease pathology is a prerequisite for HP provision. This perception was formed based on their formal training and lived experience from practice. Furthermore, this study identified the perception "hospital is an ideal place for HP" as being associated with nurses using their smart devices to access supportive information during practice in order to educate patients about medication and the importance of regular check-ups. Evidence abounds regarding the efficacy of the HP effectiveness of nurses linked to organizational culture [8] as demonstrated in hospital settings [15]. Educating patients within healthcare institutions is a fundamental aspect of healthcare delivery. The educational roles of nurses therefore serve as a determinant in shared decision-making between nurses and patients regarding treatment adherence, improving the patients degree of satisfaction with service provision, and enhanced care. Credible sources have been noted to be key players in the dissemination of public health messages amongst

Tab. IV. Relationship between nurses' knowledge and Perception regarding HP

| Knowledge variables | Perception variables | SDA | DA | N | A | SA | p-value |
|--|---|-----|----|----|-----|-----|---------|
| I have adequate knowledge regarding the conditions patients present with in this unit to provide health promotion services | A holistic knowledge of disease pathology and processes are vital for effective care of patients | 3 | 7 | 12 | 103 | 55 | < 0.001 |
| | Hospital is an ideal place for promoting patients' health because the patients can be spoken to as a group and /or one on one | 3 | 7 | 12 | 101 | 53 | 0.001 |
| | Health promotion is a waste of time | 3 | 7 | 12 | 103 | 53 | 0.531 |
| | Patients who deliberately engage in an unhealthy lifestyle will not benefit from health promotion | 3 | 7 | 12 | 100 | 55 | 0.050 |
| | Health education, advise and counseling from nurses could positively enhance patients health | 3 | 7 | 12 | 103 | 55 | < 0.001 |
| | Patients do not want health education from nurses | 3 | 7 | 12 | 103 | 53 | 0.469 |
| I am aware of how important it is to educate my patients about their condition | A holistic knowledge of disease pathology and processes are vital for effective care of patients | 0 | 0 | 2 | 57 | 121 | < 0.001 |
| | Hospital is an ideal place for promoting patients' health because the patients can be spoken to as a group and /or one on one | 0 | 0 | 2 | 56 | 118 | 0.350 |
| | Health promotion is a waste of time | 0 | 0 | 2 | 57 | 119 | < 0.001 |
| | Patients who deliberately engage in an unhealthy lifestyle will not benefit from health promotion | 0 | 0 | 2 | 56 | 119 | 0.003 |
| | Health education, advise and counseling from nurses could positively enhance patients' health | 0 | 0 | 2 | 57 | 121 | 0.002 |
| | Patients do not want health education from nurses | 0 | 0 | 2 | 57 | 119 | < 0.001 |

SA: Strongly Agree; A: Agree; N: Neutral; DA: Disagree; SDA: Strongly disagree.

various groups [27]. Nurses occupy such a position among patients and are well suited to provide HP. Our results corroborate with the findings of Timmers et al., (2020) which demonstrated that educating patients at the point of care using prompt medical information accessed via smartphones and similar devices does enhance treatment compliance, satisfaction, and improves the eventual health outcome [28]. Although our study did not show a significant relationship between 'hospital is an ideal place for HP' and 'educating patients about their disease condition', the study of Nikitara et al., (2019) did indicate that nurses who are actively involved in educating patients with diabetes mellitus empower the patients to optimise management of their disease condition [29]. The reason for our finding of non association between hospital is an ideal place for HP and education of patient concerning their health condition could be related to the nurses lack of knowledge about specific disease entities [29].

The influence of knowledge among nurses correlated positively with regards to their HP practice in this study. It was noted that there was a statistically significant relationship between the provision of necessary guidance regarding diet and lifestyle to patients and adequate knowledge regarding the medical condition of

the patients. Sufficient knowledge [30, 31] is required in order for nurses to guide patients about smoking cessation, diet, and physical activity. However, in some hospital settings, nurses argue that it is the responsibility of specialists, such as dieticians, to provide dietary counselling to patients [30]. Despite this contention, enhancing the knowledge of nurses has proven to be a cost-effective strategy towards addressing the ever-increasing cost of healthcare [32]. In addition, optimum training and knowledge empowerment can embolden nurses to fully discharge their HP roles [32], including adequately guiding their patients on matters relating to necessary and health inducing diet and lifestyle changes.

Conclusion

This study was aimed at assessing the influence of HP knowledge and perceptions in the practice of HP amongst nurses working in a tertiary hospital. The data revealed that nurses' HP knowledge played a key role in influencing their perception of, and eventual, HP practices. Health promotion is an important public health discipline necessary, and essential, for the achievement of universal health coverage. Nurses, due to their expertise

and being regularly in touch with patients, especially those with chronic non-communicable diseases, occupy a distinctive place both in leadership and provision of HP services to their patients. A rigorous educational programme is required, in both undergraduate training and in the form of in-service training, to ensure that their knowledge of HP is updated. Future research is encouraged to interrogate the possibility of nurses achieving and sustaining a model that can bring about a realistic reform in HP.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

Conceptualization: HM; Methodology: HM, TAO, MW, PM; Software: HM, PM; Validation: HM, TAO, MW, PM; Formal analysis: PM, HM; Investigation: HM; Data Curation: HM, PM; Writing - Original Draft: HM; Writing - Review & Editing: HM, TAO, MW, PM; Visualization: HM, TAO, MW, PM; Supervision: TAO, MW.

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ORIGINAL ARTICLE

Predictors of the Social Distancing Behaviors during the COVID-19 Pandemic using Protection Motivation Theory in Iran: A cross sectional study

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Key words

Self-efficacy • Perceived severity • Intention, Behavior • Social Distancing • COVID-19

Summary

Background. Social distancing is a key behavior to minimize Coronavirus disease 2019 (COVID-19) infections. Since the change of behavior is the only way to prevent this pandemic, this study aimed to predict the social distancing behaviors during the COVID-19 pandemic using protection motivation theory (PMT).

Methods. This cross-sectional study was conducted through a convenience sampling method on 796 individuals over 15 years old from urban and rural areas of different cities in Iran during 2020. The data were collected online using demographic characteristics form, PMT and social distancing behaviors questionnaires. Afterward, the obtained data were analyzed in SPSS software (version 16) through linear correlation coefficient and hierarchical regression tests.

Results. The Mean \pm SD score of social distancing behaviors was obtained at 4.42 ± 0.31 . The results of the hierarchical linear

regression model showed that after adjusting the effect of socio-demographic variables, self-efficacy (Beta = 0.238, $P < 0.001$) was the strongest predictor of social distancing behaviors during the COVID-19 pandemic, followed by intention (Beta = 0.233, $P < 0.001$) and perceived severity (Beta = 0.083, $P = 0.028$). PMT constructs and intention was able to predict 40% of social distancing behaviors in total.

Conclusions. In the prevalence of infectious diseases, individuals differ in adherence to social distancing behaviors. The PMT was a useful framework for prediction social distancing behaviors during the COVID-19 pandemic. Therefore, this theory can be used as a framework in designing educational programs to increase self-efficacy and encourage individuals to observe social distancing behaviors as a result.

Introduction

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes Coronavirus Disease 2019 (COVID-19) was first detected in Wuhan, China, in December 2019 and has since increased dramatically worldwide. The World Health Organization declared COVID-19 as an epidemic on March 11, 2020 [1]. The virus, which is usually transmitted through the respiratory droplets of infected people [2], is highly contagious, and its transmission rate is higher than that of the flu virus. SARS-CoV-2 can be transmitted by both symptomatic and asymptomatic individuals [1]. Global statistics indicate that this disease has spread rapidly in a short time so that many countries, including Iran, have been involved with the disease from the time of its outbreak (late December 2019) to the time of conducting this study (Jun 15, 2020). So to this day (11 Jan 2022), the number of confirmed infected cases and deaths caused by this disease has been estimated at 308,458,509 and 5,492,595 worldwide, respectively. Furthermore, the total number of confirmed infected cases and deaths caused by this disease has been estimated at 6,208,337 and 131,915 in Iran, respectively [3].

Considering the fact that no effective medication-assisted treatment or definitive vaccine has yet been developed for the new coronavirus [1], various countries have adopted non-pharmacological interventions to reduce virus transmission and contact levels in the population [4]. Social distancing is the most important advice to limit and delay the spread of the virus along with the basic hygiene recommendations, such as regular hand washing and the use of masks [5].

Social distancing is an important health-protective behavior [6] and one of the most effective measures in reducing viral pandemics, including COVID-19 [7]. It means staying away from the community, avoiding large gatherings, and keeping a distance from others (approximately 6 feet or 2 meters) if possible [8]. According to Imperial College London, social distancing occurs when all families limit their communication with communities outside the home, such as school and workplace by 75% [9].

Social distancing not only reduces the risk of infection among high-risk populations but also delays and reduces the size of the epidemic, which in turn eases the burden felt by health care systems and workers [2]. Furthermore, this approach has also been used as

an effective method to reduce the human-to-human transmission infection during previous epidemics [10]. After the outbreak of COVID-19, Iran the same as other countries also followed recommendations and instructions, such as closing schools and universities, mosques, shrines, Friday prayers, and cultural centers; reducing office hours; closing government jobs, except for essential jobs; restricting religious and cultural gatherings, as well as mourning and wedding ceremonies; and restricting/banning the movement of vehicles [11]. However, these recommendations were not observed by all the people.

The effectiveness of many non-pharmacological health measures depends on how people react to them [10]. Therefore, individuals' response and observation of social distancing recommendations is critical in controlling the spread of the COVID-19 virus and optimization of the outcomes during this pandemic [7]. In the confrontation with the prevalence of influenza, it is important to know the factors affecting the individuals' behavior in order to reduce the infection risk, transmission, and severity of the disease [12]. Knowledge about the psychological factors of behavioral responses to infectious diseases is also critical in shaping interventions during infectious disease epidemics [13]. Sociologists, psychologists, and anthropologists have proposed a range of different theories and models to explain the factors that affect behavior, especially health behaviors. Protection Motivation Theory (PMT) is one of the used theories for the evaluation of the factors that affect motivation and health behavior [14].

The PMT deals with the of risk perception in individuals and assesses the intention of individuals to take protective measures which are significantly affected by high levels of perceived risk [15]. In this theory, it is assumed that the acceptance of behavior and decision to participate in risk-preventing behaviors is based on the individuals' motivation to protect themselves against threats, such as epidemics [2, 9]. This theory includes two stages of threat appraisal and coping appraisal along with fear construct [16].

Threat appraisal is a cognitive process that people use to estimate the extent of a threat [2] and includes the perceived vulnerability (the individual's perception of his/her sensitivity to harm), perceived severity (the individual's perception of the severity of the potential harm) and response rewards (perceived benefits of the current methods) [2, 17]. Furthermore, coping appraisal, which refers to the assessment of an individual's ability to perform risk-preventive behaviors [2], includes self-efficacy (the individual's perception of his or her ability to perform behaviors), response efficiency (the individual's perception of the impact of recommended preventive behaviors on risk eliminating), and response costs (cost of performing the recommended behavior) constructs [2, 17].

The outcome of these two stages is protection motivation (protection intention) and behavior [16]. In other words, protection motivation is synonymous

with behavior intention and causes the stimulation or continuation of protective behavior. It also acts as an intermediary construct between the two stages (threat appraisal and coping) and protective behavior [17]. Several previous studies have investigated health-protective behaviors against the flu using the theory of protective motivation. In a study conducted in London (2012), the PMT was used to investigate the intentions to engage in protective behaviors (including social distancing) during a hypothetical influenza epidemic. According to the results of the study, the intention to stay at home during the epidemic (i.e., social distancing behavior) was associated with all PMT components. Moreover, self-efficacy was the strongest predictor of the intention to perform protective behaviors during a hypothetical epidemic [6]. In a study conducted in Scotland (2015), the results showed that PMT variables did not predict social distancing behavior in the computer game scenario. However, the three PMT components (i.e., fear, response efficiency, and self-efficacy) were important predictors of the intention to participate in social distancing [13]. Therefore, protection motivation theory provides a useful conceptual framework on the way individuals respond to a threat to their health. In other words, it leads to a better understanding of the predictors of protective behaviors in the face of the threat posed by epidemics, such as flu [12].

It should be noted that preventive behaviors is the most important issue in new influenza, and social distancing behavior is one of the most effective measures to reduce viral pandemics, including COVID-19. In addition, preventive and protective behaviors constitute the bases of PMT, and its constructs are oriented toward increasing the intention of preventive behaviors. Considering the fact that protective behaviors should be evaluated separately in each society and since predicting factors of social distancing behavior in COVID-19 has not yet been studied in Iranian society, this study aimed to determine predictors of social distancing behavior in response to the COVID-19 pandemic using protection motivation theory.

Methods

STUDY DESIGN AND SAMPLING

This cross-sectional study was conducted on urban and rural populations of different cities in Iran from Jun 15, 2020, to August 1, 2020. The sample size was estimated at 796 cases considering confidence level, power test, and small effect size of 99%, 95%, and 0.15, respectively. The sampling was performed using the convenience sampling method. Due to the pandemic nature of the disease and the presence of the disease in all the country provinces, the samples were collected from all over the country. The inclusion criteria were the age over 15 years, willingness to participate in the study, and residence in Iran.

DATA COLLECTION

The data were collected using online questionnaires sent to people in different cities through social networks, such as Telegram and WhatsApp, which were selected due to traffic restrictions in the country as a result of the COVID-19 outbreak. At the beginning of the questionnaire and before entering the statements page, the objectives of the study were briefly explained to the participants, and they were assured that their information will remain anonymous and confidential. Following that, the participants who agreed to attend the study were redirected to the statement page by clicking the "I agree" option.

MEASUREMENTS

1. Demographic characteristics form

This form covered such information as age, gender, marital status, place of residence, level of education, income level, social class, history of physical and mental illness, and knowledge of social distancing.

2. Protection Motivation Theory questionnaire

The PMT questionnaire is a researcher-made scale including six constructs and 39 statements and has been designed based on a 5-point Likert scale. The constructs of the questionnaire include:

- A) Perceived vulnerability: This construct consists of five statements and is rated on a 5-point Likert scale from 1=strongly agree to 5 = strongly disagree. It should be mentioned that one statement was scored in reverse.
- B) Perceived severity of the disease: This construct consists of seven statements and is rated on a 5-point Likert scale from 1 = strongly disagree to 5 = strongly agree. It should be mentioned that two statements were scored in inverse.
- C) Response rewards: This construct consists of four statements and is rated on a 5-point Likert scale from 1 = strongly agree to 5 = strongly disagree.
- D) Self-efficacy: This construct consists of seven statements and is rated on a 5-point Likert scale from 1 = strongly disagree to 5 = strongly agree. It should be mentioned that one statement was scored in reverse.
- E) Response efficacy: This construct consists of five statements and is rated on a 5-point Likert scale from 1 = strongly disagree to 5 = strongly agree.
- F) Response costs: This construct consists of six statements and is rated on a 5-point Likert scale from 1 = strongly agree to 5 = strongly disagree.
- G) Fear: This construct consists of five statements and is rated on a 5-point Likert scale from 1 = strongly disagree to 5 = strongly agree.

It should be noted that the mean score in each construct is obtained by adding the scores and dividing the sum by the number of the statements.

The validity of this questionnaire was assessed based on the content validity using both qualitative and

quantitative methods. In the qualitative method, the questionnaire was prepared using valid references and new studies. Afterward, 10 faculty members were asked to provide their corrective comments on the questionnaire. Furthermore, the coefficients of content validity ratio (CVR) and content validity index (CVI) were used to evaluate the content validity quantitatively. Following that, 10 experts were asked to rate each item based on a 3-point scale in which 3 = necessary, 2 = useful but not necessary, and 1 = not necessary to determine the CVR, and the responses were analyzed using the Lawshe formula. According to the Lawshe table of determining the minimum value, expressions with CVR numerical value higher than 0.62 (based on the evaluation of 10 experts) were preserved in this study [18, 19]. At this stage, by the removal of two items in the questionnaire, the number of items was reduced to 39. The CVI of the remaining items in this instrument was also calculated in this study. Regarding the Waltz and Bausell's CVI, three criteria of simplicity, specificity (relevance), and clarity were rated separately by 10 experts on a 4-point Likert scale in which 4 = completely related, 3 = related, 2 = somewhat related, and 1 = unrelated. Afterward, to calculate the CVI of each item, the total number of the experts that selected scores 3 and 4 (the highest scores) for that item was divided by the total number of the experts ($n = 10$). The criterion to accept the item was the attainment of the CVI score higher than 0.79 [19]. Accordingly, the items with a score below 0.79 were excluded from the questionnaire [20]. However, at this stage, all the items obtained a score higher than 0.79 and were maintained in the study. Regarding the reliability of the questionnaire, the internal consistency of the scale was determined by 20 respondents who were asked to complete the questionnaire. As a result, the reliability value of PMT questionnaire were confirmed by Cronbach's alpha coefficient of 0.86. In this study, an alpha value of 0.7 was considered appropriate.

3. Behavioral Intentions Questionnaire

This scale consists of five statements and is rated on a 5-point Likert scale from 1 = strongly disagree to 5 = strongly agree. It should be noted that the mean score in this questionnaire is obtained by adding the scores and dividing the sum by the number of the statements.

The validity of the content of the questionnaire was confirmed using the opinions of 10 experts and its reliability was confirmed by calculating Alpha Cronbach 0.74.

4. Social Distancing Behaviors Questionnaire

The social distancing behaviors questionnaire lists 22 behaviors in line with social distancing recommendations prepared by the research team. Each behavior is rated on a 4-point Likert scale of 1 = never/rarely, 2 = sometimes, 3 = often, and 4 = always. The mean score in this questionnaire was obtained by adding the scores and dividing the sum by the number of the statements.

The validity of the content of the questionnaire was

confirmed using the opinions of 10 experts and its reliability was confirmed by calculating Alpha Cronbach 0.82.

ETHICAL CONSIDERATIONS

The study was approved by the Ethics Committee of Gonabad University of Medical Sciences, Gonabad, Iran (Ethical code No: IR. GMU. REC.1399.045). The participants were assured of their voluntary participation in the study. Identity information, such as the respondents' first and last names, was not asked to maintain confidentiality.

STATISTICAL ANALYSIS

All statistical analyses were performed using SPSS software version 16.0. Frequency (percent) and mean \pm standard deviation (SD) were used to describe qualitative and quantitative variables, respectively. The normality assumption of quantitative variables was checked using the Kolmogorov-Smirnov test. The Spearman correlation test was used to assess the correlation between the PMT constructs and the social distancing behaviors. The hierarchical linear models were used to identify the predictors of the intention and also the behaviors concerned with social distancing during the COVID-19 pandemic based on the PMT constructs, after controlling for the influence of individual characteristics. For this purpose, the individual characteristics were entered in Block 1 and the constructs of the PMT were entered in Block 2 of the model. The assumptions of the linear hierarchical models, including normality, homoscedasticity of variance, and independence of the residuals were assessed using Kolmogorov-Smirnov test, plots of standardized residuals versus predicted values, and residual time series plot, respectively. The assumption of multicollinearity was also checked using the variance inflation factor (VIF). A two-tailed P-value of < 0.05 was considered statistically significant.

Results

CHARACTERISTICS OF THE PARTICIPANTS

A total of 796 Iranian people participated in the study, and completed the questionnaires. The mean age of participants was 36.9 ± 12.0 , ranging between 16 and 80 years old. The other characteristics of the participants have shown in Table I.

THE CORRELATION BETWEEN THE PMT CONSTRUCTS, INTENTION, AND SOCIAL DISTANCING BEHAVIORS DURING THE COVID-19 PANDEMIC

The Spearman correlation test showed that there is a significant correlation between the PMT constructs, intention, and social distancing behaviors during the COVID-19 pandemic (all P-value is less than 0.001). The results have shown in the Table II.

Tab. I. Characteristics of the study participants.

| Characteristics | N (%) |
|--|------------|
| Gender | |
| Male | 331 (41.6) |
| Female | 465 (58.4) |
| Marital status | |
| Married | 569 (71.5) |
| Single/widowed/divorced | 227 (28.5) |
| Place of living | |
| City | 699 (87.8) |
| Village | 97 (12.2) |
| Educational level | |
| High school or below | 163 (20.5) |
| Associate or Bachelor degree | 401 (50.4) |
| Master degree or higher | 232 (29.1) |
| Family income level | |
| Low | 139 (17.5) |
| Moderate | 591 (74.2) |
| High | 66 (8.3) |
| Social class (subjective) | |
| Low | 147 (18.5) |
| Middle | 583 (73.2) |
| High | 66 (8.3) |
| History of chronic diseases | |
| Yes | 133 (16.7) |
| No | 663 (83.3) |
| History of mental disorders | |
| Yes | 17 (2.1) |
| No | 779 (97.9) |
| The history of infection with COVID-19 in people around you | |
| Yes | 130 (16.3) |
| No | 666 (83.7) |
| The history of COVID-19 dying in people around you | |
| Yes | 92 (11.6) |
| No | 704 (88.4) |
| Information sources about COVID-19 | |
| TV & Radio | 294 (36.9) |
| Internet | 374 (47.0) |
| Health staff | 112 (14.1) |
| Urban advertising | 9 (1.1) |
| Friends/relatives/neighbors | 25 (3.1) |

PREDICTORS OF THE INTENTION AND BEHAVIORS CONCERNED WITH SOCIAL DISTANCING DURING THE COVID-19 PANDEMIC

The assumptions of the linear hierarchical models, including normality, homoscedasticity of variance, and independence of the residuals were met. Also all the VIFs were less than 2.5 indicating that there was not serious multicollinearity between the predictors [21].

The results of the hierarchical regression model I (the outcome variable: intention) indicated that among individual characteristics, higher age ($t = 3.395$, $P = 0.001$), female gender ($t = 2.167$, $P = 0.031$), and having a history of chronic disease ($t = 3.211$, $P = 0.001$) had a significant positive association with the intention variable, and the variance explained by

Tab. II. Mean, standard deviation, and correlations between PMT constructs and social distancing behaviors during the COVID-19 pandemic.

| Variable | Mean (SD) | Spearman correlation coefficients† | | | | | | | | |
|----------------------------|-------------|------------------------------------|------|------|------|------|------|------|------|-----|
| | | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| 1. Perceived vulnerability | 4.18 (0.65) | --- | | | | | | | | |
| 2. Perceived severity | 4.27 (0.58) | 0.39 | --- | | | | | | | |
| 3. Response Rewards | 3.92 (0.76) | 0.32 | 0.44 | --- | | | | | | |
| 4. Self-efficacy | 4.12 (0.61) | 0.38 | 0.46 | 0.50 | --- | | | | | |
| 5. Response efficacy | 4.56 (0.52) | 0.30 | 0.41 | 0.29 | 0.52 | --- | | | | |
| 6. Response cost | 3.80 (0.74) | 0.24 | 0.35 | 0.51 | 0.52 | 0.36 | --- | | | |
| 7. Fear arousal | 3.71 (0.76) | 0.13 | 0.37 | 0.24 | 0.21 | 0.27 | 0.22 | --- | | |
| 8. Intention | 4.18 (0.67) | 0.27 | 0.41 | 0.49 | 0.62 | 0.50 | 0.44 | 0.36 | --- | |
| 9. Social distancing | 4.42 (0.31) | 0.55 | 0.69 | 0.74 | 0.75 | 0.61 | 0.70 | 0.54 | 0.75 | --- |

SD: Standard Deviation; †For all P-value is less than 0.001.

the first step of the model (including the individual characteristics) was 10.1% (Adjusted $R^2 = 0.101$). Taking into consideration of standardized regression coefficients (Beta), the most significant predictors of intention variables were age (Beta = 0.102), followed by history of chronic disease (Beta = 0.091), and gender (Beta = 0.058).

At step 2, the results showed that among the constructs of the PMT, four components including self-efficacy (Beta = 0.426, $t = 12.338$, $P < 0.001$), fear arousal (Beta = 0.177, $t = 6.233$, $P < 0.001$), response efficacy (Beta = 0.156, $t = 4.912$, $P < 0.001$), and response rewards (Beta = 0.155, $t = 4.801$, $P < 0.001$) were the most significant predictors of intention variables, respectively. According to the results, a change of one standard deviation in self-efficacy, fear arousal, response efficacy, and response rewards was associated with a change of 0.426, 0.177, 0.156, and 0.155 standard deviations of intention, respectively. With the inclusion of step 2 variables (PMT constructs) in the model, the variance explained was considerably increased from 10.1% to 55.1%, which was statistically significant (Adjusted $R^2 = 0.551$, $\Delta F = 107.821$, $P < 0.001$) (Tab. III).

The results of the hierarchical regression model II (the outcome variable: behavior) indicated that among individual characteristics, higher age ($t = 2.845$, $P = 0.005$), female gender ($t = 10.139$, $P < 0.001$), and college educational level ($t = 2.877$, $P = 0.005$) had a significant positive association with the social distancing behaviors, and the variance explained by the first step of the model (including the individual characteristics) was 16.8% (Adjusted $R^2 = 0.168$). Based on the Beta values, the most significant predictors of behavior were gender (Beta = 0.317), followed by age (Beta = 0.100), and educational level (Beta = 0.087).

At step 2, the results showed that self-efficacy (Beta = 0.238, $t = 5.427$, $P < 0.001$), intention (Beta = 0.233, $t = 5.474$, $P < 0.001$), and perceived severity (Beta = 0.083, $t = 2.203$, $P = 0.028$) were the most significant predictors of behavior variables, respectively. According to the results, a change of one standard deviation in self-efficacy, intention, and perceived severity were associated with a change of 0.238, 0.233, and 0.083 standard deviations of behavior,

respectively. With the inclusion of step 2 variables (PMT constructs and intention) in the model, the variance explained was considerably increased from 16.8% to 40.0%, which was statistically significant (Adjusted $R^2 = 0.400$, $\Delta F = 37.045$, $P < 0.001$) (Tab. III).

Discussion

This study aimed to predict social distancing behaviors during the COVID-19 pandemic in Iranian society based on PMT. The results indicated a significant correlation between PMT constructs with social distancing intention and behaviors during the COVID-19 pandemic. Regarding the predictors of intention to perform social distancing behaviors during the COVID-19 pandemic, linear regression analysis showed that female gender, older age, and history of chronic disease were associated with the intention to perform social distancing behaviors. After controlling the effect of these variables, the results of the present study revealed that the four constructs of PMT, including self-efficacy, response efficiency, response rewards, and fear arousal, were significant predictors of the intention to perform social distancing behaviors.

According to the results of a study conducted in 2020, self-efficacy, response efficiency, response rewards, and perceived severity were important cognitive factors that motivate individuals to perform social distancing behavior, which is consistent with the findings of the present study [22]. The results of the present study were also in line with the findings of a study conducted in the United Kingdom (2015) which concluded that three PMT constructs (i.e., fear, self-efficacy, and response efficiency) were important predictors of the intention to participate in social distancing behaviors in the computer game scenario [13]. Furthermore, a study was conducted in Finland (2020) on voluntary PMT-based self-isolation during the COVID-19 pandemic. The results revealed that perceived severity and self-efficacy had a positive effect on self-isolation intention [23], which was consistent with the findings of the present study.

The findings of the present study indicated that fear was effective in the motivation or intention of individuals to preserve social distancing in the COVID-19 pandemic,

Tab. III. Hierarchical regression analysis predicting social distancing intention and social distancing behaviors by individual characteristics and PMT constructs.

| Dependent Variable | | Predictors | | Beta | S.E. | t | P | Model Summary |
|--------------------|--------|--|--------|---------|--------|---------|---|---------------|
| Model I | | | | | | | | |
| Intention | Step 1 | Age | 0.102 | 0.002 | 3.395 | 0.001 | R ² = 0.111 ΔR ² = 0.111 Adjusted R ² = 0.101 ΔF = 10.352 P < 0.001 | |
| | | Gender: Female ^a | 0.058 | 0.037 | 2.167 | 0.031 | | |
| | | Educational level: College ^b | -0.011 | 0.044 | -0.411 | 0.681 | | |
| | | Place of living: City ^c | -0.024 | 0.053 | 0.911 | 0.362 | | |
| | | Social class: Low ^d | -0.037 | 0.044 | -1.456 | 0.146 | | |
| | | Marital status: Married ^e | 0.011 | 0.040 | 0.409 | 0.682 | | |
| | | History of mental illness: Yes ^f | 0.009 | 0.120 | 0.323 | 0.747 | | |
| | | History of chronic disease: Yes ^f | 0.091 | 0.051 | 3.211 | 0.001 | | |
| | Step 2 | History of infection with COVID-19 in people around the participants: Yes ^f | -0.029 | 0.047 | -1.135 | 0.257 | | |
| | | Perceived vulnerability | -0.007 | 0.030 | -0.247 | 0.805 | R ² = 0.561 ΔR ² = 0.450 Adjusted R ² = 0.551 ΔF = 107.821 P < 0.001 | |
| | | Perceived severity | 0.002 | 0.038 | 0.052 | 0.958 | | |
| | | Response Rewards | 0.155 | 0.028 | 4.801 | < 0.001 | | |
| | | Response cost | 0.019 | 0.028 | 0.604 | 0.546 | | |
| | | Self-efficacy | 0.426 | 0.038 | 12.338 | < 0.001 | | |
| | | Response efficacy | 0.156 | 0.041 | 4.912 | < 0.001 | | |
| Fear arousal | 0.177 | 0.025 | 6.233 | < 0.001 | | | | |
| Model II | | | | | | | | |
| Behavior | Step 1 | Age | 0.100 | 0.001 | 2.845 | 0.005 | R ² = 0.177 ΔR ² = 0.177 Adjusted R ² = 0.168 ΔF = 17.834 P < 0.001 | |
| | | Gender: Female ^a | 0.317 | 0.020 | 10.139 | < 0.001 | | |
| | | Educational level: College ^b | 0.087 | 0.024 | 2.877 | 0.005 | | |
| | | Place of living: City ^c | 0.034 | 0.029 | 1.133 | 0.258 | | |
| | | Social class: Low ^d | -0.041 | 0.024 | -1.401 | 0.162 | | |
| | | Marital status: Married ^e | -0.008 | 0.022 | -0.241 | 0.810 | | |
| | | History of mental illness: Yes ^f | 0.020 | 0.065 | 0.640 | 0.523 | | |
| | | History of chronic disease: Yes ^f | 0.014 | 0.028 | 0.430 | 0.668 | | |
| | Step 2 | History of infection with COVID-19 in people around the participants: Yes ^f | -0.023 | 0.026 | -0.791 | 0.429 | | |
| | | Perceived vulnerability | -0.019 | 0.016 | -0.568 | 0.570 | R ² = 0.414 ΔR ² = 0.236 Adjusted R ² = 0.400 ΔF = 37.045 P < 0.001 | |
| | | Perceived severity | 0.083 | 0.021 | 2.203 | 0.028 | | |
| | | Response Rewards | -0.014 | 0.016 | -0.362 | 0.718 | | |
| | | Response cost | -0.019 | 0.016 | -0.520 | 0.603 | | |
| | | Self-efficacy | 0.238 | 0.023 | 5.427 | < 0.001 | | |
| | | Response efficacy | 0.061 | 0.023 | 1.626 | 0.104 | | |
| Fear arousal | | 0.050 | 0.014 | 1.491 | 0.136 | | | |
| Intention | 0.233 | 0.020 | 5.474 | < 0.001 | | | | |

Beta: Standardized coefficient; S.E.: Standard Error; ^a Reference category = Male; ^b Reference category = High school or less; ^c Reference category = Village; ^d Reference category = Middle or high; ^e Reference category = Single/widowed/divorced; ^f Reference category = No.

which in turn led to behavior change and adherence to social distancing. This finding is consistent with the results of other studies [13]. Fear is one of the first emotional reactions during an epidemic and acts as a defensive system in dealing with ecological threats [24, 25]. In the present study, self-efficacy was identified as the strongest construct related to intention. Therefore, if a person feels that she/he is able to perform a behavior and can overcome external influencing factors, his/her intention for social distancing will increase and she/he deals with the resulted problems and complications more easily. This finding was in line with that of previous studies on preventive behaviors in the case of an influenza pandemic, which indicated that perceived self-efficacy was the strongest predictor of the intention to stay at home out of other PMT constructs [6, 26].

In the present study, the total predictability rate of four constructs of the model (i.e., self-efficacy, response efficiency, response rewards, and fear arousal) for the prediction of the intention to perform social distancing behavior was estimated at 55.1%, indicating that PMT theory could serve as an appropriate model for the prediction of one's intention to perform social distancing behavior. The results of this study are consistent with those of another study in which the model was able to explain 55% of the interpersonal variance in the participants' motivation for performing social distancing behavior [22].

Regarding the predictors of social distancing behaviors during the COVID-19 pandemic, linear regression analysis in this study showed that among individual characteristics, female gender, older age, and higher

education level were significantly associated with the behavior, which was in line with the results of the previously conducted studies [27-29].

Considering the other predictors of social distancing behaviors during the COVID-19 pandemic and after controlling the effect of individual variables, the results of linear regression analysis showed that self-efficacy, intention, and perceived severity were significant predictors of social distancing behavior. The results of this study were in line with the findings of a study conducted in Japan (2020) which demonstrated that out of four PMT constructs, perceived severity and self-efficacy were significant predictors of staying at home and social distancing during the COVID-19 pandemic [28]. According to another study performed in 2020, self-efficacy, response efficiency, perceived severity, and vulnerability had a positive effect on adherence to social distancing [25]. In the same line, a study was conducted in 2015 to reveal whether or not PMT was a useful framework for understanding social distancing behavior in response to an simulated infectious disease epidemic. The study results indicated that PMT constructs did not predict social distancing behavior in the computer game scenario [2], which contradicts the results of the present study. The difference between the results of the two studies can be attributed to the real conditions of the disease in the present study, the high prevalence of the disease in Iran, and the fact that in a short time, a large number of people were hospitalized and many have died as a result of this infectious disease.

In present study, self-efficacy was identified as the strongest construct associated with performing social distancing behavior. This finding is consistent with the results of other studies in which self-efficacy was the most predictive variable for stay at home during the COVID-19 pandemic [28].

The intention is a mental state and involves a person's decision to act. Moreover, it is the last advisory step before performing a behavior and the most important cognitive predictor of behavior [4]. Studies have shown that although the intention is considered a good predictor of the person's behavior, and more intended individuals are more likely to perform a behavior, the intention does not always lead to engaging in a behavior. Furthermore, internal or external factors can change one's intention to perform a behavior over time, which should be considered for the promotion of the respective behaviors [28].

According to the findings of the present study, in order to transform the intention of social distancing into a behavior, one should focus on self-efficacy and perceived severity in individuals. Those who perceive COVID-19 as a severe illness with a high mortality rate and are also reported as having higher self-efficacy (e.g., they believed they could prevent infection) may be more motivated and engaged in preventative behaviors (i.e., social distancing) to minimize or eliminate the threats.

In the present study, the PMT constructs (self-efficacy and perceived severity) and intention can predict 40% of social distancing behavior in total, which indicates

that PMT theory can be used as a suitable model for the prediction of social distancing behaviors. According to another study conducted in 2020, the predictability of staying at home during the COVID-19 pandemic by the two PMT constructs (self-efficacy and perceived severity) was estimated at 21%, which was lower than that obtained in the present study [28].

This finding is important because significant behavioral changes are needed to slow the transmission of the virus during a pandemic [30].

Regarding the limitations of the present study, it should be mentioned that although a cross-sectional study was used to investigate the relationship between predicting variables and outcome at a specific point in time, longitudinal predictions could not be made in this study. Therefore, it is suggested that longitudinal research and randomized controlled studies be designed and implemented to investigate causal relationships in this field. Furthermore, the generalizability of the data in this study is affected by the fact that convenience sampling of available volunteers was conducted in a web-based approach in order to prevent the dissemination of the disease. Eventually, the assessment of self-reported behavior rather than measuring objective behavior was another limitation of the study.

Conclusion

According to the results of the present study, PMT is a useful model to explain the individuals' motivation to protect themselves against COVID-19 infection through social distancing. Furthermore, the PMT constructs (self-efficacy and perceived intensity) and intention were regarded as significant predictors of social distancing behavior during the COVID-19 pandemic. Therefore, the implementation of interventions to increase the perceived intensity of the disease and self-efficacy with the purpose to encourage people to adhere to social distancing behavior based on this theory can play an important role in slowing down or stopping the spread of COVID-19 in the long run.

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Conflict of interest statement

There are no conflicts of interest.

Authors' contributions

FHT, FM, ADN: Study conception and design. ADN,

FHT: Acquisition of data. FM: Analysis and interpretation of data. FHT, FM: Drafting of manuscript. FHT: Critical revision. All authors have read and approved the final manuscript.

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ORIGINAL ARTICLE

Maternal social capital, health status and wellbeing of mothers of children under five years in Ibadan, Nigeria

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Key words

Maternal social capital • Wellbeing • Health status

Summary

Introduction. *This study investigated the influence maternal social capital has on the health and wellbeing of mothers of under-five children in a semi-urban local government area in Ibadan, Nigeria.*

Methods. *A descriptive cross-sectional study that utilised a three-stage sampling technique was adopted to select 385 respondents from 4 primary health care centres in Ibadan, Nigeria. Data collection was done using a semi-structured questionnaire to assess mothers' social capital, wellbeing and body Mass Index (BMI). Data analysis was done using*

descriptive and inferential statistics at the significant level of $P < 0.05$.

Results. *Benefits derived from participating in social groups such as: useful health information ($p = 0.005$; $p = 0.000$) and child care support ($p = 0.003$; $p = 0.002$) were significantly associated with wellbeing and health status of mothers respectively.*

Conclusions. *Mothers should be encouraged to engage in networks that are of healthful benefits to ensure effective knowledge sharing in sustaining promotion of health and wellbeing among mothers of under-five children.*

Introduction

Health is a concept that defines man's state of wellbeing. The World Health Organisation (WHO) defines health as "a state of complete physical, mental, social wellbeing and not merely the absence of disease or infirmity" [1], and later in 1986, at the Ottawa Charter in Canada, it was furthered explained that "health is a resource for everyday life and not just an 'object for living'". The WHO highlights a clear connection between health and wellbeing and emphasises health as a human right that necessitates both physical and social resources for sustainability.

Social capital's implications for health and socio-economic factors have made it a widely studied subject in many research work. Research has highlighted a connection between social networks, social support, as well as health, in public health research in much earlier times. There was later on an established connection between the concept of social capital and health [2]. Social capital is a means whereby people are able to access unavailable information and resources through their involvement and interactions in social networks, interpersonal relationships and other social structures. Social capital is also said to be related with better mental health among mothers and it is considered a mental health promotion strategy among women [3].

Social capital may be a mediating factor between and within communities, having a positive influence on health inequalities, which emanates from social isolation, low level of support and low self-confidence.

Strong networks, good level of support and positive relationships may have influence on individuals' sense of connectedness and belonging, confidence and self-esteem. They also have the ability to bring about change in people's or in their community, which serves as a protective factor in relation to health. Social capital as a concept can be divided into two elements; structural and cognitive elements. Characteristics of structural elements includes the tangible and easily observable aspects of social capital such as network connections, roles, rules, precedents and procedure. Cognitive social capital on the other hand includes intangible elements such as dispositions, reflexes, reliance and behavioral pattern people exhibit through learning and acting in the society [4]. According to Ivković, Ham and Mijoč [5], the subjective dimension of wellbeing can be related to individual perception of the quality of life in the society; wellbeing can be measured with indicators like income, health and education, which are the most commonly used.

Mothers are faced with a wide range of challenges which are peculiar to each and every mother. Motherhood creates new experiences that necessitates efforts directed towards a balanced life, which when not attended to can impair their health and wellbeing and consequently the health of their children. Report by UNICEF highlights poor economic status, inadequate maternal nutrition and deficient prenatal care as some of the challenges faced by mothers of under-five children in tackling nutritional challenges among small children. These challenges are characterised in high levels of disparities in health

issues faced by 40 million childbearing aged women in Nigeria [6]. Other challenges faced by mothers are mostly social capital related and they include challenges such as emotional disturbance, social isolation and risk of developing depressive illnesses especially among young mothers. These challenges can be associated with feelings of isolation, loneliness and low self-esteem [7], as a result of their inability to pull resources from social networks. Many studies have focused on mothers' social capital and child health outcomes but there is a dearth of studies in Nigeria that have focused on the corresponding health and wellbeing of the mothers. This study investigated the social capital status of mothers of under-five children in two dimensions (structural and cognitive) with indicators such as social networks, trust, togetherness, cohesiveness, participation and membership in groups among mothers of under-five, and how they relate to mothers' health and wellbeing.

Methods

A descriptive cross-sectional study design was employed to randomly select 385 consenting mothers of under-five children in four Primary Health Care (PHC) centres in Ibadan, Oyo State, Nigeria. A three-stage sampling technique was employed in selecting Mothers of under-five children from the PHCs selected in the LGA. In the first stage, the number of PHCs (11) were identified in the LGA; In the second stage, a purposive selection of 4 Primary Health Care Facilities was done based on their location in the LGA and population of mothers who attended on immunization days; In the third stage, consenting mothers were selected, through random selection, from each of the 4 health facility in the following proportions, based on population of attending mothers: 50 percent (193) of the total population was selected from PHC1, 30 (116) percent from PHC2, 15 (57) percent from PHC3 and 5 (19) percent from PHC4. The instrument employed for data collection was a semi-structured interviewer-administered questionnaire which assessed the social capital status, health status and wellbeing status of the mothers of under-five children. To measure the independent variable (maternal social capital), the Short Adapted Social Capital Assessment Tool (SASCAT) developed by Harpham et al. [2] was adopted for the study. The tool was used to measure both structural and cognitive aspects of social capital. The dependent variable (wellbeing) was measured by adapting the Warwick Edinburgh Mental Health Scale (WEMWBS) as a measure for subjective wellbeing. To further ascertain the mothers' health status, anthropometry measures of the mothers of under-five children was carried out using height and weight for BMI which served as index for mother's nutritional status. In establishing the reliability of the instruments, a pre-test of the data collection instruments were carried out among approximately 10% of the total study sample population (40 mothers of under five children) in another representative population in Ibadan. A Cronbach Alpha

measurement and reliability co-efficient measure was done and a co-efficient of 0.649 Cronbach's Alpha was obtained.

A coding guide was developed along with the data collection tool in order to facilitate its analysis. The data collected was carefully entered into the Statistical Package for Social Science (SPSS IBM version 22) statistical software and analysed using descriptive statistics such as mean, median and mode and inferential statistics such as Chi-square and logistic regression.

Structural social capital (SSC) was measured with questions on attendance and level of participation in social groups, a 21 point scale was used with scores < 6 were categorised as low SSC, 7-13 categorised as average SSC and 14-21 categorised as high SSC. The cognitive social capital (CSC) was measured using questions on trust and togetherness with a 7 point scale with scores ≤ 3 were categorised as low CSC and 4 ≥ 7 categorised as high CSC. Overall social capital status (SCS) was measured with a 32 point scale with categorisation scores of ≥ 15 as low and 15 ≥ 32 as high social capital. Wellbeing was measured with a 64 point scale with ≤ 21 categorised as low, 22 ≥ 42 categorised as average and ≥ 43 categorised as high and BMI was categorised based on WHO Global data base for BMI. The data was analysed using descriptive and inferential statistics (multinomial regression analysis) at the significant level of $P < 0.05$.

Ethical approval (Ref. No: AD 13/479/1448) was sought and obtained from the Oyo State Ministry of Health Nigeria Research Ethics Committee before data collection. To ensure confidentiality of research participants, identifiers such as names and other information that could reveal the identity of research participants were not included in the research instruments. The nature of the study, benefits and objectives were explained to the respondents and they were assured that the information given would be treated with utmost confidentiality. Consent was obtained from respondents before commencement of data collection and they were informed about the opportunity to withdraw their consent freely at any point during the study. Confidentiality of each research participant was maximally maintained during and after the collection of their information. Information gathered from the respondents was stored in a password protected computer for analysis and copies of the research instruments were kept for maximum safety.

Results

SOCIO-DEMOGRAPHIC CHARACTERISTICS OF RESPONDENTS

Majority (60%) of the mothers were between the ages 21 to 30 year and almost all of the mothers (97.9%) were married. About half (50.4%) of the mothers had secondary level education, while 39.7% had tertiary education. Many (41.0%) were traders and artisans (31.4%) and earned between N11,000-N30,000

(\$50-\$100) every month (53.2%) and 27% earned below that. Many (59.5%) had 1-2 children (Tab. I).

RESPONDENTS' SOCIAL CAPITAL STATUS

Structural social capital (SSC) that measured social support groups for the mothers mainly included family and friends (44.4%) and religious groups (38.4%). Others were community leaders (11.2%), government (11.2%), cooperative group (10.6%) and charity organisations (5.5%). Types of social support mothers got included financial support from family and friends (40.3%) and

from religious leaders (29.1%). Benefits mothers derived from social support/network groups included useful health information (64.7%), childcare support (65.2%), easy access to health facility (57.7%), invitation to social function (41.8%), access to health care finance (29.6%) and financial and material support (29.1%).

Cognitive social capital (CSC) included trust in people in their neighbourhood (41%) and community (37.4%), feeling of being part of their community (63.1%), get along well with people in their community (65.7%) and majority of the people in their community generally get along well with each other (63.9%).

The result showed that almost all mothers (99.7%) had average level of SSC. Many (59.7%) had high CSC. Overall Social capital status (SCS) result showed that majority of the mothers (86.2%) had low SCS and only 13.8% had high SCS.

Tab. I. Respondents' Socio-demographic characteristics (N=385).

| Characteristics | Frequency | Percentage (%) |
|------------------------------------|-----------|----------------|
| Age | | |
| < 20 | 18 | 4.7 |
| 21-30 | 231 | 60 |
| 31-40 | 120 | 31.2 |
| 41-50 | 13 | 3.4 |
| > 50 | 3 | 0.8 |
| Marital Status | | |
| Single | 8 | 2.1 |
| Married | 377 | 97.9 |
| Religion | | |
| Christianity | 202 | 52.5 |
| Islam | 181 | 47 |
| Traditional | 2 | 0.5 |
| Ethnicity | | |
| Yoruba | 354 | 91.9 |
| Igbo | 18 | 4.7 |
| Hausa | 1 | 0.3 |
| Others | 12 | 3.1 |
| Highest level of Education | | |
| No formal education | 10 | 2.6 |
| Primary | 28 | 7.3 |
| Secondary | 194 | 50.4 |
| Tertiary | 153 | 39.7 |
| Occupation | | |
| Civil servant | 12 | 3.1 |
| Artisan | 121 | 31.4 |
| Professional | 18 | 4.7 |
| Trader | 158 | 41.0 |
| Teachers | 44 | 11.4 |
| Farmers | 7 | 1.8 |
| Students | 17 | 4.4 |
| Cleric | 1 | 0.3 |
| Unemployed | 7 | 1.8 |
| Average income per month(N) | | |
| 0-10000 | 105 | 27.3 |
| 11-30000 | 205 | 53.2 |
| 31000 and above | 75 | 19.5 |
| Number of Children | | |
| 1-2 | 229 | 59.5 |
| 3-4 | 137 | 35.6 |
| 5-6 | 18 | 4.7 |
| 7-8 | 1 | 0.3 |

WELLBEING OF RESPONDENTS

Majority (73.2%) of mothers were often times optimistic about the future, 74% often times felt useful and relaxed (66.5%). Many (59%) have often times felt interested in other people, dealt well with their problems (52.7%), been able to think clearly (64.4%) and felt good about themselves (67.3%). Furthermore, 66.2% have often times been felt confident, felt loved (67.5%) and felt cheerful (67.3%). Majority (72%) of the respondents were on the high level of wellbeing scale. A three point likert scale was used with rarely (1), Sometimes (2) and often times (3) with the aggregate score of 126, scores below 21 were labelled low level of wellbeing, scores 22-42 was labelled average level of wellbeing and scores 43-63 was labelled high level of wellbeing. There was no statistical relationship between mothers' social capital and wellbeing.

BODY MASS INDEX (BMI) STATUS OF MOTHERS (HEALTH STATUS)

Less than half of the mothers (46.5%) were of normal weight, many (39.1%) were over-weight, 11.8% were obese and very few 2.7% were under weight.

RELATIONSHIP BETWEEN BENEFIT DERIVED FROM PARTICIPATION IN SOCIAL GROUP AND HEALTH STATUS OF MOTHERS

Findings indicated that there was a statistically significant relationship between benefits: useful health information ($X^2 = 19.496$; $p = 0.000$), childcare support ($X^2 = 15.277$; $p = 0.002$), easy access to health facilities ($X^2 = 15.171$; $p = 0.001$), satisfaction from involvement in decision making ($X^2 = 9.220$; $p = 0.048$) and health status using BMI (Tab. II).

MULTINOMIAL REGRESSION ANALYSIS ON RELATIONSHIP BETWEEN BENEFITS DERIVED FROM SOCIAL GROUPS AND HEALTH STATUS

Results of multinomial regression analysis of relationship between benefits derived from social group participation and health status using BMI showed that there was a significant association between mothers who

Tab. II. Relationship between benefits derived from social groups and health status of mothers.

| | | Underweight Freq. (%) | Normal weight Freq. (%) | Overweight Freq. (%) | Obese Freq. (%) | X ² | P-value |
|--|-----|--------------------------|-------------------------------|-------------------------|-----------------------|----------------|---------|
| Useful health information | | | | | | | |
| | Yes | 4(1.8) | 124(54.6) | 75(33.0) | 24(10.6) | 19.496 | 0.000* |
| | No | 5(4.4) | 34(30.1) | 58(51.3) | 16(14.2) | | |
| Child care support | | | | | | | |
| | Yes | 4(1.8) | 121(53.8) | 77(34.2) | 23(10.2) | 15.277 | 0.002* |
| | No | 5(4.3) | 37(32.3) | 56(48.7) | 17(14.8) | | |
| Access to health facility | | | | | | | |
| | Yes | 5(2.4) | 111(54.1) | 73(35.6) | 16(7.8) | 15.171 | 0.001* |
| | No | 4(3.0) | 47(34.8) | 60(44.4) | 24(17.8) | | |
| Health care finance | | | | | | | |
| | Yes | 3(2.9) | 49(47.6) | 37(35.9) | 14(13.6) | 1.052 | 0.802 |
| | No | 6(2.5) | 109(46.0) | 96(40.5) | 26(11.0) | | |
| Financial and Material support | | | | | | | |
| | Yes | 4(4.1) | 43(43.9) | 37(37.8) | 14(14.3) | 2.280 | 0.508 |
| | No | 5(2.1) | 115(47.5) | 96(40.5) | 26(10.7) | | |
| Access to loan | | | | | | | |
| | Yes | 2(3.6) | 32(58.2) | 14(25.5) | 7(12.7) | 5.830 | 0.101 |
| | No | 7(2.5) | 126(44.2) | 119(41.8) | 33(11.6) | | |
| Friendship and developing a sense of belonging | | | | | | | |
| | Yes | 4(4.5) | 43(48.9) | 27(30.7) | 14(15.9) | 5.851 | 0.110 |
| | No | 5(2.0) | 115(45.6) | 106(42.1) | 26(10.3) | | |
| Security | | | | | | | |
| | Yes | 2(1.7) | 55(46.6) | 40(33.9) | 21(17.8) | 7.107 | 0.650 |
| | No | 7(3.2) | 103(46.4) | 93(41.9) | 19(8.6) | | |
| Decision making | | | | | | | |
| | Yes | 1(1.3) | 32(42.1) | 27(35.5) | 16(21.1) | 7.557 | 0.048* |
| | No | 8(3.0) | 115(43.4) | 114(43.0) | 28(10.6) | | |
| Involvement in developmental activities | | | | | | | |
| | Yes | 3(2.1) | 71(49.7) | 50(35.) | 19(13.3) | 2.395 | 0.500 |
| | No | 6(3.0) | 87(44.2) | 83(42.1) | 21(10.7) | | |
| Invitation to Social function | | | | | | | |
| | Yes | 0(0.0) | 4(30.8) | 6(46.2) | 3(23.1) | 2.607 | 0.391 |
| | No | 9(2.8) | 154(47.1) | 127(38.8) | 37(11.3) | | |

got easy access to health facilities ($p = 0.038$) and those who were involved in decision making ($p = 0.014$) as a benefit derived from social group participation and health status using BMI.

RELATIONSHIP BETWEEN BENEFITS DERIVED FROM SOCIAL GROUPS AND WELLBEING OF MOTHERS

Result showed that useful health information ($X^2 = 11.119$; $p\text{-value} = 0.005$), child care support ($X^2 = 11.834$, $p\text{-value} = 0.003$), security in the neighbourhood ($X^2 = 7.579$; $p\text{-value} = 0.020$) and invitation to social functions ($X^2 = 7.414$; $p\text{-value} = 0.028$) were statistically significantly related to wellbeing of mothers (Tab. III). Further multinomial regression analysis showed no statistical significance difference between benefits derived from social groups and wellbeing of mothers.

Discussion

The study findings showed that social capital status of the mothers of under-five was low and in turn was not statistically related with their health and wellbeing status. Most of the mothers participated more in their informal and religious groups than in formal groups like political groups and cooperative groups and most of them were ordinary members in the groups they belonged to and this was reflected in the sources of social support derived. The study revealed that the hospital was a good source of useful health information and child care support, and mothers utilised it as a place where they interact with other women when they visited for their children's immunization and for other purposes. The setting provided an avenue to share experiences and ideas with others mothers, to network and ask questions. Findings also showed that most of the women had

Tab. III. Relationship between benefits derived from social groups and wellbeing of mothers

| Low level Freq. (%) | | Average level Freq. (%) | High level Freq. (%) | X ² | p-value |
|---|--------|----------------------------|-------------------------|----------------|---------|
| Useful health information | | | | | |
| Yes | 1(0.4) | 54(21.7) | 194(77.9) | 11.119 | 0.005* |
| No | 8(5.9) | 31(22.8) | 97(71.3) | | |
| Child care support | | | | | |
| Yes | 1(0.4) | 60(23.9) | 190(75.7) | 11.834 | 0.003* |
| No | 8(6.0) | 25(18.7) | 101(75.4) | | |
| Easy access to health facility | | | | | |
| Yes | 3(1.4) | 45(20.3) | 174(78.4) | 3.456 | 0.191 |
| No | 6(3.7) | 40(24.5) | 117(71.8) | | |
| Access to health care finance | | | | | |
| Yes | 2(1.8) | 28(25.0) | 84(75.0) | 0.722 | 0.736 |
| No | 7(2.6) | 57(20.9) | 207(75.8) | | |
| Financial and material support | | | | | |
| Yes | 0(0.0) | 28(25.0) | 84(75.0) | 4.406 | 0.106 |
| No | 9(3.3) | 57(20.9) | 207(75.8) | | |
| Easy access to loan | | | | | |
| Yes | 0(0.0) | 18(28.1) | 46(71.9) | 2.701 | 0.225 |
| No | 9(2.8) | 67(20.9) | 245(76.6) | | |
| Friendship and development of sense of belonging | | | | | |
| Yes | 2(2.0) | 31(30.4) | 69(67.6) | 5.409 | 0.057 |
| No | 7(2.5) | 54(19.1) | 222(78.4) | | |
| Security | | | | | |
| Yes | 0(0.0) | 37(26.4) | 103(73.6) | 7.579 | 0.020* |
| No | 9(3.7) | 48(19.6) | 188(76.7) | | |
| Involvement in decision making | | | | | |
| Yes | 0(0.0) | 25(27.5) | 66(72.5) | 4.292 | 0.115 |
| No | 9(3.1) | 60(20.4) | 225(76.5) | | |
| Satisfaction from developmental activities | | | | | |
| Yes | 0(0.0) | 17(20.2) | 67(79.8) | 2.562 | 0.310 |
| No | 9(3.0) | 68(22.6) | 224(74.4) | | |
| Invitation to social function | | | | | |
| Yes | 0(0.0) | 35(21.7) | 126(78.3) | 7.414 | 0.028* |
| No | 9(4.0) | 50(22.3) | 165(73.7) | | |
| Other benefits | | | | | |
| Yes | 0(0.0) | 2(15.4) | 11(84.6) | 0.293 | 0.810 |
| No | 9(2.4) | 83(22.3) | 280(75.3) | | |

a considerably good level of wellbeing status which was significantly associated with benefits derived from participating in social groups such as useful health information, child care support, security in the neighbourhood and invitation to various social functions. Results highlighted that getting useful health information on issues relating to health and benefitting from child care support were the main benefits that were associated with the wellbeing of mothers of under-five children. Rocco and Suhrcke [8], affirms that individuals who are more involved in continuous social interactions such as with family, friends, social events involvement, meetings, partisanship in formal and informal organisations, are often more probable to have access to information on preventive and curative measures of disease than those who are not. Kawachi and Berkman [9] also describes social capital as a mechanism

through which community social capital affects health by providing channels for health promotion through which there is a rapid dissemination of health-related knowledge and information in social networks. It is also a means of creating and ensuring healthy behavioural norms (e.g. regular physical exercise, healthy eating and so on) and exerting social control over harmful health behaviours (e.g. smoking and drinking). Study findings also showed that most of the mothers received social support from their families and friends. This indicates that family and friends play a good role in helping women overcome major challenges through provision of financial resources for health care and other basic needs provision. Studies [10, 11] revealed that women who receive emotional, economic and social support from their families are well able to deal with life challenges and problems in more logical and easier

way. Family social supports for women who require extra care in dealing with difficult situations can help achieve a crisis period with less psychological burdens. Social family ties create support systems that reduce the rate of physical infirmity and also create an avenue for recuperation to an individual's normal life.

Health status was measured using Body Mass Index (BMI). This was due to the fact that prevalence of obesity has been on the increase in recent times having impacts on morbidity, quality of life and public health. This study showed a relationship between certain benefits derived from participating in social networks (useful health information, child care support, easy access to health facility and involvement in decision making) and BMI status. Rohrer et al. [12], reported that obesity is more common among women who live in low income societies and have large family sizes but do not receive support from their parents than those with large family sizes and parental supports. Social support gotten through networks of friends and family have been correlated with improved participation in networks that supports diet and physical activity interventions; and among postpartum mothers who are overweight; social support was shown to influence healthy behaviours that ensures healthy weight. Possible channels identified that could stand as a mediating factor between health and social capital include the improvement of norms of health-related behaviours such as community/group prevalent norms and values such as avoiding sugars and trans-fat take up. Others are collective efficacy, such as advocating situations and conditions that allows for exercise and healthy eating habits; and exchange of social support which could be in form of nutritional advice and support [13].

Recommendations

Health promotion and behavioural change recognises the role of communities in improving various health outcomes and thereby many health interventions are taken through communities to achieve their goal and get to the target audience. Therefore health intervention planning should take into consideration the structural and cognitive social capital strength of the community so as to ensure knowledge transfer and sustainability of interventions carried out. Health education and promotion programmes should make efforts towards strengthening social groups and networks in the community and also ensuring solidarity, reciprocity of kind gestures, togetherness and trust especially among mothers. This will facilitate easy access into the community and increased knowledge acceptability and retention.

Conclusions

Findings highlights that the level of social capital does not predict the wellbeing of the women in this study

but may influence their health status using their Body Mass Index. Therefore, mothers should be encouraged to engage in meaningful and resourceful networks that will facilitate easy access to useful health information and many other benefits needed for considerable level of health and wellbeing status.

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Conflict of interest statement

The authors declare no competing interest.

Authors' contributions

Both authors have contributed substantially to the conception, design, analysis, interpretation, writing and reviews of the manuscript.

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ORIGINAL ARTICLE

Measuring the Structures of the Health Belief Model Integrated with Health Literacy in Predicting University Students' Adoption of Smoking Preventive Behaviors

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Key words

Health Belief Model • Health Literacy • Smoking • Preventive Behaviors

Summary

Objectives. One of the priorities of public health in reducing smoking is to prevent young people from becoming smokers. Health literacy (HL), smoking, and preventive behaviors are related. Moreover, HL has a potential impact on strengthening the Health Belief Model (HBM). Considering the high prevalence of smoking among university students, the current study was conducted to measure the structures of the HBM integrated with HL in predicting university students' adoption of smoking preventive behaviors.

Methods. This was a cross-sectional descriptive study. Three hundred and forty dormitory students of Shahid Beheshti University of Medical Sciences (Teheran, Iran) in 2016, were selected through single-stage cluster sampling for the study. The data gathering tool was a researcher-made questionnaire based on the

HBM and the HL inventory for adults (HELIA). The data were analyzed using the SPSS software version.16.

Results. The multiple regression analysis showed that the application of health information from five dimensions of HL, perceived susceptibility, self-efficacy, and decision-making dimensions were the predictors of smoking prevention. Also, the structures of this integrated model were able to anticipate 36.5% of the behavioral changes.

Conclusion. The HBM integrated with HL can be used as an appropriate framework for designing educational programs to encourage university students to adopt smoking preventive behaviors.

Introduction

Smoking is one of the most important risk factors for chronic disease in the world and its use is growing rapidly among adolescents and youth [1]. It is estimated that the number of smokers enhanced from 1.3 billion to 1.6 billion people in 2025. Its mortality is estimated to increase to 8.3 million people in 2030 from 4.8 million in 2006 [2]. Various studies indicate that the prevalence of smoking among the students of some medical universities in Iran is more than 20% [3, 4].

The results of studies show that there is a significant association between HL and smoking status [5]. The studies on this issue have concluded that low HL could be considered as an independent risk factor for smoking [6-8], smoking recurrence [9], and weaker results of smoking cessation programs [10]. One of the latest study revealed that HL should be considered when developing targeted tobacco prevention strategies [11]. Also, Atri et al., concluded that improving the level of

HL can lead to change people's behavior in relation to smoking [12]. HL is a dynamic and multidimensional concept encompassing the ability of individuals to achieve the goal, communicate, and understand basic health information and services needed for proper decision-making in health care [13]. Benefiting from HL can enhance health behaviors and improve access to health care [14]. Regarding the level of HL among students, studies by Deghankar et al. [15] and Sajadi et al. [16] showed that more than one-third of students had inadequate and problematic HL.

A review of previous studies has shown that the HBM is a good model for education regarding the prevention of smoking [17]. The HBM is an appropriate model for anticipating smoking-related behaviors; due to its inclusion of the two categories of health beliefs and social factors [18]. Glanz et al. believe that the dimensions of the HBM can be useful in understanding health behaviors in multicultural groups [19]. Having a high perceived self-efficacy and high perceived susceptibility can reduce smoking among people [18]. Various researchers have also suggested using the

HBM in educational programs to promote smoking preventive behaviors [20-22].

On the other hand, HL has a potential impact on strengthening the HBM. As the variable of knowledge and acting as a facilitating factor, it can enhance people's perception of susceptibility [20].

According to some researchers' views, to better understand the causes of complex behaviors such as smoking [17], the potential impact of HL on the structures of HBM [20], and the role of HL in smoking, poorer smoking cessation outcomes, and return to smoking [6-10], it seems that integrating the HBM with HL can help further enhance the success of this model in promoting the smoking prevention. Therefore, considering the increasing trend of smoking among university students [3, 4, 20], the current study was designed and implemented to measure the structures of the HBM integrated with HL in predicting the adoption of smoking preventive behaviors among university students.

Method

This study was a cross-sectional descriptive-analytical study that was conducted on the dormitory students of Shahid Beheshti University of Medical Sciences (SBMU) in 2016. In this study, 355 students were selected through a single-stage random cluster sampling method. At first, a list of all the 14 dormitories where students from different medical sciences were living was prepared. Then, 4 dormitories (2 dormitories for girls and 2 dormitories for boys) were selected randomly and all the students residing in them were enrolled on the condition that they had the inclusion criteria.

The sample size estimation was done based on Cochran's sample size formula. The sample size was estimated to be 322 people according to a review of previous studies [23] and considering $P = 0.30$ for smoking preventive behaviors and $d = 0.05$. 355 subjects were included in the study based on the opinion of a statistics expert and a 10% probability of falling.

The inclusion criteria were the tendency of the subjects for inclusion, being a student, Iranian citizenship, studying at the undergraduate grade, being in the second or third year of study, and living in the dormitories of SBMU. In addition, unwillingness to continue participating in the study and not completing the questionnaire was considered as the exclusion criteria. It is noteworthy that the data of 15 students were omitted because they did not complete the questionnaire and the final analysis was performed on 340 questionnaires (response rate: 95.8%). In this study, the students were contractually considered to have the experience of smoking if they had smoked at least one cigarette during their lifetime. A student who smoked daily or occasionally at the time of the study was also referred to as a smoker. A student who did not have a history of smoking even a single cigarette during the time of the research was referred to as a non-smoker [3]. The data gathering tool was a questionnaire with 4 parts: A) the first part was about some demographic

and background characteristics and determining the smoking or nonsmoking status of the students. B) the second was a researcher-made questionnaire that was used to measure the HBM constructs regarding smoking and its risks. This questionnaire included perceived susceptibility (n: 4 questions), perceived severity (n: 6 questions), perceived barriers (n: 6 questions), perceived benefits (n: 7 questions), perceived self-efficacy (n: 6 questions), and cues to action (n: 2 questions). In the section on the HBM constructs, the Likert scale was used with 5 choices of strongly agree (5 points), agree (4 points), no comment (3 points), disagree (2 points), and strongly disagree (1 point). It should be noted that among the questions of perceived susceptibility, only the first question followed the above rule, and the other questions were reversely scored. In the section related to cues to action, the students were asked about the ways they used to obtain information about the dangers of smoking and the benefits of preventing smoking and their responses were calculated by frequency. C) The third part was related to the questions measuring the rate of adoption of smoking preventive behaviors (n: 15 questions). The scoring method in the behavior questions gave the score of 2 points to the best answer, the score of zero points to the worst answer, and the score of one point to the intermediate answer. According to previous researches, the preventive behaviors were classified into three levels of poor (with the score of below 50% of the total score), moderate (with the score of 50-75% of the total score), and good (with the score of over 75% of the total score) [24]. D) The fourth part was related to the HL questionnaire of Iranian urban population aged 18-65 (HELIA). This questionnaire included 33 questions measuring five major dimensions including reading, gain access, understanding, appraisal, health information decision-making and application. The scores on the total questionnaire ranged from 0 to 100 where higher scores indicated better conditions. The scores between 0-50, 50.1-66, 66.1-84.0, and 84.1-100 were considered as inadequate HL, problematic HL, sufficient HL, and excellent HL, respectively. The psychometric properties of the questionnaire were well documented [25]. Furthermore, in the study of Panahi et al., the validity and reliability of the aforementioned questionnaire were tested in a sample of university students. Drawing on the results of confirmatory factor analysis, this questionnaire was a desirable fit. Furthermore, in the study, Cronbach's alpha coefficient was desirable. Overall, the results of the study showed that the HELIA questionnaire could be used for university students [26].

To determine Content Validity Ratio (CVR) and Content Validity Index (CVI), the HBM questionnaire was given to a handful of professors and experts and their ideas were considered in modifying or deleting the questions. Accordingly, reliability was calculated in the pilot study (which was conducted on 30 students) and the following results were finally obtained: perceived susceptibility (CVR = 0.88, CVI = 0.90, Cronbach's alpha = 0.85),

perceived severity (CVR = 0.97, CVI = 0.99, Cronbach's alpha = 0.70), perceived barriers (CVR = 0.84, CVI = 0.93, Cronbach's alpha = 0.81), perceived benefits (CVR = 0.79, CVI = 0.91, Cronbach's alpha = 0.90), perceived self-efficacy (CVR = 0.89, CVI = 0.96, Cronbach's alpha = 0.83), and smoking preventive behaviors (CVR = 0.91, CVI = 0.90, Cronbach's alpha = 0.85). Validity and reliability were not calculated for questions related to cues to action because they were in objective form and did not measure the students' ability to comprehend [20]. The alpha coefficients for the dimensions of reading, access, understanding, appraisal, decision making, and use of health information, and the whole HELIA questionnaire were 0.84, 0.85, 0.90, 0.77, 0.86, and 0.94, respectively.

After observing the ethical and research standards that included receiving an Ethics Code (IR.TMU.

REC.1394.172) and obtaining consent from the participants, the questionnaires were given to the participants. The questionnaires were completed by self-report and took 45 minutes. After the nature of the study and its aims were described to the students, they were asked to answer the questionnaire questions with complete honesty and were assured that all the information requested in the questionnaire would be used confidentially. Furthermore, the questionnaires were completed in the students' dormitories and the presence of a researcher. After data collection, the data were analyzed using the SPSS software version.16, descriptive statistical, Pearson correlation coefficient, multiple regression, and independent T-test. The significance level in this study was considered less than 0.05.

Tab. I. The demographic and background information of the students participating in the study.

| Variables | | No. (%) |
|--|----------------------------|------------|
| Gender | Female | 204 (60) |
| | Male | 134 (40) |
| Education years | Sophomore | 139 (40.9) |
| | Junior | 201 (59.1) |
| Marital status | Single | 295 (86.8) |
| | Married | 41 (12.1) |
| | Divorce or death of spouse | 4 (1.2) |
| Having a smoker in the family | Yes | 121 (35.6) |
| | No | 219 (64.4) |
| Probation history | Yes | 12 (3.5) |
| | No | 328 (96.5) |
| Physical activity per week | Everyday | 18 (5.3) |
| | Most days | 41 (12.1) |
| | Sometimes | 140 (41.2) |
| | Rarely | 111 (32.6) |
| | Never | 30 (8.8) |
| Father's job | Employee | 73 (21.5) |
| | Worker | 29 (8.5) |
| | Self-employed | 131 (38.5) |
| | Retired | 78 (23) |
| | Other | 29 (8.5) |
| Mother's job | Housewife | 269 (79.1) |
| | Employee | 51 (15) |
| | Self-employed | 4 (1.2) |
| | Worker | 1 (0.3) |
| | Other | 15 (4.4) |
| Education field | Health | 74 (21.8) |
| | Nursing | 63 (18.5) |
| | Nutrition | 52 (15.3) |
| | Midwifery | 21 (6.2) |
| | Optometry | 20 (5.9) |
| | Physiotherapy | 18 (5.3) |
| | Other fields | 92 (27) |
| Having a friend who smokes | Yes | 199 (58.5) |
| | No | 141 (41.5) |
| The status of the individual in terms of smoking | Smoker | 81 (23.8) |
| | Non-smoker | 201 (59.1) |
| | Has experienced | 58 (17.1) |

Tab. II. The comparison of the mean and standard deviation of the constructs of the HBM integrated with HL and the adoption of smoking preventive behaviors among smoking and non-smoking students

| Variables | Smokers | | Non-smokers | | Total | | P-value |
|--------------------------|---------|--------------------|-------------|--------------------|-------|--------------------|---------|
| | Mean | Standard deviation | Mean | Standard deviation | Mean | Standard deviation | |
| Perceived susceptibility | 13.64 | 4.673 | 17.46 | 2.782 | 16.55 | 3.70 | 0.000 |
| Perceived severity | 23.67 | 4.610 | 25.95 | 3.533 | 25.41 | 9.32 | 0.000 |
| Perceived barriers | 23.11 | 3.947 | 24 | 4.211 | 23.79 | 4.16 | 0.084 |
| Perceived benefits | 26.05 | 5.738 | 29.61 | 4.238 | 28.76 | 4.87 | 0.000 |
| Self-efficacy | 23.11 | 4.577 | 26.59 | 3.410 | 25.76 | 4.001 | 0.000 |
| Health literacy | 67.34 | 15.26 | 73.10 | 12.93 | 70.52 | 14.12 | 0.001 |
| Preventive behaviors | 37.90 | 22.41 | 39.36 | 19.16 | 39.01 | 19.96 | 0.036 |

Results

The mean (SD) of the participants' age was 22.93(4.05) years. Table I shows the other demographic and background information of the participating students. Table II shows the scores obtained from the constructs of the HBM, HL, and the adoption of smoking preventive behaviors among smoking and non-smoking students. The results of this table show that the mean scores of all the integrated model constructs (except for the perceived barriers) and the adoption of smoking preventive behaviors were significantly higher in nonsmokers than in smokers. According to the results, the percentages of students with inadequate, problematic, adequate, and excellent HL levels were 9.2% (31 people), 28% (94 people), 43% (145 people), and 19.8% (67 people), respectively. The percentages of students with poor, moderate, and good smoking preventive behavior levels were 72% (245 people), 23.3% (79 people), and 4.7% (16 people), respectively. In addition, the dimensions of understanding and access had the highest mean scores, whereas the health information decision-making and application dimensions had the lowest mean scores among the five dimensions of HL.

The results showed that the internet (64.1%) and interaction with friends and acquaintances (38%) were the most important resources from which the participating students routinely obtained information about the dangers of smoking and the benefits of preventing it. Table III shows the correlation coefficients among the constructs of the HBM integrated with HL and the adoption of smoking preventive behaviors as

well as the correlation coefficients between the different constructs of this model. The results of this table showed that there was a significant and direct correlation among all the constructs of this model. The highest correlation was observed between self-efficacy and perceived benefits ($r = 0.615$), perceived benefits and perceived severity ($r = 0.595$), and perceived susceptibility and HL ($r = 0.574$). The results also demonstrated that the adoption of smoking preventive behaviors among students had a significant correlation only with perceived susceptibility ($r = -0.102$), perceived self-efficacy ($r = 0.167$), and the HL variable ($r = 0.144$) ($P < 0.05$). Table IV shows the results of the multiple regression analysis in determining the predictors of the adoption of smoking preventive behaviors and the predictive level of behavior by these constructs in the integrated HBM. Overall, the results of this table show that the constructs of the HBM integrated with HL predicted 36.5% of the adoption of smoking preventive behaviors. Among the studied constructs, perceived susceptibility, perceived self-efficacy, and health information decision-making and application out of the five dimensions of HL were significantly predictive of behavior. Among these variables, perceived susceptibility was the strongest predictor of behavior. Perceived severity, perceived barriers, and perceived benefits, and the other four dimensions of HL were not significant predictors of behavior.

Discussion

The current study was designed and implemented to measure the structures of the HBM integrated with HL in

Tab. III. The correlation coefficient matrix of the constructs of the HBM integrated with HL and the adoption of smoking preventive behaviors

| Variables | Perceived susceptibility | Perceived severity | Perceived barriers | Perceived benefits | Self-efficacy | Health literacy | Preventive behaviors |
|--------------------------|--------------------------|--------------------|--------------------|--------------------|---------------|-----------------|----------------------|
| Perceived susceptibility | 1 | | | | | | |
| Perceived severity | 0.555* | 1 | | | | | |
| Perceived barriers | 0.163* | 0.433* | 1 | | | | |
| Perceived benefits | 0.515* | 0.595* | 0.447* | 1 | | | |
| Perceived self-efficacy | 0.551* | 0.382* | 0.382* | 0.615* | 1 | | |
| Health literacy | 0.574** | 0.419* | 0.158 | 0.357 | 0.418** | 1 | |
| Preventive behaviors | -0.102** | 0.026* | -0.017 | 0.008 | 0.167** | 0.144** | 1 |

Significant correlation was less than 0.01. ** Significant correlation was less than 0.05.

Tab. IV. Multiple regression analysis: the predictors of the adoption of smoking preventive behaviors in the HBM integrated with HL.

| Constructs | β | P-value Enter Method | F (P-value) | R (R ²) |
|--|---------|-------------------------|----------------|---------------------|
| Perceived susceptibility | 0.327 | 0.001 | 11.875 (0.001) | 0.515 (0.365) |
| Perceived severity | -0.100 | 0.268 | | |
| Perceived barriers | -0.059 | 0.408 | | |
| Perceived benefits | 0.150 | 0.084 | | |
| Self-efficacy | 0.194 | 0.028 | | |
| Dimension of reading | -0.084 | 0.189 | | |
| Dimension of access | 0.003 | 0.972 | | |
| Dimension of understanding | 0.076 | 0.388 | | |
| Dimension of appraisal | -0.076 | 0.342 | | |
| Dimension of decision-making and use of health information | 0.190 | 0.018 | | |

predicting the adoption of smoking preventive behaviors among university students. Based on the results, the structures of the HBM integrated with HL, in general, predicted 36.5% of the adoption of smoking preventive behaviors. The structures of perceived susceptibility and self-efficacy were significant predictors of behavior. Also, among the five dimensions of HL, the dimension of health information decision-making and application significantly predicted behavior.

Based on the results of the studied constructs, perceived susceptibility was the strongest predictor of the adoption of smoking preventive behaviors. This finding was in line with the findings of the study by Boroujeni et al. [27]. Moreover, the findings of this section are in contrast to the findings of the studies of Lee et al. [18], Mokhtari Laleh et al. [17], and Mohammadi et al. [28]. For the contradiction between the results of these three studies and those of the present study, it can be said that in the first two studies only male students participated and it is conceivable that their sensitivity to smoking and exposure to cigarette smoke were lower than those of girls. A possible reason for the differences between the results of Mohammadi et al. and those of the present study could be the differences between the samples studied in the two studies because adolescents may be less sensitive than students to smoking and exposure to cigarette smoke because of their lower awareness. Regarding other reasons for the significance of perceived susceptibility in predicting the adoption of smoking preventive behaviors, the presence of HL can be mentioned because it can influence behavior by increasing the perceived susceptibility [20].

In this study, perceived self-efficacy was another important construct in predicting smoking prevention. These findings are in agreement with the findings of the studies by Boroujeni et al. [27] and Mohammadi et al. [28], while they are in contrast to the results of the studies by Lee et al. [18], and Mokhtari Laleh et al. [17]. One possible reason for this discrepancy is that in the studies of Lee et al. and Mokhtari Laleh et al., no self-efficacy construct was used among the questionnaire questions. Regarding other reasons for the significance of perceived self-efficacy in predicting the adoption of smoking preventive behaviors, the presence of HL in this study can be mentioned because

it can act as a mediator between self-efficacy and behavior change [20].

In this study, perceived barriers could not predict the adoption of preventive smoking behaviors. The findings of the present study are in contrast with the one of other studies such as Boroujeni et al. [27], Mohammadi et al. [28], Mokhtari Laleh et al. [17], and Lee et al. [18]. One might argue about this contradiction that some of the questions used to measure the structure of perceived barriers including such statements as "easy access to smoking can cause the beginning of smoking behaviour" were not considered by the students as barriers to the adoption of smoking preventive behaviors and the majority of these students cited such statements as "not having fun and leisure time can cause people to smoke" as barriers to the adoption of smoking preventive behaviors.

In this study, perceived benefits did not affect the adoption of smoking preventive behaviors. The results of this section are in line with the findings of studies by Boroujeni et al. [27], Mohammadi et al. [28], and Mokhtari Laleh et al. [17], whereas they contradict the results of a study by Lee et al. [18]. These differences appear to be due to the differences in the target groups and the tools used. Furthermore, the questions used to measure the constructs of perceived benefits in the current study may not fully represent all the benefits of the adoption of smoking preventive behaviors for health from the students' point of view and most of them cited the statement "not smoking reduces the risk of cancer" as an important benefit of the adoption of smoking preventive behaviors. Another possible reason could be the possible overlap of HL with the perceived benefits and its potential impact on this construct.

The results of the present study showed that perceived severity did not affect the adoption of smoking preventive behavior. These results are consistent with the findings of the studies by Boroujeni et al. [27], Mohammadi et al. [28], and Mokhtari Laleh et al. [17]. Regarding this case, the structure of perceived severity was influenced by medical information and knowledge. Since the participants in the study were medical students, the items in the structural assessment section were probably not comprehensible enough to represent all of the disabilities and diseases caused by smoking or exposure

to smoke. Concerning other reasons that perceived severity was not significant for predicting behavior, it is possible to overlap some of the HL questions used in this study (HELIA) with several questions related to the perceived severity construct.

The results also showed that among the dimensions of HL, only the dimension of decision making and the use of health information had an impact on the adoption of smoking preventive behaviors. This result was in line with the findings of the study of Martin et al. [29]. Concerning the reason for the effect of one of the five dimensions of HL on the adoption of smoking preventive behaviors, it can be said that probably the dimension of decision making and use of health information could be more related to the adoption of smoking preventive behaviors than the other dimensions of HL because this dimension is homogeneous with this behavior. In the study of Arabzadeh et al., the dimension of using health information had the highest relationship with the adoption of smoking preventive behaviors [30]. Another reason could be that the study population consisted of medical students. As stated earlier, the lowest mean score among the dimensions of HL was related to decision-making and the use of health information. Therefore, it can be said that the students may have had sufficient ability to read, gain access, understand, and evaluate health information but were not able to take appropriate action based on their abilities and knowledge.

The results of the correlation test reflected that there was a significant and direct correlation between all the structures of this model. The significant correlation between the model constructs in this study indicated that the sum of these constructs and dimensions together can constitute the attitudes and capacities necessary for the adoption of smoking preventive behaviors. These results are consistent with the results of the study by Boroujeni et al. [27] and Peyman et al. [31]. In addition, the results indicated that the adoption of smoking preventive behaviors among the students was significantly correlated only with perceived susceptibility and perceived self-efficacy. These findings are also consistent with the findings of the study of Boroujeni et al. [27]. Thus, it can be concluded that any intervention to increase perceived susceptibility and self-efficacy can also influence the adoption of smoking preventive behaviors.

There was also a significant but weak correlation between the adoption of smoking preventive behaviors and HL. These findings are in agreement with the findings of the studies by Peyman et al. [31], Panahi et al. [1, 13, 20, 32-35], Dehghankar et al. [36] and Arabzadeh et al. [30]. It can be added that although some of the studies have identified the association between HL and preventive behaviors [32], it is probably not possible to prove such a relationship for low levels of HL skills. Therefore, planning and designing communication interventions to improve these skills can lead to the establishment of the relationship between HL skills and the adoption of health behaviors.

Conclusion

Taken together, the results of this study suggest that the HBM integrated with HL can be used as an appropriate framework for designing educational programs to encourage students to adopt smoking preventive behaviors. However, among the constructs of the above model, perceived susceptibility, perceived self-efficacy, and the dimension of decision making and use of health information from the five dimensions of HL had the most impact on the adoption of smoking preventive behaviors and should be investigated further.

The present study was the first to evaluate the constructs of the HBM integrated with HL in predicting the adoption of smoking preventive behaviors. Given that this study was conducted only among undergraduate medical students and dormitory students, the findings of this study cannot be generalized to other age groups and students. Therefore, it is recommended that further studies be conducted on different populations and groups (in terms of age, education, and residence) using this model.

One limitation of the current study was the lack of studies on the integration of the HBM with the structures of different health education and health promotion models which limited the comparability of the findings and demonstrated the need for further studies in this area. The data were collected through self-reporting which was another limitation of this study.

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Conflict of interest statement

There is no conflict of interest.

Authors' contributions

Rahman Panahi, Nooshin Hosseini: implementation and collection of data, content collection, and writing the paper. Ali Ramezankhani: advisor, contributing to writing the paper. Mohamad Anbari, Mohiadin Amjadian: contributing to writing the paper. Leila Dehghankar: contributing to writing the paper. Shamsaddin Niknami: supervisor, corresponding author.

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ORIGINAL ARTICLE

Handwashing knowledge, attitudes, and practices in Ghana

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Key words

Handwashing Knowledge • Attitudes • Practices • Ghana • Handwashing facilities.

Summary

Introduction. Handwashing has been recognized as a convenient, effective, and cost-effective means of preventing communicable diseases. However, many people overlook the importance of handwashing when engaging in activities that require handwashing due to various factors. The objectives of this study were to assess the level of handwashing knowledge, attitudes, and practices and determine their relationships and how they are affected by sex, educational background, and age.

Methods. A cross-sectional survey was conducted among 636 respondents who received and completed an online questionnaire that was disseminated to the contacts of the researchers via WhatsApp, Email, LinkedIn, and Facebook. Respondents were presented with several statements to assess their handwashing knowledge, attitudes, and practices.

Results. Overall, 82.2% of respondents had good knowledge, 91%

had a positive attitude, and 48.4% adhered to good handwashing practices. Having a high school level of education ($OR = 0.193$, $p = 0.034$), ($OR = 0.145$, $p = 0.000$) and ($OR = 0.448$, $p = 0.049$) decreased the likelihood of having good knowledge, positive attitudes, and good practices than in persons with tertiary level education. Predictors of good handwashing practices were knowledge ($OR = 1.059$, $p = 0.37$) and attitude ($OR = 1.095$, $p = 0.000$). These results suggest that having a higher level of education could increase a person's knowledge and attitude, which in turn enhances the likelihood that the person would adhere to most handwashing and hand hygiene practices.

Conclusions. Enhancing people's handwashing practices requires positive attitudes and good knowledge about handwashing. These need to be complemented by enhanced access to handwashing facilities and innovative measures to enforce and encourage compliance.

Introduction

The World Health Organization (WHO) declared the novel coronavirus disease (COVID-19) outbreak as a public health emergency of international concern on 30 January 2020. By 4th May 2020, a total of 3,407,747 cases with 238,198 deaths had been confirmed in 215 countries, areas, or territories [1]. The WHO then issued some precautionary measures to the public to protect themselves and others from the spread of COVID-19. The measures include regular and thorough hand cleaning with an alcohol-based hand rub or washing them with soap and water and covering the mouth and nose with bent elbow or tissue when coughing or sneezing.

Elaborating on the appropriate hand hygiene protocol, UNICEF (Ghana) published on its website an article titled "Everything you need to know about washing your hands to protect against coronavirus [2]. The article highlighted, among others, (a) how to wash the hands properly, (b) when hands should be washed, (c) how to help children wash their hands, (d) types of water required for washing hands, (e) whether and how washed hands should be dried, (f) whether washing hands is more effective than using hand sanitizer, and (g) what to do in the absence of soap.

Ghana had its first two confirmed cases of COVID-19 on 12th March 2020 and by 5th May 2020, the cases had increased to 2,719 with 294 recoveries and 18 deaths. In the statement announcing the two cases on 12th March, the Minister for Health entreated all Ghanaians to observe the precautionary measures, which include regular and thorough washing of hands with soap under running water and the use of alcohol-based hand sanitizers [3]. By 14th March, Ghana had recorded a total of six cases and on 15th March, the President of Ghana gave his first national address on the pandemic [4]. Among others, the President banned all public gatherings and instructed establishments such as offices, supermarkets, shopping malls, restaurants, nightclubs, hotels, and drinking spots to observe enhanced hygiene procedures by providing hand sanitizers, running water, and soap for washing of hands. Furthermore, he asked the Ministry of Transport to work with private and public transport operators to ensure enhanced hygienic conditions in all vehicles and terminals, by providing hand sanitizers, running water, and soap to wash hands. The Ministry of Local Government and Rural Development was also tasked to coordinate with the Metropolitan, Municipal, and District Assemblies to enhance hygiene conditions in markets across the country.

As a result of the President's directives, many

organizations started providing hand hygiene facilities at work and in public places. There was even an apparent shortage of alcohol-based sanitizers on the market. For that reason, on 16th March 2020, the President met with leaders of Ghana's pharmaceutical industries to discuss the local production of materials, including sanitizers, and liquid soaps as part of the COVID-19 response in Ghana. Accordingly, the Food and Drugs Authority fast-tracked the registration of hand sanitizers, and by 10th April 2020, it had approved 327 hand sanitizers for the COVID-19 fight [5]. There was heightened production, purchase, and display of handwashing facilities such as Veronica buckets and hand cleaning products at public spaces, workplaces, and similar locations.

Handwashing has been a convenient, effective, and cost-effective means of preventing communicable diseases in developing countries. Many infections start when hands are contaminated with disease causing-organisms, and this can happen after using the toilet, coughing or blowing the nose, handling garbage, and touching other contaminated surfaces [6]. Most diseases such diarrhea and pneumonia, which are transmitted mainly by contaminated hands can be prevented by handwashing with soap [7]. However, many people overlook the importance of handwashing when engaging in activities that require the washing of hands. For example, less than 40% of zoo visitors are reported to wash their hands upon exiting animal contact areas [8]. A study in 54 countries in 2015 found that, on average, 38.7% of households practiced handwashing with soap [9].

Factors such as hygiene education, adequate organizational factors including the availability of handwashing materials, and strong examples from influential persons, could effectively increase adherence to hand hygiene practices and reduce the incidence of infections [10, 11]. In an observational study, it was reported that people who lived in urban districts, with high educational levels and sufficient knowledge on infectious diseases have a high handwashing compliance rate [12]. In addition, women are more likely to wash their hands than men after controlling for washroom characteristics and clustering effects associated with social norms [13]. Several studies have examined attitudes and perceptions toward hand hygiene and found, for example, that most healthcare workers held positive attitudes and perceptions [14-16].

In contrast, few studies have focused on people's knowledge, attitudes, perceptions, and practices toward hand hygiene during a pandemic. A few studies were undertaken to identify the factors that most effectively motivated people to adopt certain protective measures, including hand hygiene during the H1N1 epidemic

and SARS pandemic, mainly in Hong Kong, China, Singapore, and South Korea [17-20]. A post-Ebola virus disease epidemic study in Nigeria showed that a higher proportion of respondents had a good knowledge of the risk factors of the disease but had a poor practice of hand hygiene for infection control [21].

This current study assessed the handwashing knowledge, attitudes, and practices of the public (i.e., people 15 years or older living in Ghana) during the COVID-19 pandemic. The objectives were to determine if handwashing knowledge, attitude, and practices differ by sex, educational background, and age, and assess the level of handwashing knowledge, attitudes and practices, and the relationships among them. This study provides insights into the level of knowledge and attitudes Ghanaians have about hand hygiene, especially handwashing, and identifies the knowledge gaps as well as issues that must be addressed to always enhance hand hygiene practices including during pandemics and epidemics.

Methodology

A quantitative method was employed. The study was conducted between July and October 2020 when the Ghana Health Service was urging everyone to adhere to the COVID-19 preventive protocols. Handwashing knowledge was assessed by providing a set of questions and statements with corresponding options for the study participants to choose correct answers (Tab. II). Handwashing attitudes were assessed by providing statements for the respondents to indicate whether they agreed with them or not (Tab. III). Handwashing practices were assessed by providing a list of the prescribed hand hygiene practices (as publicized at the onset of the COVID-19 pandemic) to the participants to indicate whether they adhere to the practices or not (Tab. IV).

Because of the restrictions on movements due to the COVID-19 pandemic, the data was collected using an online link to the questionnaire linked to the KoBo Toolbox. The online survey link was shared with the contacts of the researchers via WhatsApp, Email, and LinkedIn. The researchers appealed to all the contacts who had received the online link to also share with their contacts. The study was approved by the Council for Scientific and Industrial Research Institutional Review Board with approval no: RPN 004/CSIR-IRB/2020. An introductory statement was included in the survey that informed participants about the purpose of the survey, assured them of the confidentiality of the data, and gave them the option to opt out if they felt uncomfortable.

Tab. I. Regional distribution of respondents.

| Region | No. | Region | No. | Region | No. | Region | No. |
|-----------|-----|---------------|-----|------------|-----|---------------|-----|
| Ahafo | 4 | Central | 27 | Northern | 11 | Upper West | 4 |
| Ashanti | 39 | Eastern | 24 | Oti | 28 | Volta | 125 |
| Bono | 2 | Greater Accra | 305 | Savannah | 6 | Western | 7 |
| Bono East | 6 | North East | 1 | Upper East | 5 | Western North | 1 |

Tab. II. Statements and responses on handwashing knowledge.

| Handwashing knowledge statements | Authors' Marking scheme | % of respondents who gave correct responses | % of respondents who gave wrong responses |
|---|--|---|---|
| MATERIALS USED FOR HANDWASHING | | | |
| Water is a material used for handwashing | Yes | 94.0 | 6.0 |
| Soap is a material used for handwashing | yes | 93.9 | 6.1 |
| Antiseptics are materials used for handwashing | No | 84.9 | 15.1 |
| An alcohol-based sanitizer is a material used for handwashing | No | 51.1 | 48.9 |
| Level of knowledge on materials used for handwashing | Good knowledge = 82.2%; Fair knowledge = 17.0%; Poor knowledge = 0.8% | | |
| BENEFITS OF HANDWASHING | | | |
| Handwashing is a part of personal hygiene | Yes | 96.9 | 3.1 |
| Handwashing prevents diseases | Yes | 93.9 | 6.1 |
| Prevents mosquito bites | No | 96.7 | 3.3 |
| Handwashing Protects children against ill-health | Yes | 75.9 | 24.1 |
| Handwashing Limits spread of infections | Yes | 93.4 | 6.6 |
| Level of knowledge on benefits of handwashing | Good knowledge = 90.4%; Fair knowledge = 8.0%; Poor knowledge = 1.6% | | |
| DISEASES PREVENTABLE BY HANDWASHING | | | |
| Cholera is preventable by handwashing | Yes | 93.1 | 6.9 |
| Malaria is preventable by handwashing | No | 97.0 | 3.0 |
| Hypertension (a No is correct) | No | 97.2 | 2.8 |
| COVID-19 is preventable by handwashing | Yes | 98.4 | 1.6 |
| Common cold, Catarrh is preventable by handwashing | Yes | 40.1 | 59.9 |
| Typhoid is preventable by handwashing | Yes | 52.8 | 47.2 |
| Diarrhea is preventable by handwashing | Yes | 77.4 | 22.6 |
| Level of knowledge on diseases preventable by handwashing | Good knowledge = 87.3%; Fair knowledge = 11.6%; Poor knowledge = 1.1% | | |
| KNOWLEDGE ABOUT HANDWASHING DAY | | | |
| 15 th October is Global Handwashing Day | Yes | 24.3 | 75.7 |
| Level of knowledge on Global Handwashing Day | Good knowledge = 14.8%; Fair knowledge = 47.0%; Poor knowledge = 38.2% | | |
| The Overall level of Knowledge about handwashing | Good knowledge = 84.1%; Fair knowledge = 14.5%; Poor Knowledge = 1.4% | | |

DATA ANALYSIS

A total of 679 respondents completed the survey, of which 645 were from Ghana and 34 were from other countries. However, of the respondents in Ghana, nine (9) did not complete the questionnaire; hence those cases were discarded in addition to the cases by respondents outside Ghana. The analysis presented here is thus based on 636 respondents who were residents in Ghana at the time of the survey.

ASSESSMENT OF KNOWLEDGE ABOUT HANDWASHING

The questions were categorized into (1) materials used for handwashing, (2) benefits of handwashing, (3) diseases preventable by handwashing, and (4) knowledge about the Global Handwashing Day. A correct response attracted 1 point, while a wrong response attracted 0 points. The total correct points were calculated in terms

of absolute numbers and percentages. A criterion was developed to determine the level of knowledge: a score of 70-100% = Good knowledge; a score of 50-69% = Fair knowledge; and a score of 0-49% = Poor knowledge.

ASSESSMENT OF ATTITUDE ABOUT HANDWASHING

An agreed response implied a negative attitude while a disagreed response indicated a positive attitude. An agreed response attracted -1, while a disagreed response attracted +1 point. The total point for attitude was calculated by adding the positive and negative points. A negative total implies a negative attitude, and a positive total suggests positive attitude.

ASSESSMENT OF HANDWASHING PRACTICE

Any handwashing practice adhered to attracted 1

Tab. III. Respondents' attitudes to handwashing.

| Statements | Disagree (positive attitude) % | Agree (negative attitude) % |
|---|--------------------------------------|-----------------------------------|
| You will NOT wash your hands after using the toilet if you feel your hands are clean | 82.5 | 17.5 |
| You will NOT wash your hands after using the toilet if you are in a hurry and have no time to wash your hands | 83.8 | 16.2 |
| You will NOT wash your hands after using the toilet if you feel handwashing is cumbersome | 85.1 | 14.9 |
| You will NOT wash your hands after using the toilet if there is not enough water | 76.9 | 23.1 |
| You will NOT wash your hands after using the toilet if there is no soap | 75.2 | 24.8 |
| You will NOT wash your hands after using the toilet if the water is too cold | 87.1 | 12.9 |
| You will NOT wash your hands after using the toilet if handwashing is not your habit | 78.5 | 21.5 |
| You will NOT wash your hands after using the toilet if there is no paper or cloth napkin or hand dryer | 87.4 | 12.6 |
| You will NOT wash your hands after using the toilet if you feel the water is not clean | 49.1 | 50.9 |
| Do you think handwashing is important? | 97.5 | 2.5 |
| Would you feel guilty if you did not wash your hands before eating? | 94.0 | 6.0 |
| The overall level of attitude | 91.0 | 9.0 |

Tab. IV. Respondents' handwashing and hand hygiene practices.

| Practice | % of respondents practicing |
|--|---|
| Using hand sanitizer | 65.4 |
| Using hand wipes | 64.0 |
| Keeping hand sanitizer in your bag/pocket when out of home | 74.8 |
| Washing your hands after blowing your nose | 74.4 |
| Washing your hands after visiting a public place, e.g. markets, church, or mosque | 66.5 |
| Washing your hands after touching surfaces outside of the home, e.g. money, Automated Teller Machine | 78.9 |
| Washing your hands before eating | 50.6 |
| Washing your hands when you return home from work/town | 61.5 |
| Washing your hands after using the toilet | 50.8 |
| Washing your hands when your hands are visibly dirty | 50.3 |
| Washing your hands after shaking hands | 72.3 |
| Washing your hands before entering your office or workplace | 81.0 |
| Washing your hands before entering a supermarket | 84.7 |
| The overall level of practice | Good practice = 48.4% Fair practice = 19.8% Poor practice = 31.8% |

point while a practice not followed attracted 0 points. The points were summed up and the equivalent percentages calculated. A criterion was developed as follows to determine the level of practice: a score of 70-100% = Good practice; a score of 50-69% = Fair practice; and a score of 0-49% = Poor practice.

Initial data analysis included descriptive statistics and cross-tabulations (chi-square tests) where the influence of sex, age, and educational background on respondents' responses was examined. The cross-tabulation analysis on knowledge scores yielded some results where the expected cell counts were less than 5; hence the knowledge scale was dichotomized into 'good knowledge' and 'fair knowledge'. Also, correlations and crosstabulations were performed to assess the relation of handwashing knowledge and attitude with handwashing practices. Furthermore, in cases where chi-square tests were significant, logistic or multinomial regression was

used to determine the relationships. Finally, odds ratios (OR), p-values, and confidence intervals were reported for each level of the variables.

Results

The respondents were made up of 52.3% male and 43.7% female, with 58.5% being youthful (15-35 years) and 41.5% being older (36-80 years). About 77.3% had tertiary level of education while 15.7% and 6.9% had high school and basic school level education, respectively. The regional distribution of the respondents is shown in Table I as per the 16 regions of Ghana. The regional distribution of respondents appeared to have been influenced by the networks of the researchers. Table II shows the proportion of respondents who gave correct or wrong responses. A total of 82.2% of

Tab. V. Cross tabulations of educational level against handwashing knowledge, attitude and practices.

| Cross tabulations of educational level against handwashing knowledge, attitude and practices | | | | |
|--|---------------|---------------|----------------|-------|
| | Basic School | High School | Tertiary level | Total |
| Good knowledge | 4.7% | 10.1% | 69.3% | 84.1% |
| Fair Knowledge | 2.2% | 5.7% | 8.0% | 15.9% |
| Positive attitude | 6.3% | 11.5% | 73.4% | 91.2% |
| Negative attitude | 0.6% | 4.3% | 3.9% | 8.8% |
| Good practice | 3.6% | 3.8% | 41.0% | 48.4% |
| Fair practice | 1.1% | 6.9% | 11.8% | 19.8% |
| Poor practice | 2.2% | 5.0% | 24.5% | 31.8% |
| Cross tabulations of handwashing practices against knowledge and attitude | | | | |
| | Good practice | Fair practice | Poor practice | Total |
| Good knowledge | 42.8% | 14.6% | 26.7% | 84.1% |
| Fair Knowledge | 5.7% | 5.2% | 5.0% | 15.9% |
| Positive attitude | 46.3% | 17.2% | 27.7% | 91.2% |
| Negative attitude | 2.2% | 2.7% | 3.9% | 8.8% |

respondents had good knowledge of the materials that are used for handwashing. However, about 51% said alcohol-based sanitizers are among materials used for handwashing, probably because they were unclear about the difference between handwashing and hand sanitizing, which does not involve the use of water. Also, 90.4% of respondents had good knowledge about the benefits of handwashing but 24.1% did not know that handwashing could protect children against ill-health. Furthermore, 87.3% had good knowledge about diseases that could be prevented by handwashing but 59.9% and 47.2% of respondents did not know that common cold and typhoid, respectively were preventable by handwashing. Only 387 out of 636 respondents were aware of the existence of the Global Handwashing Day (GHWD) and just 24% of the 387 knew the date on which the GHWD is commemorated. Overall, 90.4% of respondents had good handwashing knowledge, 8% had fair knowledge, and 1.6% had poor knowledge.

On handwashing attitudes, overall, 91% of respondents had a positive attitude towards handwashing, with 75-98% showing a positive attitude for each statement except the statement “You will not wash your hands after using the toilet if you feel the water is not clean” where 50.9% portrayed a negative attitude (Tab. III). Also, 21-25% of the participants showed a negative attitude by agreeing that they would not wash their hands after using the toilet (a) if there is not enough water (23.1%), (b) if there is no soap (24.8%), and (c) if handwashing is not their habit (21.5%).

In terms of handwashing practices, Table IV shows that overall, less than 50% of respondents undertake most of the prescribed handwashing practices. About 32% of respondents exhibited poor handwashing practices as they did not adhere to most of the prescribed practices. The practices that most respondents adhered to were ‘washing their hands before entering an office or workplace’ (81.0%), ‘washing their hands before entering a supermarket’ (84.7%), and ‘washing hands after touching surfaces outside of the home’ (78.9%).

Cross-tabulation of the level of handwashing knowledge

with sex, age, and level of education yielded a significant Pearson chi-square statistic only for the level of education (Tab. V). Also, a Chi-square test was performed for handwashing practices against knowledge and attitude and the results were statistically significant (Tab. V). Hence logistic regression analysis was performed to assess how educational background influences handwashing knowledge, attitude, and practices as well as how handwashing knowledge and attitude influence practices (Tab. VI).

The logistic model (Tab. VI) showed that having a basic level of education ($OR = .136$, $p = .024$) and high school level of education ($OR = 0.193$, $p = 0.034$.) decreased the likelihood of having good knowledge about handwashing by 0.136 and 0.193 times, respectively than in persons with tertiary level education. The results suggest a statistical association between level of education and level of knowledge about handwashing, however, basic and high school levels of education is not significant in predicting fair level knowledge. Results also showed that having a high school level of education ($OR = 0.145$, $p = 0.000$) decreased the odds of showing a positive attitude towards handwashing by 0.145 times than in people with tertiary level education. This suggests a statistical association between level of education and having a positive rather than negative handwashing attitude, however, this is not statistically significant in persons having a basic level of education. Similarly, persons having a high school level of education ($OR = 0.448$, $p = 0.049$) were 0.448 times less likely to exhibit good handwashing practices than in persons with a tertiary level of education after controlling for the other factors in the model. Furthermore, a person with a high school level of education ($OR = 2.860$, $p = 0.000$) is 2.860 times more likely to exhibit fair handwashing practices compared to poor handwashing practices than in persons with a tertiary level of education after controlling for the other factors in the model. These results suggest that having a higher level of education could enhance one’s handwashing attitude and practices compared to a lower level of education.

Tab. VI. Logistic regression for the influence of educational background on handwashing knowledge, attitude, and practices, and the influence of handwashing knowledge and attitude on handwashing practices.

| | | Sig. (p-value) | Odds ratio | 95% C.I. for EXP(B) | |
|---|-----------------|-------------------|------------|---------------------|-------|
| | | | | Lower | Upper |
| Influence of educational background on handwashing knowledge, attitude and practices. (Reference categories: Poor knowledge, Negative attitude, Poor practice, Tertiary education) | | | | | |
| Good knowledge | Basic School | 0.024 | 0.136* | 0.024 | 0.773 |
| | High School | 0.034 | 0.193* | 0.042 | 0.884 |
| Fair Knowledge | Basic School | 0.467 | 0.511 | 0.083 | 3.126 |
| | High School | 0.934 | 0.936 | 0.196 | 4.463 |
| Positive attitude | Basic School | 0.269 | 0.536 | 0.178 | 1.618 |
| | High School | 0.000 | 0.145* | 0.080 | 0.264 |
| Good practice | Basic School | 0.959 | 0.982 | 0.491 | 1.964 |
| | High School | 0.049 | 0.448* | 0.255 | 0.789 |
| Fair practice | Basic School | 0.935 | 1.040 | 0.403 | 2.684 |
| | High School | 0.000 | 2.860* | 1.680 | 4.869 |
| Influence of handwashing knowledge and attitude on level of handwashing practices (Reference categories: Poor practice) | | | | | |
| Good Practice | Knowledge score | 0.037 | 1.059* | 1.004 | 1.119 |
| | Attitude score | 0.000 | 1.095* | 1.043 | 1.149 |
| Fair Practice | Knowledge score | 0.570 | 0.983 | 0.928 | 1.042 |
| | Attitude score | 0.004 | 0.931* | 0.886 | 0.977 |

* Significant Odds ratio at $p < .05$

In terms of the influence of knowledge and attitude on handwashing practices, firstly, correlations analysis showed that handwashing knowledge ($r = 0.154$, $p < 0.001$) and handwashing attitude ($r = 0.197$, $p < 0.001$) had significant positive associations with handwashing practices. In contrast, the knowledge score ($r = 0.394$, $p < 0.001$) had a positive association with the attitude score. These suggest that people would adhere to most handwashing practices if they had a positive attitude toward handwashing and have good knowledge about handwashing. Secondly, the logistic regression model showed that increasing the knowledge score ($OR = 1.059$, $p = 0.37$) by 1 unit increased the likelihood of having good handwashing practices compared to poor practices by 1.059 times after controlling for the other factors in the model. This result showed a statistical association between a person's handwashing knowledge score and the level of handwashing practices exhibited; however, the association is not significant in terms of predicting a fair level of handwashing practice. Results also showed that if a person increases his/her handwashing attitude score ($OR = 1.095$, $p = 0.000$) by 1 unit the odds of exhibiting good practices compared to poor practices would be expected to increase by 1.095 units while holding all other variables in the model constant. Similarly, the odds for exhibiting fair handwashing practices compared to poor practices would be expected to decrease by 0.931 units if a person's attitude score ($OR = .931$, $p = 0.004$) increased by a unit. These suggest that the more positive one's attitude is towards handwashing, the greater the likelihood that the person would adhere to most handwashing and hand hygiene practices.

Discussion

This study assessed whether handwashing knowledge, attitude and practices differ by sex, educational background and age or not and determined the level of handwashing knowledge, attitude and practices and their relationships. Although 82.2% of respondents had good knowledge of the materials used for handwashing, about half of the respondents indicated that alcohol-based sanitisers were among materials used for handwashing. This indicates that some people did not know the distinction between handwashing, which entails washing hands with non-antimicrobial or antimicrobial soap and water, and other means of ensuring hand hygiene. It is important for hygiene educators and promoters to emphasise the difference and note which hand hygiene methods should be promoted under specific conditions. For example, in poor communities where access to hand sanitizers may be a challenge, it is critical to promote handwashing with water and soap that may be easily accessible. Although sanitizers are used to maintain hand hygiene, it is important to emphasize that it is not the same as handwashing. Similarly, antiseptics are not used for handwashing, but antiseptic agents may be contained in antimicrobial soaps that are used for handwashing [22]. In this case, it is important for public health educators to distinguish between antiseptic hand-wash, which entails washing hands with water and soap or other detergents containing an antiseptic agent, and an antiseptic hand rub which involves applying a waterless antiseptic agent to all surfaces of the hands to reduce the number of microorganisms present [22].

Handwashing provides several benefits that could contribute to changing people's attitudes and behaviors towards handwashing. Most respondents in this study had good knowledge about the benefits of handwashing,

however about one-third did not know that handwashing could protect children against ill-health. Good knowledge about this handwashing benefit is very critical because of the vulnerability and susceptibility of children to microbial infections. According to the WHO diarrhoeal disease, which is a symptom of infections caused by a host of bacterial, viral, and parasitic organisms, most of which are spread by feces-contaminated water, is the second leading cause of death in children under five years old, killing around 525,000 children each year [23]. Therefore, the importance of handwashing for the prevention of infectious disease especially, in children, has been established and is advocated for [24-27]. It is estimated that about one-third of infections are preventable by practicing correct handwashing [28]. Regarding the specific diseases preventable by handwashing, the overall knowledge level is good in 87.3% of respondents. This is not different from a study by Suen et al. [29], who found that majority of their respondents could differentiate between the diseases that could or could not be transmitted through poor hand hygiene. Notwithstanding the overall good knowledge, the findings showed that about 60% of respondents did not know that the common cold could be prevented by handwashing, while 47% did not know the power of handwashing in preventing typhoid infection. These findings suggest that more education is needed on the various health benefits of handwashing, especially for endemic infectious diseases. In Ghana, typhoid fever was ranked among the top twenty causes of outpatient morbidity and accounted for 1.2%, 1.7%, and 1.3% of hospital admissions in 2017, 2016, and 2015, respectively. The transmission of typhoid fever occurs through the fecal-oral route; hence hygienic procedures such as handwashing are important for preventing and controlling the infection [30]. A study in Jakarta, Indonesia, where typhoid is endemic, found that households that do not use soap for handwashing are at a significantly higher risk of contracting typhoid [31]. Handwashing with soap could prevent respiratory infections by 16-21%, reduce pneumonia by 25%, and protect about 1 of 5 young children with respiratory infections [32-34]. The low-level knowledge with respect to specific illnesses calls for the need for more education on the various health benefits of handwashing as well as common diseases it could help prevent. Overall, the majority (91.2%) of the respondents had a positive attitude towards handwashing, with over 70% showing a positive attitude for each statement except for three. The highest proportion of respondents (97.5%) showed a positive attitude towards the statement 'handwashing is important aligning with a study where 89.8% agreed to this statement [35]. For the statement "You will not wash your hands after using the toilet if you feel the water is not clean", about half of the respondents portrayed a negative attitude which calls to question the kind of water that can be used for handwashing. This is critical, especially in communities where water may be prone to contamination. However, it is critical to emphasize that water for handwashing

does not have to be as clean as drinking water because research has found that washing hands with soap and even very contaminated water from the municipal water supply still delivered health benefits including diarrhea reduction [36]. Also, about 21-25% of the respondents showed a negative attitude by agreeing that they would not wash their hands after using the toilet (a) if there is not enough water (23.1%); (b) if there is no soap (24.8%), and (c) if handwashing is not their habit (21.5%). Although handwashing with soap is substantially more effective at removing dirt and germs from hands, the use of water alone does help reduce the risk of diarrhea [37]. Thus, it is preferable to wash hands with only water to not wash at all because of the absence of soap. In hygiene education, where there is no water, it is important to emphasize other hand hygiene practices such as the use of hand sanitizers. The findings bring to the fore the importance of ensuring the provision, availability, and access to handwashing materials or hand hygiene materials. Handwashing is a repetitive action that may lead to the formation of a habit, and habits can influence behaviour [38]. However, about 78.5% of respondents were of the view that even if they had not developed the habit of handwashing, they would wash their hands after using the toilet. This positive attitude could be the result of their understanding of the benefits of handwashing. Handwashing practices are the actual activities that will lead to disease prevention. Hence, it was quite unsatisfactory that overall, less than 50% of respondents undertook most of the COVID-19 prescribed handwashing and hygiene practices while one-third of respondents exhibited poor hand washing practices. Similar findings were reported by Fielmua et al. [39] and UNICEF [33], where only 20% of the Ghanaians population were found to wash their hands with soap while awareness about the importance of the practice remains low, with a handwashing growth rate of 8% over the period 2014-2017 [33]. Similar findings were reported by Rabbi and Dey [40], where 90% of their respondents had knowledge about the importance of handwashing before eating, but only 21% did so. The practices that most respondents adhered to were 'washing hands before entering an office' (81.0%), 'washing hands before entering a supermarket' (84.7%), and 'washing hands after touching surfaces outside of the home' (78.9%). These results could be attributed to the COVID-19-related directives by the Ghana government, where handwashing and hand hygiene facilities were supposed to be provided at public spaces, including offices, supermarkets, churches, and bus stations. These facilities were not only provided, but there were also persons stationed near the facilities to enforce compliance by people visiting these public spaces. The provision of these facilities in shops and other public spaces has also been reported in a study conducted in Northern Ghana [39]. However, contrary to our findings, they found that adherence to COVID-19 safety protocols at shopping centres was very poor, with about 91.3% of the customers not practicing handwashing before entering the shops although handwashing facilities

were provided. They also report that non-adherence to COVID-19 protocols was higher in shops where there was no pressure to conform to the protocols.

Gender and age of respondents had no significant influence on the level of handwashing knowledge, attitude and practices. However, the educational level of respondents was found to significantly influence the level of handwashing knowledge, such that the higher the educational level the better the knowledge in issues related to handwashing. Similar findings were reported by Suen et al. [29], in which having a tertiary education level improved handwashing knowledge. On the contrary, they found that gender and age influence handwashing knowledge, whereas being female and middle-aged significantly enhanced handwashing knowledge. Our findings also differ from Fielmua et al. [39], who found that youth and children had a poor attitude towards the COVID-19 protocol practices including, handwashing, compared to adults. In Ghana, before the COVID-19 pandemic, messages on handwashing were rarely shared with the public; hence most people who knew might have read about it themselves or were taught during their formal education. In Ghana, where the illiteracy rate among persons 15 years and older is 21% World Bank [41], it will be useful to integrate handwashing messages in non-formal educational programs as well as during church and funeral programs, festivals and other social gatherings. It is also critical to incorporate handwashing lessons in all educational curricula starting from preschool through basic to tertiary levels.

The positive correlations found among handwashing knowledge, attitude, and practices suggest that people would adhere to most handwashing practices if they had a positive attitude towards handwashing and had good knowledge about handwashing procedures and benefits. This was confirmed in the logistics regression analyses where there were statistical associations between a person's handwashing knowledge score, positive attitude, and handwashing practices. Thus, a higher handwashing knowledge score and a positive attitude towards handwashing are likely to increase a person's adherence to the prescribed handwashing practices. Fielmua et al. [39] also found that attitude is critical to handwashing behavior and the fight against the COVID-19. These findings are in line with Garba and Uche [42], who found that level of knowledge and attitude toward proper handwashing practices were significantly associated with the adherence to the practice.

One major limitation of the study is that all the data are based on self-reports by the respondents, which the authors could not verify because the study was online based. In addition, regional influence on the results was not assessed because of their uneven representation, which reflects the sampling technique employed.

Conclusions

This study assessed the handwashing knowledge, attitudes, and practices of people living in Ghana during

the COVID-19 pandemic. Handwashing knowledge was found to be generally good among the respondents; however, in terms of the distinction between handwashing and hand sanitizing materials as well as the specific diseases that are preventable by handwashing, a lot more public education is required. It is also important to create more awareness about Global Handwashing Day and sensitize people on the importance and significance of the Day. Furthermore, handwashing knowledge, attitude, and practices were found to be statically associated with the educational background of respondents; hence it is important to take advantage of this and incorporate handwashing education in formal educational curricular as well as non-formal educational programs to address the needs of people who may not be literates.

Most respondents generally had a positive attitude to handwashing and were of the view that handwashing is important, especially after visiting the toilet. However, it is important for public health and hygiene educators to clearly explain what types of water could be used, whether soap should necessarily be used, and what to do when there is inadequate or no water and/or soap. Despite the general good knowledge and positive attitudes to handwashing, most respondents exhibited poor adherence to the prescribed handwashing and hand hygiene practices except in a situation where measures had been put in place to enforce compliance.

This study has revealed that enhancing people's handwashing practices requires positive attitudes towards handwashing as well as good knowledge about the appropriate materials used for handwashing and the health benefits of handwashing. These need to be complemented by enhanced access to handwashing facilities and innovative measures to enforce and encourage compliance with most hand hygiene practices, especially during pandemics such as COVID-19 and epidemics such as cholera and other endemic infectious diseases.

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Ethical approval

The study was approved by the Council for Scientific and Industrial Research Institutional Review Board with approval no: RPN 004/CSIR-IRB/2020.

Conflict of interest statement

The authors declare no potential conflicts of interest.

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Authors' contributions

RO and FZ designed the study. RO, SBT, FZ, WA participated in the data collection and analysis. RO drafted the manuscript. All authors read, revised, and approved the manuscript.

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ORIGINAL ARTICLE

Factors related to the voluntary interruption of pregnancy in Spain

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Key words

Voluntary interruptions of pregnancy • Abortion • Sexual and Reproductive Health • Socioeconomic factors • Spain

Summary

Introduction. *The voluntary interruption of pregnancy (VIP) is a complex process, influenced both by health and psychosocial factors, which in turn affect the health and well-being of the women. The objective of this study is to determine the factors related to the voluntary interruption of pregnancy in Spain, in women with more than one interruption, according to their origin.*

Methods. *A cross-sectional study of the VIP episodes carried out at the request of the women themselves in Spain during 2018. The factors related to repeat VIPs are described according to the origin of the women, estimating the crude and adjusted prevalence odds ratio (OR).*

Results. *The highest rates of VIP occurred in women aged 20 to 24 years. The probability of a second VIP, both in Spanish women and those of foreign origin, increased with age, with the size of the population (> 50,000 inhabitants), and with dependent children.*

Conclusions. *All women should have the possibility of planning their reproductive life, for which they have the right to have access to adequate information, to effective contraceptive methods, and to be able to interrupt an unplanned pregnancy with all the guarantees of quality, confidentiality and safety.*

Introduction

Voluntary Interruption of Pregnancy (VIP) is an important global public health issue, conditioned by diverse health and socio-demographic factors. Its incidence serves as a “proxy” for the frequency of unwanted pregnancies, which in turn, give an idea of the difficulties that exist regarding the functioning of family planning and primary care services, and women’s access to them, as well as the barriers to the access and use of contraceptives [1].

Forty-eight percent of all pregnancies that occur worldwide are unintended and, of these, 61% end in an abortion, which represents approximately 73 million abortions per year (39/1000 women aged 15 to 49 years), with higher rates occurring in low-income countries [2]. In Spain, abortion was decriminalized in certain cases in 1985 [3]; it was at that time that the official VIP Register was initiated by the Ministry of Health [4]. Currently, the law regulating VIPs in Spain is Organic Law 2/2010, of March 3, on sexual and reproductive health and the voluntary interruption of pregnancy, which “recognizes the right to freely decide maternity. Amongst other things, this means that women can make the initial decision about their pregnancy and that this conscious and responsible decision be respected”, allowing free access to VIP during the first 14 weeks of gestation and, if there is a serious risk to the life or health of the pregnant woman or the fetus, up until week 22 [5]. Outside of the essential legal requirements, abortion remains a crime in Spain as covered by the Penal Code [6].

Despite there being a slight increase in the number

of VIPs in the two years following the establishment of the 2010 Law, this trend gradually decreased over subsequent years. The steepest falls were among women in the younger age groups (under 24 years of age), although slight rises have been seen in almost all age groups over the past two years [7].

Various studies affirm that a high percentage of women who have undergone a VIP in Spain belong to the most vulnerable sections of the population [8]. Among the characteristics that have been most frequently related to VIP are age, over the passing of which more or less relevance may be given to socioeconomic variables such as the presence or not of a stable partner [9-13], migration [9-11, 14], and a poor educational level [9, 11]. Nevertheless, a higher rate of VIP has also been described in very young women with a higher educational level, or students who do not want motherhood to prevent them from completing their studies and improving their future opportunities [10, 12]. Something similar occurs with the employment situation – although VIP is generally related to women who are unemployed or facing precarious work situations [9, 13, 14], there have been cases described of women resorting to VIP so as not to lose job opportunities, either young people at the beginning of their professional careers or older women trying to consolidate positions that might be lost due to motherhood [12]. Age is also often interwoven into the reproductive life of women, who resort to abortion to postpone the onset of motherhood, or to avoid having more children they do not want [9-14]. Likewise, they resort to VIP when they cannot access contraceptive methods due to financial or administrative

problems; this is especially the case amongst immigrant women [10, 15].

Research on the characteristics and factors associated with the demand for more than one VIP (repeat VIP) is scarce, despite very high percentages of repeat VIPs having been described in different countries, even in adolescents [16-19], and hardly any data have been published on this in Spain, where repeat VIPs have been associated with immigrant women who have resided a long time in the country, and with situations of persistent social vulnerability [9].

The complexity of the elements affecting VIP and repeat VIP makes it necessary to continue studying and quantifying them so that it is possible to better understand the conditions under which they occur, to understand their implications on the safety and quality of care, and to minimize possible health problems for women, both physical and mental [20]. In order to draw up more effective sexual and reproductive health promotion strategies, we intend to improve knowledge about the factors related to the repeated voluntary interruption of pregnancy in Spain, according to the origin of the women.

Methods

This is a descriptive cross-sectional observational study on the episodes of Voluntary Interruptions of Pregnancy (VIPs) carried out in Spain during 2018. Of the 95,917 cases recorded that year (representing a rate of 11.12 per 1000 women), we have selected the 86,749 episodes (90.4%) in which the interventions were requested by the women themselves.

Our source of information is the computerized database on Voluntary Interruptions of Pregnancy (2018) of the Ministry of Health's General Sub-directorate for Health Promotion and Public Health Surveillance in Madrid. This agency compiles notifications on VIPs from the different Autonomous Communities collected via a joint questionnaire, which is automatically recorded and filtered through a Ministry of Health online application, ensuring the women's anonymity by omitting their personal identification data and those of the health centres where the VIPs are conducted.

The data collected by the specific questionnaire and analysed in our study comprise socio-demographic information on the pregnant women (date of birth, place of residence, country of birth, nationality, living arrangements, level of education, income, and employment status) and reproductive health information (living daughters or sons, previous VIPs, and use of contraceptives). To study the possible factors associated with the existence of a previous VIP, starting from the variable "Number of previous VIPs", we create the dichotomous variable "Previous VIP": yes, no.

STATISTICAL ANALYSIS

The variables are presented by their absolute and relative frequencies, except for the age variable, which

is presented with its mean and standard deviation. To analyse the relationship of the different variables to the women's origin, the chi-square test was used for the categorical variables and the Mann-Witney U test to compare the means of the "age" variable. The relationship of the different factors with the existence of a previous VIP was studied by calculating the crude prevalence odds ratios (ORs) and their 95% confidence intervals. Logistic regression models were fitted to estimate the possible factors independently associated with repeat VIP. All analyses were disaggregated by the women's origin variable. The analyses were carried out using the Stata statistical program (version 15.0).

Results

Of the 86,749 VIPs registered in Spain during 2018 that were requested voluntarily by the women themselves, 63.2% corresponded to women of Spanish origin.

Twelve percent of the VIPs occurred in Spanish women aged 19 and younger, five percentage points higher than in women of foreign origin of the same age, for whom the VIPs were more numerous in the older age groups. This is consistent with the higher percentages of Spanish women who say they are students (14.5%) and who live with their parents or relatives (28%). Among the Spanish women, the group attending university is almost double that of the women of foreign origin (17.2% compared to 9.7%). Thirty-six percent of foreign women and 38% of Spanish women do not have their own income. On the other hand, 43% of Spanish women and 55% of those of foreign origin have dependent children. Half of the foreign women and 38% of the Spanish women did not regularly use any type of contraceptive method.

Of the women who requested a VIP in 2018, 34% of Spanish women and 44% of those of foreign origin had previously had a VIP; 11.7% of Spanish women and 16.9% of foreign women had had more than one previous VIP (Tab. I).

In performing the multivariate analysis, when adjusting the factors associated with the existence of previous VIPs, it is observed that, in women of Spanish origin (Tab. II), the probability of having a second VIP increased with age up to the 30-39-year-old group (ORa = 2.97), decreasing a little in the older groups.

It also increased with the size of the population, being 33% higher in populations of more than 50,000 inhabitants (ORa = 1.33). The probability of a second VIP was 26% higher in unemployed women (ORa = 1.26) and double if they had dependent children (ORa = 2). Living with a family or partner decreased the probability of a second VIP. In foreign women (Tab. III), the probability of having a second VIP also increased with age, with an ORa of 3.25 in those aged 40 and over. It was also higher in populations with a greater number of inhabitants and almost double when they had dependent children (ORa = 1.82). However, in foreign women, living with a partner (ORa = 1.14) or family (ORa = 1.12) increased the probability of a second VIP. In both the Spanish

Tab. I. Socio-demographic, economic and sexual and reproductive health characteristics of women having a VIP at their own request in Spain during 2018 (n = 86,236).

| | Spanish origin | Foreign origin | P-value* |
|---|----------------|----------------|-----------|
| | No. (%) | No. (%) | |
| Total | 54,511 (63.2) | 31,725 (36.8) | |
| Median age (IQR) | 28 (22-34) | 29 (24-35) | < 0.001** |
| Age | | | < 0.001 |
| ≤ 19 yr | 6,660 (12.2) | 2,234 (7.0) | |
| 20-24 yr | 12,104 (22.2) | 6,917 (21.8) | |
| 25-29 yr | 12,019 (22.0) | 7,291 (23.0) | |
| 30-34 yr | 10,619 (19.5) | 7,209 (22.7) | |
| 35-39 yr | 8,824 (16.2) | 5,775 (18.2) | |
| ≥ 40 yr | 4,285 (7.9) | 2,299 (7.3) | |
| Place of residence by number of inhabitants | | | < 0.001 |
| ≤ 10,000 | 7,850 (14.4) | 2,605 (8.3) | |
| 10,001-50,000 | 14,874 (27.3) | 6,915 (21.9) | |
| 50,001-500,000 | 22,371 (41.1) | 12,442 (39.4) | |
| ≥ 500,001 | 9,391 (17.2) | 9,602 (30.4) | |
| Educational level | | | < 0.001 |
| Does not read/write | 454 (0.8) | 865 (2.8) | |
| Primary education | 8,776 (16.2) | 5,484 (17.5) | |
| Middle school | 20,709 (38.2) | 12,997 (41.4) | |
| Secondary school | 14,712 (27.2) | 8,719 (27.8) | |
| University education | 9,290 (17.2) | 3,048 (9.7) | |
| Others | 199 (0.4) | 250 (0.8) | |
| Employment situation | | | < 0.001 |
| Self-employed | 1,826 (3.4) | 1,284 (4.1) | |
| Employed | 29,926 (55.6) | 17,905 (57.6) | |
| Pensioner | 237 (0.4) | 38 (0.1) | |
| Student | 7,800 (14.5) | 2,342 (7.5) | |
| Unemployed / looking for first job | 11,207 (20.8) | 6,886 (22.2) | |
| Unpaid care work | 2,330 (4.3) | 2,232 (7.2) | |
| Others | 516 (1.0) | 415 (1.3) | |
| Cohabitation/Living Arrangements | | | < 0.001 |
| Alone | 13,034 (24.3) | 8,413 (27.2) | |
| With partner | 24,450 (45.5) | 15,988 (51.6) | |
| With parents / relatives | 15,058 (28.1) | 5,117 (16.5) | |
| Other situations | 1,148 (2.1) | 1,462 (4.7) | |
| Dependent children | | | < 0.001 |
| With dependent children | 21,649 (43.3) | 14,393 (54.6) | |
| No dependent children | 28,359 (56.7) | 11,972 (45.4) | |
| No. of previous VIPs | | | < 0.001 |
| 0 | 35,812 (65.7) | 17,661 (55.7) | |
| < 2 | 12,319 (22.6) | 8,695 (27.4) | |
| ≥ 2 | 6,380 (11.7) | 5,369 (16.9) | |
| Use of contraceptive methods | | | < 0.001 |
| Yes | 27,289 (61.9) | 11,338 (49.2) | |
| No | 16,827 (38.1) | 11,689 (50.8) | |

* p values for Chi-square test. ** p value for Mann-Whitney U test. IQR: Interquartile Range.

women and the foreign women, a higher education level was associated with a lower probability of having a second VIP.

Discussion

This study highlights some of the factors affecting

the decision of women who requested a voluntary interruption of pregnancy in Spain in 2018. Our results indicate that, regardless of their country of origin, women have certain factors in common related to their demographic, economic and reproductive situation that support their decision to abort, something that has already been described in other studies [11, 13].

Tab. II. Factors independently related to having a second VIP in Spanish women (Spain, 2018).

| | ORa (95% CI) | P-value |
|---|------------------|---------|
| Age | | |
| ≤ 19 yr | 1 | |
| 20-29 yr | 2.81 (2.57-3.07) | 0.000 |
| 30-39 yr | 2.97 (2.70-3.27) | 0.000 |
| ≥ 40 yr | 2.18 (1.93-2.45) | 0.000 |
| Place of residence by no. of inhabitants | | |
| ≤ 10,000 inhabitants | 1 | |
| 10,001-50,000 inhabitants | 1.15 (1.08-1.23) | 0.000 |
| ≥ 50,000 inhabitants | 1.33 (1.25-1.41) | 0.000 |
| Educational level | | |
| No education/Primary | 1 | |
| Secondary education | 0.75 (0.71-0.79) | 0.000 |
| Higher education | 0.38 (0.35-0.41) | 0.000 |
| Employment situation | | |
| Working | 1 | |
| Unemployed | 1.26 (1.20-1.32) | 0.000 |
| Student/pensioner | 0.61 (0.57-0.67) | 0.000 |
| Cohabitation/Living arrangements | | |
| Alone+others | 1 | |
| Partner | 0.88 (0.84-0.93) | 0.000 |
| Family | 0.93 (0.88-0.98) | 0.010 |
| Dependent children | | |
| No | 1 | |
| Yes | 2.00 (1.91-2.10) | 0.000 |

ORa: Adjusted Odds Ratio.

According to our data, of the women who requested a VIP in 2018 in Spain, 34% of Spanish women and 44% of those of foreign origin had had at least one previous VIP; these figures are above the 23% found in Aberdeen (UK) and 16% in Uruguay [21, 22], but are similar to those found in populations in China [16, 18], Glasgow (UK) [23] and France [24], and are below the 48 % described in New York, USA [25]. In general, while rates of VIP appear to be decreasing, rates of repeat VIP are increasing worldwide [19].

In Spain in 2018, the highest rates of VIP occurred in women aged 20 to 24 (18.6 per 1000 women), while the lowest rates of VIP were identified in the group aged 40 and over, followed by those under 20 years of age (9 per 1000 women). Age is one of the factors most frequently related to requesting a VIP, sometimes for wanting to delay motherhood, other times for not wanting to increase the number of children that they already have [9, 13]. In our study, the probability of having a repeat abortion increased with age among Spanish women up to the 30 to 39-years-old group, while in foreign women, the probability continued to increase up to the 40-and-over age group; this is in line with other studies that also attribute higher risk to older ages [26]. Some studies have stated that the probability of a second abortion is lower the older the women are at the time of their first VIP [17] – this is something that could be happening in more mature Spanish women, but not in those of

Tab. III. Factors independently related to having a second VIP in women of foreign origin (Spain, 2018).

| | ORa (95% CI) | P-value |
|---|------------------|---------|
| Age | | |
| ≤ 19 yr | 1 | |
| 20-29 yr | 2.40 (2.11-2.73) | 0.000 |
| 30-39 yr | 3.14 (2.74-3.60) | 0.000 |
| ≥ 40 yr | 3.25 (2.75-3.83) | 0.000 |
| Place of residence by no. of inhabitants | | |
| ≤ 10,000 inhabitants | 1 | |
| 10,001-50,000 inhabitants | 1.06 (0.96-1.18) | 0.250 |
| ≥ 50,000 inhabitants | 1.14 (1.04-1.26) | 0.006 |
| Educational level | | |
| No education/Primary | 1 | |
| Secondary education | 0.91 (0.85-0.97) | 0.006 |
| Higher education | 0.51 (0.46-0.56) | 0.000 |
| Employment situation | | |
| Working | 1 | |
| Unemployed | 0.96 (0.90-1.01) | 0.145 |
| Student/pensioner | 0.58 (0.51-0.65) | 0.000 |
| Cohabitation/Living Arrangements | | |
| Alone+others | 1 | |
| Partner | 1.14 (1.08-1.22) | 0.000 |
| Family | 1.12 (1.03-1.21) | 0.006 |
| Dependent children | | |
| No | 1 | |
| Yes | 1.82 (1.71-1.93) | 0.000 |

ORa: Adjusted Odds Ratio.

foreign origin, perhaps related to lower utilization of family planning services at these ages. Contrary to our results, many studies show a higher probability of repeat VIP in younger women [21, 24]. It is possible that older women, especially those of foreign origin, may not be having regular gynaecological check-ups nor receiving a prescription for contraceptives [21], and that they are using less effective methods or methods poorly adapted to their life circumstances [27, 28].

In both study groups, Spanish women and foreign women, the probability of a repeat VIP is higher when women live in larger municipalities, which may be related to better access to SRH (Sexual and Reproductive Health) and VIP resources, and may also be related to less social pressure in large cities than in small ones, since abortion is still a taboo subject and closely related to gender stereotypes, which means that women who resort to VIP are judged negatively and rejected socially, especially where there is greater religious or anti-abortion group pressure [20, 29]. The study by Liu et al. in China does not describe a relationship between a second VIP and the rural or urban area of residence, but with the region's level of development, so that the probability is greater the greater the development of the area [18].

In our study, a higher level of education has been associated with a decrease in the probability of having a second VIP in both groups of women, which coincides with the majority of studies that find more repeat

abortion in women with limited education [26, 16, 18], or where no relationship is found with the educational level [18, 23]. This might be due to the fact that people with a higher level of education are more likely to know about and apply preventive measures to avoid unwanted pregnancies [26].

Our data show a lower frequency of repeat VIP in female pensioners, while the probability of having more than one VIP is higher in unemployed Spanish women, which would correspond to a more depressed socioeconomic situation, something already described in other studies [16, 21]. In the women-of-foreign-origin group, the relationship between unemployment and repeat VIP does not appear, perhaps due to the weight of the possible structural inequality suffered by immigrants, with less access to education, health services and economic resources [26], and also less access to the world of work [16, 18]. In addition, our data show a lower probability of having a repeat VIP among female students, of any origin, which coincides with lower abortion repetition in younger women, something observed by other authors [16, 18], whereas Bajos et al. in France describe female students as one of the groups with the highest risk of repeat VIP, due to their difficulty in managing daily contraception [27].

The probability of requesting a second VIP is lower in Spanish women who live with a partner or with relatives; this coincides with other studies that find more repeat abortions in women who live alone [24]. However, our data show that, among foreign women, the probability of a second VIP is higher in those who live with the family or with a partner, in line with that published by other authors [24], reporting unstable relationships or problems with the partner, in which intimate partner violence is frequently mentioned [23-25]; this is something that should be systematically explored in the case of any woman requesting more than one VIP. It has also been described, worldwide, that the rate of VIP is higher in married women in almost all sub-regions, while in the developed world the rates in married women are lower [28].

Regardless of the woman's type of cohabitation, a factor strongly related to repeat VIP (in our study and in others) is the woman having dependent children [16-21]. This, together with socioeconomic aspects such as limited income or a precarious work situation, is generally a factor associated with the VIP request [30].

Among the reproductive characteristics, approximately half of the foreign women and almost 40% of the Spanish women did not regularly use any type of contraception. These data coincide with a study carried out in Denmark, where it was observed that the non-use of contraceptives was common, mainly among immigrant women [30], although there are studies that show that a significant percentage of women used them when they became pregnant, which may indicate that they are used incorrectly or the use of ineffective means [21, 23], highlighting the need to improve reproductive health advice, especially in women who have already had a VIP.

Conclusions

Although VIP is legal in Spain, women who require this service encounter numerous barriers in meeting this need, since only 14% of the interventions are carried out in National Health Service centres [7], the vast majority depending on the existence of private centres in their area. The fact of calling this act a voluntary interruption gives it a negative moral connotation which falls on the woman, who is perceived as requiring this service on a whim [31], with no attention paid to their life circumstances. Such moral judgement is felt most by women who resort to abortion on more than one occasion [22] and this becomes clear to all women when they have to confront anti-abortion groups protesting in front of the clinics, with no one preventing the protests [32, 33], thus increasing the stigma, feelings of helplessness, and psychological pain in the women [29].

All women, Spanish and foreign, should have the possibility of planning their reproductive life and decide if they want to have children, in what number and when, for which they have the right to access adequate information, to effective contraceptive methods and to be able to interrupt an unplanned (or desired) pregnancy via the public health service, with all the guarantees of quality, confidentiality and safety.

STUDY LIMITATIONS AND ADVANTAGES

The data used in our study are based on the information provided by the Ministry of Health's database on VIPs, preventing us from knowing other relevant factors related to VIPs that are not included in said database. On the other hand, as it is a cross-sectional study, it is not possible to establish the temporality of the factors studied or to estimate the risk of performing a VIP. However, as far as we know, this is the first study in Spain that attempts to explain the factors associated with repeat abortions; and although we cannot estimate risks due to the cross-sectional study design, our results are given greater internal validity having worked with all the national data on abortions taking place in 2018 that were requested by the women themselves.

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Conflict of interest statement

This paper presents independent results. The views expressed are those of the authors and not necessarily those of the Institute of Health Carlos III, the Ministry of

Health, or the University Hospital Complex of Cáceres. We declare no competing interests.

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Authors' contributions

SGS and MARA conceived and designed the experiments, performed the data collection and analysed the data; SGS and MCR wrote the paper.

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Evaluation of Breast Self-examination Training in Turkish Women Living in Northwestern Turkey

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Key words

Breast self-examination training • Turkish women • Knowledge • BSE skills

Summary

Introduction. Breast cancer (BC) is one of the most significant health problems among the women. Breast self-examination (BSE) is an examination method which is used by women to detect breast cancer as much early as possible. Training of women about BSE is crucial.

Methods. The current study was semi-experimentally single-group pretest-posttest designed in order to evaluate breast self-examination (BSE) training efficacy on Turkish women's knowledge and skills. The study was performed on 119 Turkish women. The data were collected with a three questionnaires and BSE Training Skills Evaluation Form in three phases.

Results. 81.5% of the women did not perform BSE regularly.

Rate of correct responses about knowledge on BC, risk factors and screening increased after posttest. Significant improvements were observed in the post-test (after training, after one month and three months training) scores for knowledge of Turkish women towards BC, risk factors and screening, steps of BSE after the intervention ($p < 0.001$). To quantify the efficiency of training, effect size (Cohen's d) was derived. For knowledge and ability to do BSE scores, Cohen's d was $1.01 \leq$ with large effect size indicating highly effective impact of the training.

Conclusions. It seems that BSE training is beneficial in women. However, women should receive regular BSE training to renew their knowledge and skills. Long follow-up is required.

Introduction

Breast cancer (BC) is the most frequent cancer among women and rate of death is increasing day by day [1, 2]. Furthermore, because of the increase in aging, 19.3 million new cases of cancer are estimated to occur in 2025 and more than half of cancer deaths are expected to be seen in less developed regions around the world. In Turkey, BC incidence has increased about two times in the last two years [3]. Increased BC incidence leads more health spending and high death rates. On the other hand, maintaining an effective cancer screening is one of the most important factors to assess the outcomes of diagnosis, and treatment. Due to this reason, BC should be controlled and prevented through early diagnosis and screening program [2, 3]. Mammography, clinical breast examination (CBE) and breast self-examination (BSE) are a crucial for early diagnosis of BC [2, 4].

Breast cancer screening increases quality of life and success of cancer treatment. Besides, it reduces social, economic, and psychological difficulties for the patients and their relatives. Additionally, early diagnosis provides cheaper and more effective treatment, reduces labor loss, and contributes to economic development of a country [5]. BSE, which is recommended to be performed every month, is an easy, cheap, safe, and effective non-invasive screening method for the BC and does not require special equipment. This screening method, which can be easily performed by every woman, may be effective if the women are willing to conduct BSE regularly [2]. Furthermore, performing

regular BSE improve breast awareness and encourage women to take more responsibility for their own health [6]. In a randomized controlled study conducted by Thomas et al. [7], it was found that mortality rates did not change in the 10-year follow-up of women who trained in BSE, however there was an increase in benign biopsy rates among women trained in BSE. Self-detection and rapid diagnosis of breast abnormalities is an important strategy for early diagnosis. Even though BC screening programs in Turkey are free and easily accessible, participation of Turkish women to these programs is relatively low since they do not have sufficient knowledge about breast cancer and consider themselves to be at low-risk group. Consequently, they consider BSE as unnecessary and do not regularly perform BSE [8-11]. Results of the previous studies had similar findings [6, 12-15]. These studies showed that low participation of women in breast cancer screening has still been a global problem around the world.

Success of BC screening program depends on the awareness of the target population. Training of women about BC and screening methods is crucial. Studies showed that lack of knowledge about BSE was the primary reason behind the reluctance of the women to perform BSE and that training on BSE could encourage them to perform BSE and contribute to health-seeking behaviors and cancer control [16-18]. During the BSE training, health professionals should provide information, encourage positive health behaviors, and change the existing incorrect behaviors to maintain the sustainability of women's health. These training programs should deal with the importance of early diagnosis and treatment in cancer control, demonstrate how to perform

BSE and underline the importance of regular BSE [15, 17-20]. The aim of this study was to evaluate the efficiency of the BSE training on Turkish women aged between 20 and 69 years.

Methods

A pre-experimental study with one group pre-and posttest design study was conducted with 119 women between March and June 2016.

PARTICIPANTS AND SETTINGS

A total of 228 women who aged 20 and 69 years were enrolled and regularly participated to sewing, knitting, marbling, wood painting and cake making courses of a municipal women training center located in Safranbolu-Karabuk in Northwestern Black Sea region of Turkey. Turkish Ministry of Health Breast Cancer Screening Program considers the women between 20 to 69 ages as eligible for BSE practice. Raousoft sample size calculator was used to calculate the sample size. With 90% reliability and 5%, the error margin sample size was calculated as 127 women. The sample comprised 119 women, who agreed to take part in the study and participated to all the three sessions of the BSE training.

MEASUREMENTS

The data were obtained using the three questionnaires developed by researchers according to relevant literature [1, 2, 21, 22] and the Breast Self-Examination Training Skills Evaluation Form.

Personal Information Questionnaire (Q1)

This questionnaire included 13 items on age, profession, marital and education status, age at menarche and first pregnancy, parity, duration of breastfeeding, use of birth control pills, receiving postmenopausal hormone therapy and radiotherapy, smoking habits, regular performance of BSE and family history of breast cancer among first-and-second degree relatives.

The Women's Knowledge about Breast Cancer, Risk Factors and Screening Questionnaire (Q2)

This questionnaire was composed of 12 items, which asked the participants to self-evaluate their knowledge on BC and screening on a three-point scale (Yes, no, I don't know). In our study, Cronbach's alpha was 0.82.

Women's Knowledge on Performing Breast Self-Examination Questionnaire (Q3)

This survey was consisted of 11 items, which asked the respondents to self-evaluate their knowledge on BSE on a three-point scale (Yes, no, I don't know). In our study Cronbach's alpha was 0.85.

BSE Training Skills Evaluation Form (Q4)

This form was prepared by Taskin [23] and was published in the book, entitled "Birth and Women's Health Practice

Guide for Nurses and Midwives". The form listed the stages to be performed during BSE and was composed of 26 items. Researchers asked the women to perform BSE on their bodies or a mannequin and evaluated their practice by using this questionnaire. Each of the 26 items was scored one point and proper BSE practice was scored five points. Higher scores mean better practice of BSE, with the total score ranging from 1-31 [23].

DATA COLLECTION

The study was carried out in three phases: the first phase (pre-training phase) and the second phase (training phase) and the third phase (post-training phase).

First phase (pre-training)

One week before, Safranbolu Cultural Activities Center managers announced that training about BC, screening and BSE would be provided to all women who were attending courses at the center. On the day of the training, the researcher went to the center two hours before the training and completed the preparations for the meeting room. Later, women were gathered in the meeting room. To evaluate the pre-test and post-test, researcher wanted to write nickname from women.

Second phase (training phase)

Before the training began, the purpose of study was explained by the researcher. At the beginning of this phase, pink ribbons were given to women and explained pink ribbon as the symbol of breast cancer. Pink pencils were delivered to complete data forms. All questionnaires for pre-test were distributed before the training. Women completed the questionnaire in about 20 minutes. The training provided for women aimed to improve their knowledge about BC and screening and to promote their practical performance of BSE. In the training, a power point presentation was given by the researcher to women for improving their knowledge of BC and screening, which took 120 minutes. Specifically, a phase of the training program included BC and risk factors, symptoms, screening methods for the early detection of BC. Researcher emphasized the importance of BSE. Additionally, researcher showed the practice of BSE on the model and then were asked to practice BSE on their own bodies once. At the end of the training, brochures that were designed and illustrated BSE steps were handed out to the women.

Third phase (post-training)

After a 15-minute break, Q1, Q2 and Q3 were distributed again for evaluation of impact of the training. Women filled in their questionnaires again after one month and three months. Women's responses for the pre- and post-intervention questions were obtained via face-to-face interviews (after one month and after three months). The study continued for 12 weeks.

STATISTICAL ANALYSIS

Data was analyzed using Statistical Package for the Social Sciences (SPSS 20.0, IBM Corp.; Armonk, NY, USA).

Descriptive characteristics of the women and their level of knowledge were analyzed by percentage and frequency analysis. Multivariate variance analysis was used to analyze the relationships between training and knowledge of BC and screening, knowledge on steps of BSE and skills. Pearson's correlation analysis was used to analyze the relationship between knowledge of the women towards steps of BSE and their skills. The effect size of the significant difference in the measurements was calculated by Cohen's d effect size analysis [24]. Statistical significance level was taken as $p < 0.05$.

ETHICAL CONSIDERATION

Ethical approval for the study was obtained from the ethical review committee of Karabuk University (2015/08, protocol no: 33479383/35) and institutional permission was obtained from the administration of Safranbolu-Karabuk-Turkey Cultural Activities Center. Permission to use the BSE Training Skills Evaluation Questionnaire was received via e-mail from the Turkish author. The women were assured of anonymity and confidentiality, and they were informed that the completion of the questionnaire can be carried out in private and at the respondents' leisure. All data were stored in a secure, locked safe. The Turkish women were assured that their participation in the study was not obligatory. Also, they had the right to withdraw from the study at any time.

Findings

Some personal characteristics of the women have been presented in Table I. Mean age of the women was 37.4 ± 2.9 , 76.5% were married, 39.5% graduated from high school and 60.5% were housewives. Only, 18.5% of women performed BSE regularly.

Table II reports the knowledge of women on BC, risk factors and BCS before and after the training. In present study, women' correct response rate about knowledge on BC, risk factors and BCS increased after the training.

Table III indicates that the knowledge of women towards steps of BSE. As the table depicts, the rate of correct answers towards steps of BSE increased after the post test. Table IV shows the comparison of mean on knowledge BC, screening, steps of BSE and practical competency before

and after the training. There was a statistically significant increase on scores of knowledges towards BC, risk factors, screening, steps of BSE and practical competency before and after the training periods ($F = 8.968$, $p \leq 0.001$; $F = 38.113$, $p \leq 0.001$; $F = 117.000$, $p \leq 0.01$, respectively) with very large effect size (Cohen $d = 1.01 \leq$)

Table V reports the correlation between women' knowledge on steps of BSE and women' ability to do BSE after immediately, one month and three months. There was a positive correlation between knowledge on steps of BSE and BSE skills before and after the training ($p < 0.001$).

Discussion

BSE is an important screening method since it empowers women against BC, encourages them to take their own responsibility and improves their awareness on cancer [22]. In present study, it was found minority (18.5%) of the women performed BSE regularly. Previous studies reported the percentage of women's that regularly performed BSE ranged between 14 and 65% [10, 11, 25, 26]. All these studies and our study suggest that women are dismissing the importance of BSE in the early diagnosis of BC. On the other hand, the low percentage of women that performed BSE in our study was not desirable.

In the present study, it was determined that women's knowledge of breast cancer risk factors and screening was not at a satisfactory in pretest phase. Previous studies have reported that women's knowledge towards BC, risk factors and screening was low [11, 25-28]. Relatively lower rates of correct answers in these studies may be related with the fact that the participants different characteristics like age, education, occupation etc. On the other hand, these findings show insufficient knowledge of breast self-examination before training, thus there are needed to investigate the barriers and facilitators.

World Health Organization recommends women to perform BSE regularly as a part of the program to promote health [22]. Effectiveness of BSE among women depends on the development of programs to improve knowledge and awareness on and to encourage attitudes towards performing BSE. Training provided by health professionals may increase the awareness of women on breast cancer and may enable them to perform BSE on a regular basis [17, 28]. In our study, it was reported that women' correct response rate about knowledge on BC, risk factors and BCS increased after the training. For example, many women did not know about the possibility of BC risk factors such age, being overweight, family history, diet, breast feeding, never given birth, hormone therapy, menstrual history) before training. Correct rate highly increased after training (above 95%). Previous studies indicated that BC, risk factors and early detection stated more given correct answers in the post training test compared to the pretraining period. For example, In Turkey, Yılmaz et al. [29] stated that knowledge scores of women were increased significantly from the pretest to the post test after four weeks, Ozerdogan et al. [30] reported after three weeks training, similarly Bayık Temel et al. [31] showed after six months training.

Tab. I. Descriptive characteristics of Turkish women (n = 119).

| Variables | | n (%) |
|----------------------------------|---------------|-----------|
| Mean of age 37.4 ± 2.9 | | |
| Marital status | Married | 91 (76.5) |
| | Single | 28 (23.5) |
| Education | Primary | 44 (37.0) |
| | High school | 47 (39.5) |
| | University | 28 (23.5) |
| Profession | Housewife | 72 (60.5) |
| | Civil servant | 10 (8.4) |
| | Employee | 37 (31.1) |
| Performs BSE regularly (Monthly) | Yes | 22 (18.5) |

Tab. II. Knowledge of women on BC, risk factors and BCS before and after the training (n = 119).

| Answers given related with BC, risk factors and screening | Correct response in pre-test n (%) | Correct response in post-test n (%) |
|---|------------------------------------|-------------------------------------|
| Breast cancer is the most common cancer among women | 117 (98.3) | 119 (100.0) |
| Being overweight, family history, personal history of BC increases the risk of BC | 21 (17.6) | 108 (90.8) |
| No history of breastfeeding, never given birth increase the risk of BC | 7 (5.9) | 114 (95.8) |
| Receiving postmenopausal hormone therapy, menstrual history increases the risk of BC | 14 (11.8) | 117 (98.3) |
| Diets with red meat and animal fat, lack of exercise increase the risk of BC | 19 (16.0) | 117 (98.3) |
| Change in size, shape, or direction of nipples may an indicator of BC | 37 (31.1) | 108 (90.8) |
| If there is a lump or mass in the breast, sore in nipples, nipple retraction, appearance like an orange peel, or a lump or swelling in the underarm area, a woman should visit a hospital | 77 (64.7) | 119 (100.0) |
| Mammography, clinical breast examination (CBE), and breast self-examination (BSE) is very crucial of BC early diagnosis. | 34 (28.6) | 119 (100.0) |
| BSE should be practices every month after the age 20. | 28 (23.5) | 119 (100.0) |
| BSE should be performed monthly | 22 (18.5) | 119 (100.0) |
| CBE should be practiced by a doctor once in 2-3 years in women aged between 20-40 and every year in women older than 40 years. | 27 (22.7) | 110 (92.4) |
| Women who do not have a risk factor for BC should start mammography at the age of 40 | 20 (16.8) | 108 (90.8) |

Tab. III. Knowledge of women towards steps of BSE before and after the training (n = 119).

| Knowledge on steps of BSE (n = 119) | Correct response in Pre-test n (%) | Correct response in Post-test n (%) |
|--|------------------------------------|-------------------------------------|
| BSE should be performed monthly | 22 (18.5) | 119 (100.0) |
| Visual examination is the first stage of BSE | 56 (47.1) | 119 (100.0) |
| A woman should check for an asymmetry between your two breasts. | 53 (44.5) | 119 (100.0) |
| Proper positioning and diagnosis technique are crucial for BSE | 70 (58.8) | 119 (100.0) |
| You should stand before a mirror that reflects upper part of body | 25(21.0) | 98 (82.4) |
| Breasts are controlled in front of a mirror in point of shapes, size, appearance with arms at sides, arms on hips | 25 (21.0) | 114 (95.8) |
| Hands are pressed against hips, shoulders and elbows are placed in front by bending towards mirror and breasts are watched | 32 (26.9) | 108 (90.8) |
| Control nipples for discharge by kindly squeezing | 42 (35.3) | 113 (95.0) |
| Use 2 nd , 3 rd , and 4 th fingers of your hand to touch every part of your breast. During this phase, fingers should be kept close | 25 (21.0) | 102 (85.7) |
| Examination should be done over breasts by circle and horizontal movements slowly | 35 (29.4) | 110 (92.4) |
| During the examination, all of breast should gradually slow, moderate, and strong pressures. | 40 (33.6) | 108 (90.8) |
| Hand examination should be done by both lie-flat position and standing. Each breast should control at least for five minutes. | 25 (21.0) | 110 (92.4) |
| Clasp your hand behind your head and look carefully for any changes in the shape of your breasts | 40 (33.6) | 108 (90.8) |
| Put a pillow or towel under your shoulder for the breast to be examined while lying down | 15 (12.6) | 113 (94.5) |
| While standing or lying down, underpins are examined by hand after breasts by palpation | 20 (16.8) | 115 (96.6) |

Studies in other countries have also reported that BSE training improved the knowledge levels of women about BC [15, 16, 32, 33] in a similar way to our research.

In the current study, it was indicated that women' correct response rate about steps of BCS increased one and three months after the training. Despite the existence of research, which evaluated the effectiveness of BSE training, we

did not find any studies that used the BSE training skills evaluation form. However, Ayran et al. [25] reported that there were significant differences in BSE skill levels before and after BSE education given to enhance the ability to do BSE. Bayik Temel et al. [31] determined that the behavior change for BSE in the sixth month post-training. Similarly, Qadir Ibrahim et al. [34] showed that there was a highly

Tab. IV. Comparison of mean differences on knowledge BC, BCS and steps of BSE and practical competency before and after the training periods.

| Knowledge on BC, risk factors and screening | X±SS | df | Wilks' lambda | Effect size (Cohen's d) | F* | p |
|---|---------------|----|---------------|-------------------------|---------|---------|
| Pre-test | 5.54 ± 1.594 | 3 | 0.812 | 2.94 ^a | 8.968 | < 0.001 |
| Post- test | 8.67 ± 1.176 | | | 1.30 ^b | | |
| Re-test after 1 month | 7.32 ± 1.096 | | | 1.35 ^c | | |
| Re-test after 3 months | 7.37 ± 1.065 | | | | | |
| Knowledge of steps of BSE | | 3 | 0.504 | | 38.113 | < 0.001 |
| Pretest | 5.44 ± 2.342 | | | 1.75 ^d | | |
| Post-post test | 8.83 ± 1.392 | | | 1.25 ^e | | |
| Re-test after 1 month | 7.82 ± 1.315 | | | 1.34 ^f | | |
| Re-test after 3 months | 7.96 ± 1.245 | | | | | |
| BSE skills | | | | | 117.000 | < 0.01 |
| Pretest | 16.36±1.462 | 2 | 0.926 | 7.06 ^g | | |
| Post-test | 26.39 ± 1.376 | | | 4.90 ^h | | |
| Re-test after 1 month | 25.53 ± 2.201 | | | 4.78 ⁱ | | |
| Re-test after 3 months | 25.93 ± 2.424 | | | | | |

* Multivariate analysis (MANOVA); ^a Pre-test and post-test (large effect size), ^b Pre-test and re-test after 1 months (large effect size), ^c Pre-test and re-test after 3 months (large effect size), ^d Pre-test and post-test (large effect size), ^e Pre-test and re-test after 1 months (large effect size), ^f Pre-test and re-test after 3 months (large effect size), ^g Pre-test and post-test (large effect size), ^h Pre-test and re-test after 1 months (large effect size), ⁱ Pre-test and re-test after 3 months (large effect size).

Tab. V. Relationship between knowledge on steps of BSE and BSE skills before and after the training periods.

| Knowledge on steps of BSE | | | | |
|---------------------------|---|-----------|----------------------|-----------------------|
| BSE Skills | | Post-test | Retest after 1 month | Retest after 3 months |
| Post-test | r | .305 | - | - |
| | p | < 0.001 | - | - |
| Re-test after 1 month | r | - | .537 | - |
| | p | - | < 0.001 | - |
| Re-test after 3 months | r | - | - | .549 |
| | p | - | - | < 0.001 |

Pearson Correlation Coefficient *p < .05.

significant differences between pre and posttest regarding Iraqi women's knowledge of steps of BSE. Increased knowledge of steps of BSE may help to promote women's awareness of BC and screening and to improve the treatment success, increase benign biopsy rates, and reduce mortality rates. Therefore, this training program should organize periodically and should follow-up long term.

Knowledge of practice of BSE are crucial to maintain screening behavior. In the present study, it was seen that there was a positive correlation between knowledge of BSE steps and ability to do BSE (BSE skills). Ayran et al. [25] indicated that given BSE knowledge changes supported developing awareness about BC and BSE. Previous studies showed that similar finding that evaluated effects of knowledge on women's BSE practice [15, 31, 33, 35]. Another study conducted in Egypt found that there was a positive correlation between the knowledge, attitude and behavior scores of women and there was also a stronger correlation between the level of knowledge and skills of BSE [34]. Based on these findings, we may conclude that training on BC and screening are important to increase the awareness on BC and encourage and perform correct BSE. The study results were in line with literature.

There are some limitations of this study. Firstly, this study

was an observational study in which women underwent breast health education and BSE training. There was no control group in the study. The testing of the women consisted only of knowledge test. Thus, we cannot be distinguished what aspect of the training changed the outcomes for the women. Secondly, the study was conducted on women, who were enrolled to courses provided by Safranbolu Cultural Activities Center, thus the findings may only be generalizable to the women in Safranbolu district of Karabuk province.

Conclusions

We found that during and after the BSE training, women had the opportunity to learn about BC, risk factors and BSE, which, in turn, resulted with increase in their knowledge on BSE. Besides, the training may be an opportunity to perform BSE on a mannequin under the supervision of the BSE trainer and may help to realize and to correct wrong skills. On the other hand, knowledge level of women on BC, and BCS and steps of BSE, which were not at demanded levels before training, however improved after the BSE training. We believe that planned BSE training may help women

to perform BSE by using correct techniques three months after the training. However, this change in health behavior should be followed by long term and women should receive regular BSE training to renew their knowledge and skills. Furthermore, additional materials, such as comprehensible brochures and text messages may contribute to improve the training.

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Ethical approval

Ethical approval for the study was obtained from the ethical review committee of Karabuk University (2015/08, protocol no: 33479383/35) and institutional permission was obtained from the administration of Safranbolu-Karabuk-Turkey Cultural Activities Center.

Conflict of interest statement

The authors declare that they have no conflicts of interest

Funding sources

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Authors' contributions

Study design: I.I.A., and N.K; Data collection: N.K, Data analysis and interpretation: I.I.A., and N.K; Manuscript preparation: I.I.A., and N.K wrote the original draft. All authors approved the final manuscript for submission.

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ORIGINAL ARTICLE

Risk of disordered eating in emerging adulthood: media, body and weight-related correlates among Hungarian female university students

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Key words

Disordered eating • Sociocultural attitudes toward appearance • Body satisfaction • Eating disorders in family • Sporting • Hungary

Summary

Background. University years often are accompanied by dramatic lifestyle changes resulting in an elevated risk of disordered eating among females. We examined the associations of disordered eating with body image, weight and media-related variables.

Methods. Hungarian female university students ($n = 261$, mean age = 22.0 years; $SD = 2.2$ years) were the study participants using online data collection. The Eating Attitude Test-26 (EAT-26) was used to assess levels of and risk for disordered eating.

Results. Twenty-four percent of the sample displayed disordered eating: students with family's eating disorders ($OR = 4.73 [1.34-16.67]$, $p < 0.05$), body satisfaction ($OR = 0.23 [0.07-0.70]$, $p < 0.01$), engagement in sporting ($OR = 4.46 [1.77-11.27]$, $p < 0.01$) and past slimming ($OR = 5.63 [2.07-15.27]$, $p < 0.001$)

were particularly at risk. Multiple linear regression indicated that dieting was associated with a higher score among sporting students ($\beta = 0.18$, $p < 0.001$) and internalization of media messages ($\beta = 0.18$, $p < 0.001$). BMI was a predictor of dieting ($\beta = 0.15$, $p < 0.01$) and oral control ($\beta = -0.34$, $p < 0.001$); social media addiction for bulimia ($\beta = 0.17$, $p < 0.01$).

Conclusions. Our paper highlights the role of body dissatisfaction, sporting and slimming tendencies, sociocultural attitudes toward appearance, and family's eating pathology in understanding female university students' disordered eating. There is a limited role that social media plays in part, due to possible age-related experiences and skills related to coping with a variety of social pressures.

Introduction

Emerging adulthood [1] is that period during the life course when youth leave their childhood home and gain more freedom in making behavioral decisions. However, exploration of new behaviors has not always been positive in terms of health maintenance. University years often mean dramatic lifestyle changes which may result in an elevated risk of disordered eating, particularly among women [2]. The prevalence of diagnosed eating disorders among college students varies between 8-17% [3]. The occurrence of the risk of disordered eating can be much higher: 30.7 percent among Eastern European female students [4] and 20.1% among Hungarian students [5], with an increasing tendency among young women in their twenties [6]. Although disordered eating is common among young women, help-seeking is still remarkably low [7]. With regards to prevention, detecting the risk of disordered eating seems useful [8]. As such, using self-report measures is a good tool for screening and studying correlates without pathologizing [9].

Among potential factors impacting eating habits, foremost are body and weight-related factors. Being overweight is a key factor among college students [10]; Eastern European university students with a higher BMI were at risk to experience eating disorders, primarily among younger females [4].

Another factor is body dissatisfaction which is also related to the internalization of Western body ideals [11]. Among obese college students, the desire to be thin is closely associated with body dissatisfaction and slimming in both sexes, and with exercise intensity among males [12]. Many young people use sport as a way of maintaining/losing weight [13]; sport and physical activity can constitute a major risk factor for the development of eating disorders for those for whom obtaining an ideal body shape is relevant [14].

The family's attitudes are also crucial in the development of body image and dietary habits, particularly for females [15]. Parents' eating disorders or obesity can also increase the risk of body and weight-related concerns [16-18]. Besides family, pressure from and internalization of media messages can also contribute to dieting and disordered eating. Perceived sociocultural pressure often acts as a mediator in the relationship between internalization of the ideal body (both thin and athletic) and eating disorders [19]. Particularly, research finds that young girls are at the greatest risk for sociocultural exposure *vis a vis* mass media [20].

The 'new' forms of media, such as the Internet, and particularly social networking sites can have a great impact on forming our body image and eating concerns through social comparison [21, 22]. Among Asian undergraduate students the risk of disordered eating

attitudes was found to be associated with pathological Internet use [23]. However, the link between eating disorders and the Internet or social media addiction has not been fully developed [24]. Research reports that females are at risk for the pressure of sociocultural norms of the media at every age, especially younger girls [20]. Moreover, a recent study reported that younger persons (around 13 years) were the most prone to internalize social media messages on disordered eating [25].

Despite a growing number of studies on the risk of disordered eating among university students, additional research is needed to map a broader context of the contributing factors to this negative health outcome. Therefore, the main goals of our study include: (1) to detect the prevalence of the risk of disordered eating; (2) to examine bivariate associations of what factors contribute to disordered eating behaviors; (3) to examine the role of body, weight and media-related variables in disordered eating habits; and finally, (4) using logistic regression, to examine the risk or protective odds among a set of independent variables used to determine disordered eating behavior.

Methods

PARTICIPANTS AND PROCEDURE

Survey participants were recruited via an online questionnaire between April and June 2021. The public link was shared on websites and special Internet communication platforms (e.g., Facebook, Instagram, and others). Participation was voluntary and confidential, and participant's informed consent was obtained. The study plan was approved by the Institutional Review Board of the Doctoral School of Education, University of Szeged, Hungary (No. 6/2021), in accordance with the Helsinki Declaration. The convenience sample that was obtained, consisted of Hungarian university students ($n = 313$; ages 18–30; 83.4% females). Due to the gender disparity, we decided to analyze only women's responses ($n = 262$; mean age = 22.0 years; $SD = 2.2$ years).

MEASUREMENT

The validated, Hungarian version [26] of the Eating Attitude Test-26 (EAT-26) was used to assess levels and risk of disordered eating habits [27]. Besides a summary score (EAT_sum) of the 26 items (with one inverse item), three factors were detected: dieting (EAT_dieting; e.g., "Avoid foods with sugar in them"), bulimia (EAT_bulimia; e.g., "Vomit after I have eaten"), and oral control (EAT_oral control; e.g., "Display self-control around food"). A six-point scale with responses ranging from 'never' to 'always' was used (a score of 3, 2, and 1 was given for 'always', 'usually' and 'often', respectively, and 0 for 'sometimes', 'rarely' and 'never'). The total scores could range between 0–78. The cut-off score ≥ 20 held the meaning of being 'at risk'. Internal consistency for the scale was 0.84 with the current sample of women. Among body and weight-related variables, the following were included: Body Mass Index ($BMI = \text{weight in}$

kilograms divided by height in meters squared), body satisfaction (no = 1, yes = 2), current sporting (no = 1, yes = 2), ever slimming (no = 1, yes = 2), eating disorder/obesity in the family (no = 1, yes = 2). Besides, the Hungarian validated [28] of the Body Appreciation Scale - 2 (BAS-2) comprised of 10 items rated on a 5-point Likert-type scale (1 = never... 5 = always [29]. This scale measures respondents' acceptance and favorable opinions of, and respect for their bodies (e.g., "Despite its imperfections, I still like my body"). Higher scores reflect higher levels of body appreciation. The Cronbach's alpha coefficient in our sample (α) was 0.94. The Hungarian, validated version [30] of the Sociocultural Attitudes Towards Appearance Scale (SATAQ) is a 30-item measure used to assess internalization of sociocultural appearance standards [31]. The scale contains items on the endorsement and acceptance of unrealistic ideal images and athletic body idea, importance of various forms of media for obtaining information, and perceived pressure to achieve the media body ideal. Here summary scores were applied where higher scores indicated higher societal and media impact on the body image of the individual. Cronbach's alpha coefficient in our sample was 0.93.

Finally, the Hungarian validated form [32] of the 6-item Bergen Social Media Addiction Scale (BSMAS) [33] was used to assess problematic social media use over the past 12 months (e.g., "You spend a lot of time thinking about social media or planning how to use it"). Participants responded on a 5-point scale (never to always). The Cronbach's alpha coefficient was 0.79 in our sample.

DATA ANALYSIS

SPSS for MS Windows Release 22.0 was used to analyze the data, with a maximum significance level set at 0.05. The analysis started with an examination of the descriptive statistics for the dependent and independent variables. For appropriateness of our data to correlation and regression analyses, we carefully test normality of the variables using statistical tests and/or visual inspection: Skewness, Kurtosis, Kolmogorov-Smirnov Test. When the requirements are not met, we "transform" the data to make it "normal", namely, our normalizing transformation uses a logarithmic transformation. After that, the data meet the criteria of the normal distribution, they are suitable for parametric analyses. Bivariate relationships between the (sub)scales of disordered eating habits and other study variables were examined using Pearson correlation coefficients. The primary focus of the analyses was two-fold. First, detecting the associations between dependent variables (body image, weight and media-related) and the independent variable (EAT score) using multiple linear regression analysis. Next, binary logistic regression analyses (simple and multiple) were used to examine correlates of EAT risk by calculating odds ratios (OR). An odds ratio > 1.0 indicates that there is a positive association between the factors of interest to the baseline odds, while a value < 1.0 indicates the opposite.

Results

Descriptive statistics for the sample are presented in Table I. Nearly one-fourth (24.1%) of the students had EAT-26 scores ≥ 20 . Eating disorder in the family was reported by 6.9% and obesity by 65.9%. More than 80% of respondents said they were satisfied with their body, 64.8% reported participating in some sporting and 54.8% reported slimming behavior.

Correlations among study variables are presented in Table II. The summary EAT score was positively correlated with social media addiction, sociocultural attitudes toward appearance, familial factors, and (ever) slimming and BMI, while negatively associated with body appreciation and satisfaction. The strongest positive correlation was with previous slimming ($r = 0.39$, $p < 0.001$) and the negative ones with body appreciation ($r = -0.40$, $p < 0.001$) and body satisfaction ($r = -0.38$, $p < 0.001$). The EAT_dieting subscale was similar except for social media addiction being nonsignificant and sporting as an additional correlate ($r = 0.19$, $p < 0.01$). The EAT_bulimia subscale was also similar with social media addiction being significant ($r = 0.25$, $p < 0.001$). In the case of EAT_oral control, only past slimming ($r = -0.14$, $p < 0.05$) and BMI ($r = -0.31$, $p < 0.001$) were significant correlates.

Multiple regression estimates are in Table III. In the case of EAT_sum, sociocultural attitudes towards appearance ($\beta = 0.14$, $p < 0.05$), obesity in the family ($\beta = 0.13$, $p < 0.05$), sporting ($\beta = 0.12$, $p < 0.05$) and past slimming ($\beta = 0.19$, $p < 0.01$) were positive, while body appreciation ($\beta = -0.19$, $p < 0.01$), body satisfaction ($\beta = -0.16$, $p < 0.05$) and age ($\beta = -0.10$, $p < 0.05$) were negative predictors. In terms of dieting (EAT_dieting), besides these predictors, BMI was a significant contributor ($\beta = 0.15$, $p < 0.01$) and age was nonsignificant. The following variables proved significant predictors of EAT_bulimia: social media addiction ($\beta = 0.17$, $p < 0.01$), obesity in the family ($\beta = 0.15$, $p < 0.01$), body satisfaction ($\beta = -0.24$, $p < 0.001$) and ever slimming ($\beta = 0.18$, $p < 0.01$). In addition with growing age, bulimia also showed a decreasing tendency ($\beta = -0.10$, $p < 0.05$). Finally, the only significant predictor of EAT_oral control was BMI with a negative association ($\beta = -0.34$, $p < 0.001$). The results in Table IV, using binary (simple) logistic regression, show that all variables are significant ($p < 0.05$) except for age.

Finally, in multiple regression (Tab. V), sociocultural attitudes toward appearance (OR = 1.02 [1.01-1.04], $p < 0.05$), eating disorder in the family (OR = 4.73 [1.34-16.67], $p < 0.05$), sporting (OR = 4.46 [1.77-11.27],

Tab. I. Descriptive statistics for study variables (n = 261).

| Variables | Cronbach alpha | Min. | Max. | Mean (SD) | % |
|---|----------------|-------|-------|---------------|-------|
| Social media addiction | 0.79 | 6 | 27 | 12.95 (4.77) | |
| Sociocultural attitudes toward appearance | 0.93 | 30 | 148 | 79.33 (23.83) | |
| Eating disorder in family | | | | | 6.9% |
| Obesity in family | | | | | 65.9% |
| Body appreciation | 0.94 | 12 | 50 | 35.47 (8.25) | |
| Body satisfaction | | | | | 86.2% |
| Sporting | | | | | 64.8% |
| Slimming (ever) | | | | | 54.8% |
| BMI | | 15.06 | 39.19 | 22.21 (4.32) | |
| EAT_sum | 0.84 | 0 | 66 | 13.59 (10.32) | |
| EAT_dieting | 0.86 | 0 | 38 | 6.97 (6.50) | |
| EAT_bulimia | 0.74 | 0 | 15 | 2.06 (2.99) | |
| EAT_oral control | 0.60 | 0 | 18 | 3.55 (3.25) | |
| EAT_risk | | | | | 24.1% |

Tab. II. Correlation analysis between disordered eating habits and other study variables.

| | EAT_sum | EAT_dieting | EAT_bulimia | EAT_oral control |
|---|----------|-------------|-------------|------------------|
| Social media addiction | 0.16* | 0.03 | 0.25*** | 0.04 |
| Sociocultural attitudes toward appearance | 0.33*** | 0.34*** | 0.32*** | -0.01 |
| Eating disorder in family | 0.07 | 0.06 | 0.11 | 0.10 |
| Obesity in family | 0.22*** | 0.27*** | 0.24*** | 0.01 |
| Body appreciation | -0.40*** | -0.44*** | -0.39*** | 0.08 |
| Body satisfaction | -0.38*** | -0.40*** | -0.43*** | 0.06 |
| Sporting | 0.11 | 0.19** | -0.05 | 0.02 |
| Slimming (ever) | 0.39*** | 0.49*** | 0.38*** | -0.14* |
| BMI | 0.24*** | 0.41*** | 0.23*** | 0.31*** |
| Age | -0.08 | -0.04 | -0.07 | -0.11* |

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Tab. III. Multiple linear regression estimates for EAT summary score and subscales.

| B/SE/β | Eat_sum | Eat_dieting | Eat_bulimia | Eat_oral control |
|---|--------------------|---------------------|---------------------|---------------------|
| Media-related variables | | | | |
| Social media addiction | 0.01/0.01/0.06 | -0.01/0.01/-0.07 | 0.03/0.01/0.17** | 0.01/0.01/0.03 |
| Sociocultural attitudes toward appearance | 0.01/0.01/0.14* | 0.01/0.01/0.18*** | 0.01/0.01/0.09 | 0.01/0.01/0.01 |
| Family-related variables | | | | |
| Eating disorder in family | 0.07/0.16/0.02 | 0.07/0.18/0.02 | 0.22/0.17/0.07 | 0.21/0.18/0.07 |
| Obesity in family | 0.21/0.09/0.13* | 0.21/0.10/0.10* | 0.26/0.10/0.15** | 0.17/0.10/0.11 |
| Body-related variables | | | | |
| Body appreciation | -0.02/0.01/-0.19** | -0.03/0.01/-0.23*** | -0.01/0.01/-0.11 | 0.01/0.01/0.04 |
| Body satisfaction | -0.37/0.14/-0.16* | -0.30/0.16/-0.11* | -0.58/0.15/-0.24*** | -0.19/0.15/-0.09 |
| Sporting (ever) | 0.20/0.09/0.12* | 0.35/0.10/0.18*** | -0.04/0.09/-0.02 | 0.07/0.09/0.05 |
| Slimming (ever) | 0.30/0.10/0.19** | 0.46/0.11/0.24*** | 0.31/0.10/0.18** | -0.06/0.10/-0.04 |
| BMI | 0.01/0.01/0.01 | 0.03/0.01/0.15** | 0.01/0.01/0.01 | -0.06/0.01/-0.34*** |
| Age | -0.04/0.02/-0.10* | -0.03/0.02/-0.06 | -0.04/0.02/-0.10* | -0.03/0.02/-0.10 |
| Constant | 2.81*** | 0.96 | 1.25 | 2.92*** |
| R ² | 0.32 | 0.46 | 0.33 | 0.13 |
| F value | 11.86*** | 20.76*** | 12.48*** | 3.79*** |

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. B: Unstandardized regression coefficient, SE: Standard Error, β: standardized regression coefficients. VIF (Variance Inflation Factor) < 2.0 in each case.

Tab. IV. Simple (binary) logistic regression estimates for EAT risk.

| Predictors | Simple logistic regression | |
|---|----------------------------|------|
| | OR (95% CI) | SE |
| Media-related variables | | |
| Social media addiction | 1.06 (1.01-1.13)* | 0.03 |
| Sociocultural attitudes toward appearance | 1.03 (1.02-1.05)*** | 0.01 |
| Family-related variables | | |
| Eating disorder in family | 3.50 (1.32-9.25)* | 0.50 |
| Obesity in family | 3.07 (1.51-6.25)** | 0.36 |
| Body-related variables | | |
| Body appreciation | 0.90 (0.87-0.94)*** | 0.02 |
| Body satisfaction | 0.09 (0.04-0.20)*** | 0.40 |
| Sporting | 2.04 (1.07-3.89)* | 0.33 |
| Slimming (ever) | 12.37 (5.10-30.03)*** | 0.45 |
| BMI | 1.11 (1.04-1.18)** | 0.03 |
| Age | 0.93 (0.81-1.06) | 0.07 |

OR: Odds Ratio; 95% CI: 95% Confidence Intervals; SE: Standard Error. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

$p < 0.01$) and past slimming (OR = 5.63 [2.07–15.27], $p < 0.001$) are related to higher odds of disordered eating, while body satisfaction is related to lower odds of disordered eating (OR = 0.23 [0.07–0.70], $p < 0.01$).

Discussion

This study explores the associations between disordered eating and a set of body, weight and media-related variables among a sample of Hungarian female university students. We chose a sample of young women since female gender was typically associated with higher odds of disordered eating [4, 10]. Age was slightly related to decreased occurrence of bulimia but it did not elevate significantly the risk of disordered eating. Findings indicate 24.1 percent of risk of disordered eating which was lower than previous Eastern European studies [4] but higher than a previous Hungarian study (20.1%) [5]. While some of the correlates (particularly

sociodemographics) were already detected, our study added a variety of factors to get a more complex picture. Previous studies revealed (social) media playing important role in dieting, forming body image and weight concerns through social comparison and internalization of the ideal body type [19, 20, 22]. Our findings support the role of sociocultural attitudes toward appearance in eating disorders. It was related to higher levels of disordered eating, particularly in students' dieting behavior. While a previous study reported that younger girls were more at risk [20], older females, such as university students, remained a susceptible group. However, social media played a limited role similar to a previous study [24]; the only relevant association was with bulimia. Thus, young adults seemed less susceptible to social media messages perhaps because they learned how to cope with them. As it seemed, dieting or oral control were not influenced by social media activities in contrast with bulimia and general risk of eating disorders [6]. Interestingly, sociocultural attitudes were

Tab. V. Multiple (binary) logistic regression estimates for EAT risk.

| Predictors | Multiple logistic regression | |
|---|------------------------------|------|
| | OR (95% CI) | SE |
| Media-related variables | | |
| Social media addiction | 1.03 (0.94-1.11) | 0.04 |
| Sociocultural attitudes toward appearance | 1.02 (1.01-1.04)* | 0.01 |
| Family-related variables | | |
| Eating disorder in family | 4.73 (1.34-16.67)* | 0.64 |
| Obesity in family | 2.25 (0.89-5.70) | 0.47 |
| Body-related variables | | |
| Body appreciation | 0.95 (0.90—1.00) | 0.03 |
| Body satisfaction | 0.23 (0.07-0.70)** | 0.57 |
| Sporting | 4.46 (1.77-11.27)** | 0.47 |
| Slimming (ever) | 5.63 (2.07-15.27)*** | 0.51 |
| BMI | 0.99 (0.91-1.09) | 0.05 |
| Age | 0.85 (0.71-1.00) | 0.09 |
| χ^2 | 98.77*** | |
| <i>df</i> | 10 | |
| Nagelkerke R^2 | 0.47 | |

OR: Odds Ratio; 95% CI: 95% Confidence Intervals, SE = Standard Error. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

not significant correlates of bulimia. These findings suggest that the interactive nature of social media and posts/comments from friends may play a more decisive role than information and pressure from mass media. In dieting behavior, the situation is the reverse: internalizing messages on the ideal body from well-known people who are popular on TV or magazines.

Our results showed that past slimming was also associated with an elevated risk of disordered eating among sporting students [13, 14] where internalization of thin or athletic body types formed by the media may play a role. This finding suggests that students tend to use not only sport but also disordered eating habits to get a similar figure. Sporting students and those reporting previous slimming tendencies were more likely, while students being satisfied with their bodies were less likely to engage in disordered eating.

The role of familial factors was previously noted [16-18]. In our study, obesity in the family was related not only to the summary scores of disordered eating but also to dieting and bulimia. Familial obesity can force students to prevent their own overweight by dieting or even bulimic behavior. A previous study also revealed the importance of control strategies which are also related to gender [34], although in our study, oral control was not related to familial factors, only with BMI. In terms of the overall risk of disordered eating, however, familial eating disorders proved a predictor: these were less frequent than familial obesity but if present they played a role in elevating the likelihood of young women's disordered eating. More research is needed to clarify the background of these findings; perhaps individual psychological factors can play a role.

Weight and body-related factors were the strongest correlates, similar to previous studies [10-12], particularly body satisfaction as a protective factor and body appreciation against dieting. In addition, dieting significantly moderated the relationship between body

dissatisfaction and disordered eating in a previous study [35]. On the other hand, BMI played a limited (if any) role in multiple regression analysis (only in oral control and dieting) suggesting that (subjective) body image is more important than the more objective weight status.

Overall, five factors increased considerably the odds of disordered eating: 1) body satisfaction (negatively); 2) eating disorder in the family; 3) sporting; 4) previous slimming behavior; and 5) sociocultural attitudes toward appearance. Namely, being less satisfied with one's body, having an elevated susceptibility to mass media messages, the negative example of eating disorders in the family, and engaging in certain activities such as sporting and/or previous slimming behavior, made students more susceptible.

Study limitations

While the cross-sectional design, self-reported and online data collection (using a convenience sample) are limitations, using a broader and more inclusive number of correlates in the analysis is clearly a strength. Our paper highlights the role of body satisfaction, sporting, and previous slimming behavior, pressure from and information of the mass media and family's eating pathology/obesity in female students' disordered eating, while the limited role of social media possibly can be attributed to their age-related experiences and skills on how to cope with it. However, information about the ideal body from the media seems ideal for sporting students which can elevate their risk of disordered eating. Future research should also concentrate on other psychological variables and disordered eating such as binge eating, and the link between social media use and bulimia.

Conclusions

Females usually have higher odds of disordered eating, and it is especially increasing among young women in their twenties. While we know more about its contributors in adolescent girls, less information is available about female university students. Among a few previous studies, most of them concentrated on sociodemographic associations and psychological correlates. However, except for one study in Hungary, we have not yet explored background variables of young women's disordered eating so far. This is the first study to detect associations between disordered eating and a set of body, weight and media-related variables among a sample of Hungarian female university students. These results can trigger future studies on this issue at international level as well including more similar variables.

We concluded that a relatively high level of risk of disordered eating was detected in our sample of female university students which was lower than previous Eastern European studies but higher than a previous Hungarian study. We identified several risk factors, such as eating disorders/obesity in the family, previous slimming behavior, or internalization of sociocultural attitudes towards appearance, while body satisfaction served as protection. Sporting students are also at risk of disordered eating, while BMI and social media addiction played a limited role in this age group.

Acknowledgment

Not applicable.

Ethical approval

The study protocol was approved by the Institutional Review Board of the Doctoral School of Education, University of Szeged, Hungary (No. 6/2021), in accordance with the Helsinki Declaration.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

BFP, HK and AG designed the study. BFP conducted literature review. HK and AG were responsible for data collection and editing the questionnaire. BFP supervised the whole research project and wrote the first draft. KMF participated in the analysis and interpretation of data and finalized the manuscript. All authors contributed to and have approved the final manuscript.

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ORIGINAL ARTICLE

Which mother-headed households' parenting styles are related to children's behavior problems? A cross-sectional study

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Key words

Parenting style • Mothers • Children • Behavior problems

Summary

Introduction. Parenting styles are considered as one of the main determinants of individual and social behaviors and the use of dysfunctional styles can create child behavioral problems. The aim of this study was to determine the relationship between mother-child relationship patterns in mother-headed households and children's behavioral problems.

Methods. This is a descriptive-analytical cross-sectional study that was performed on 345 mother-headed households under the coverage of the Imam Khomeini Relief Committee in Shiraz, Iran. Mothers were selected by convenience sampling method and data were collected using several questionnaires including the mother-child relationship evaluation, the child behavior checklist, and social support appraisals scale. Data were analyzed using SPSS software version 21.

Results. The overprotective parenting style, as one of the inef-

ficient models has been used more than others by mother-headed households as well as the mothers with higher education levels used less from the child-rearing style "excessive ease", and benefited more from the support of friends and others. In addition, children of divorced and low-income mothers are more prone to externalizing behavioral problems. The final result was also determined two parenting styles "excessive ease and overprotection" are effective on children's total behavioral problems.

Conclusion. The findings highlight the need to plan and expand socio-economic and educational support services to improve living conditions and parenting skills in mother-headed households. Further research is also suggested to identify the determinants and types of interventions affecting mother-child relationships, children's behavioral problems, and finally quality of life among this low-income and vulnerable group.

Introduction

Throughout the life span, childhood and adolescence are the most important phases of life in which personality traits are formed [1]. Children are considered one of the most vulnerable groups that are exposed to many behavioral and emotional problems during development [2].

Behavior problems are all repetitive, abnormal, and annoying behaviors such as finger sucking, nail-biting, nervous habits and tic, stuttering, and beatings that disrupt the performance of the individual and the family and have negative effects on their learning, communication, and social efficacy [3, 4]. Behavior problems are divided into two broad categories: internalizing and externalizing problems [5]. Externalizing behavior problems are incompatible patterns of behavior that create difficulty for others, such as law-breaking and aggressive behavior [6], and internalizing behavior problems are actions that reflect internal state: anxiety, depression, isolation, and physical complaints [7].

Generally, behavior problems are first seen in the early years of elementary school and peak between the ages of 8 and 15 [8]. These problems as debilitating disorders significantly affect the academic and professional

performance of children and are associated with a high degree of social problems [9]. According to pathological points of view, children's behavioral and psychological problems can be affected by individual factors such as age, gender, stage of psychological and cognitive development, as well as structural factors such as divorce, separation, and remarriage of parents.[10, 11] Among the social factors that affect a child's health, the family has a crucial role. Healthy personality development and success in different areas of life are affected by the communication patterns that govern the family environment [12]. Therefore, if a family becomes a single-parent family due to reasons such as death, divorce, leaving home, and long absence, the children will face various emotional, socioeconomic, and educational difficulties [13].

Extensive research on single-parent families in recent years has shown that the impact of not having a mother or a father is different. Children living alone with their mothers, in addition to facing poverty and the absence of a father, are more likely to suffer from academic failure and behavioral problems, and are more likely to commit crimes in adulthood as well [14]. During the absence of the father, women heads of households, in addition to raising children and performing household chores,

are also the source of income and are required to work outside the home as well as the absence of the mother in childhood causes a lot of harm to the children [15].

On the other hand, mental health professionals attribute the main cause of behavioral problems in the family to the patterns of communication that exist between parents and especially mothers and children [16]. Communication patterns or parenting styles are the methods that parents use in dealing with their children [17]. Influenced by Baumrind's theory, four types of parenting styles are authoritarian, authoritative, neglectful, and permissive [18]. Research on these four patterns shows that these patterns can have positive and negative consequences in children [19]. In an authoritarian style, parents are assertive and lack intimacy and love in their behavior and speech, an authoritative style, with a combination of restraint and high emotional support, provides appropriate levels of independence and two-way communication between child and parent, a neglectful style characterized by insufficient determination, high love of parents and overprotection, and finally, in the permissive style, parents do not show enough determination and love in dealing with the child [20]. Each of these communication patterns can predict the psychological and social development or behavioral problems of children in the future [21].

Regarding the relationship between parenting style and child behavioral problems, Shafipour et al., showed in a study that authoritative parenting has an important role in preventing behavioral problems in children, and on the other hand, a neglectful style can lead to behavioral problems in children [22]. Alizadeh et al., in their study, stated that the relationship pattern of acceptance leads to a reduction in internalizing and externalizing behavioral problems in children [19]. Also in a study by Anton et al., demonstrated that the children are more exposed to externalizing behavioral problems due to the socio-economic conditions of the mother [23].

In fact, parenting styles occur in the socio-economic-cultural context and are affected by it and as result, the consequences of diverse parenting styles may be different in terms of socio-economic and cultural conditions [24]. In addition, it seems consequences of raising children by mothers in a society where support systems are active and available are different from a society where access to support services is limited [25]. Therefore, specific studies in this field can provide adequate information for planning interventions for educational authorities, and also help to take beneficial measures for the mental health of mothers and then children.

Iran is a developing country with a middle and low-income level. The aftermath of the Eight-Year War and the ensuing international sanctions have put severe pressure on the country, social welfare organizations, and public and private charities to meet the needs of disadvantaged populations. Mother-headed households are one of the poorest populations in Iranian society, often economically and socially disadvantaged, and themselves and their children may be at risk of psychological, behavioral, and social problems. Therefore, it is important to study the

parenting style and behavioral problems of their children to provide different services.

According to our research, no study has been conducted in Iran on the relationship between mother-child relationship patterns and child behavioral problems in families with mother-headed households. Therefore, the aim of this study was conducted to investigate the relationship between mother and child relationship patterns with children's behavioral problems in mother-headed households under the coverage of Imam Khomeini Relief Foundation in Shiraz, Iran.

Methods

STUDY DESIGN AND SETTING

This descriptive and correlational study was conducted from December 2018 to May 2019. Study setting were several centers under coverage of Imam Khomeini Relief Foundation (IKRF) located in Shiraz city in the south part of Iran. The IKRF is a charitable organization in the Islamic Republic of Iran, established in March 1979 to provide social and cultural services to poor families in Iran and some other countries.

STUDY POPULATION AND SAMPLE SIZE

The research population was women heads of households who were covered by Shiraz Imam Khomeini Relief Foundation. The sample size was estimated 313 people, based on the similar study [4]. Considering a 10% attrition rate, 345 women heads of households who were referred to the centers covered by Imam Khomeini Relief Foundation were selected with the convenience sampling method. The inclusion and exclusion criteria were considered based on Table I.

INSTRUMENTS

The data collection instruments included a demographic information form, the Mother-Child Relationship Evaluation (MCRE), The Child Behavior Checklist (CBCL), Social Support Appraisals (SS-A) scale. Demographic characteristics of the participants included education level, marital status, occupation, household income status, and types of housing.

Mother-Child Relationship Evaluation (MCRE)

The Maternal-child relationship was measured through the Mother-Child Relationship Evaluation (MCRE) questionnaire. This scale was developed by Robert M. Roth in 1980 and assesses the mother's attitude toward interacting with the child on four subscales including child acceptance, excessive ease, overprotection, and child rejection [26]. Each subscale has 12 items and there are totally 48 items in this questionnaire. Responses are scored on a five-point Likert scale from 1 (strongly disagree) to 5 (strongly agree). The reliability and validity of this questionnaire in Iran was confirmed by Zamiri in 2005, and Cronbach's alpha coefficient for the subscales of child acceptance, excessive ease,

Tab. I. Inclusion and exclusion criteria.

| Inclusion criteria | Exclusion criteria |
|---------------------------------------|--|
| At least elementary level of literacy | Persistent serious psychological problem |
| Having a child 4-18 years old | Doing not return the questionnaires |
| Consent to participate in the study | Defective completion of questionnaires |

overprotection, and child rejection was reported at 0.77, 0.71, 0.78 and 0.72, respectively [27]. To get the total score, the scores of the items are added together and the higher scores indicate a better attitude.

The Child Behavior Checklist (CBCL)

Behavioral problems were assessed using the parent rating form of the Child Behavior Checklist (CBCL) developed by Achenbach [28]. The 113-item questionnaire reflects the behavioral and emotional problems of children ages 4 to 18, and parents rate their child's behavior over the past six months on a three-point scale with incorrectly = 0, somewhat correct = 1, and correct = 2. This questionnaire evaluates the types of behavioral problems of children and adolescents in 8 specific areas. The list of child behavioral problems consists of three scales: total problems, externalizing, and internalizing problems [8]. The reliability and validity of the Persian version of CBCL, the parent rating form have been confirmed in a study by Ashori and Karimnezhad in 2020 and Cronbach's alpha coefficients on the subscales of externalizing, internalizing, and the total problem were 0.83, 0.90, and 0.86, respectively [29].

Social Support Appraisals Scale (SS-A)

To assess the social support of mothers, the SS-A scale was used that developed by Vaux et al, in 1986 based on Cobb's definition of social supports[30]. The SS-A measures how much a person feels loved and a member of a group such as family or friends. The SS-A measures how much a person feels loved and a member of a group such as family or friends. This 23-item questionnaire includes three areas: family, friends, and others. Questionnaire items were scored by means of a 5-point Likert scale from a score of 1 (very little) to a score of 5 (very much). The total score of the test varies from 23 to 115. The reliability of the Persian version of the questionnaire was proven by Khabaz et al, with Cronbach's alpha equaling 0.74 [31].

STATISTICAL ANALYSIS

Data analysis was performed using SPSS software version 21. Descriptive statistics (mean, standard deviation, frequency, and percentage) were used to describe the research variables. Independent t-test, one-way ANOVA, and eta squared statistic (for measuring the effect size) were used to characterize the relationship between variables at a significant level of $p < 0.05$.

ETHICAL CONSIDERATION

This study was approved by the Ethics Committee of the Shiraz University of Medical Science (No: 13847 – 42 –

01 - 95). All participants were informed that participation in the study was voluntary. Then, all participants gave informed consent. They were also assured that the data collected would remain confidential.

Results

The total number of mothers who participated until the end of the study and completed the questionnaires was 334, with a participation rate of 97%. The age range of mothers was from 25 to 53 years old with a mean age of (39 ± 2.59) and the children aged between 6 and 18 years old with a mean age of (10.64 ± 3.67). The distributions of mothers' demographic variables are presented in Table II.

According to Table II, 95.5% ($n = 319$) of the participants were literate and had the ability to read and write, 49.4% of mothers ($n = 165$) were divorced and 60.2% ($n = 201$) were unemployed, 65.6% of mothers ($n = 219$) had financial support.

Table III is demonstrated that among the independent variables, total child behavioral problems, overprotective child-rearing style, and mothers' perceived support from the family have the highest mean.

According to Table IV, it was determined that among the 4 mother-child relationship styles, there is a significant difference between the excessive ease model and the mother's education level and as the mother's education level increases, the mean score of excessive ease pattern decreases. The results also showed that there is a significant difference between mean friend support and other support (government, organizational, social, etc.) with mother's education level, and as mothers' education

Tab. II. Mothers' demographic characteristics.

| Variable | Categories | N (%) |
|-------------------|----------------------------------|------------|
| Education level | Illiterate | 15 (4.5) |
| | Up to primary school | 163 (48.8) |
| | Up to secondary school/ Graduate | 134 (40.1) |
| | Higher education | 22 (6.6) |
| Marital status | Widow | 88(26.3) |
| | Divorced | 165(49.4) |
| | Unbound | 81(24.3) |
| Mothers' job | Unemployed | 201 (60.2) |
| | Employed | 133 (39.8) |
| Types of housing | Self-owned house | 119 (35.6) |
| | Parents' home | 108 (32.4) |
| | Rented | 107 (32) |
| Financial Support | Yes | 219 (65.6) |
| | No | 115 (34.4) |

Tab. III. Differences in questionnaires' subscales.

| Variables | Categories | Mean \pm SD | 95%CI | P-value | |
|---------------------------|---------------------|------------------|-------------|-------------|-------|
| | | | Lower bound | Upper bound | |
| Child Behavioral problems | Internalizing | 1.26 \pm 0.65 | 1 | 3 | 0.000 |
| | Externalizing | 1.23 \pm 0.60 | 1 | 3 | |
| | Total | 1.27 \pm 0.64 | 1 | 3 | |
| Mother-child relationship | Acceptance of child | 26.06 \pm 2.87 | 18 | 35 | 0.000 |
| | Overprotection | 33.20 \pm 4.28 | 18 | 48 | |
| | Excessive ease | 27.99 \pm 4.48 | 15 | 43 | |
| | Child rejection | 33.07 \pm 3.32 | 24 | 43 | |
| Mother perceived support | Friend Support | 25.87 \pm 4.03 | 12 | 34 | 0.000 |
| | Family Support | 33.78 \pm 3.81 | 17 | 40 | |
| | Others Support | 31.10 \pm 4.07 | 14 | 40 | |

Significant level < 0.05.

Tab. IV. Comparison of the mean score of mothers' perceived support and types of MCRE based on level of education.

| | Subcategories | Illiterate (15) | Up to primary school (163) | Up to secondary school/ Graduate (134) | Higher education (22) | P-value* |
|----------------------------|-----------------|------------------|----------------------------|--|-----------------------|----------|
| Types of MCRE | Acceptance | 26.20 \pm 2.54 | 26.15 \pm 2.71 | 25.93 \pm 3.06 | 26.13 \pm 3.21 | 0.919 |
| | Overprotection | 34.13 \pm 5.80 | 32.99 \pm 4.04 | 33.35 \pm 4.10 | 33.22 \pm 5.83 | 0.737 |
| | Excessive Ease | 29.40 \pm 5.12 | 28.55 \pm 4.58 | 27.55 \pm 4.11 | 25.59 \pm 4.56 | 0.008 |
| | Child rejection | 32.80 \pm 3.23 | 32.92 \pm 3.30 | 33.36 \pm 3.25 | 32.54 \pm 3.94 | 0.571 |
| Mothers' perceived support | Family | 34.46 \pm 1.92 | 33.71 \pm 4.04 | 33.58 \pm 3.81 | 35.00 \pm 2.81 | .376 |
| | Friends | 24.33 \pm 2.89 | 25.13 \pm 4.10 | 26.48 \pm 3.84 | 28.63 \pm 3.65 | 0.000 |
| | others | 30.40 \pm 2.44 | 30.16 \pm 3.76 | 31.85 \pm 4.25 | 33.95 \pm 4.04 | 0.000 |

* One-way ANOVA.

level increases, the mean scores of supports of friends and others increase ($P < 0.05$).

Table V showed that there was a significant difference between the total mean score of child behavioral problems and externalizing problems with the mother's marital status. So that the mean scores of total and externalizing problems in children with divorced mothers were higher than others. Regarding the comparison of mothers' average incomes and children's behavioral problems, it was found that children's total and externalizing behavioral problems have a statistically significant

difference with the amount of mothers' income, and the mean scores of total and externalizing behavior problems in the income group "300,000-5,200,000 Rials" were higher than others.

The eta squared (η^2) statistic was used to investigate the association between child-rearing style and children's behavioral problems. According to Table VI, two child-rearing styles "excessive ease, overprotective" have a statistically significant effect on total child behavioral problems. The value of eta squared for excessive ease and overprotection showed that there is a medium

Tab. V. Comparison of the mean score of mothers' marital status and income with child behavioral problems.

| | Subcategories (n) | Internalizing problems M \pm SD | Externalizing problems M \pm SD | Total problems M \pm SD |
|----------------|----------------------|-----------------------------------|-----------------------------------|---------------------------|
| Marital status | Widow (132) | 49.96 \pm 9.65 | 49.05 \pm 8.16 | 50.48 \pm 9.55 |
| | Divorced (159) | 49.94 \pm 10.15 | 51.68 \pm 11.59 | 50.80 \pm 10.72 |
| | Unbound (43) | 50.30 \pm 10.68 | 46.69 \pm 7.38 | 45.52 \pm 7.18 |
| | P-value | 0.977 | 0.005 | 0.007 |
| Income (Rials) | 300000-5200000 (297) | 49.94 \pm 9.85 | 50.55 \pm 10.22 | 50.60 \pm 10.22 |
| | 5210000-10100000(33) | 51.13 \pm 11.64 | 45.16 \pm 5.95 | 45.40 \pm 5.97 |
| | 10110000-15000000(4) | 45.05 \pm 3.74 | 48.96 \pm 10.67 | 43.10 \pm 9.081 |
| | P-value | 0.495 | 0.013 | 0.007 |

Significant level < 0.05.

Tab. VI. The eta squared (η^2) statistic results.

| Types of MCRE Children' behavioral problems | Acceptance | | Overprotection | | Excessive Ease | | Child rejection | |
|---|------------|---------|----------------|---------|----------------|---------|-----------------|---------|
| | η^2 | P-value | η^2 | P-value | η^2 | P-value | η^2 | P-value |
| Internalizing | 0.095 | 0.243 | 0.056 | 0.893 | 0.070 | 0.687 | 0.057 | 0.877 |
| Externalizing | 0.118 | 0.232 | 0.120 | 0.212 | 0.138 | 0.072 | 0.117 | 0.133 |
| Total | 0.098 | 0.227 | 0.288 | 0.000 | 0.284 | 0.000 | 0.191 | 0.184 |

Significant level < 0.05.

effect size ($\eta^2 > 0.2$), therefore, in this study, these two parenting styles are effective on children's total behavioral problems.

Discussion

This study investigated the relationship between the child-rearing style of mother-headed households and children's behavioral problems. The results showed that the overprotective child-rearing style, as one of the inefficient models, more than three other styles has been used by mother-headed households. Lazar et al. congruent with our finding concluded that mother-headed households are more likely to use dysfunctional communication and behavioral patterns [32]. This could be because mother-headed households may have had less time, patience, and financial and emotional support, and most importantly, they have fear of losing their children. Contrary to the results of the present study, Mullins et al, stated that despite more perceived vulnerability, and stress in mother-headed households, they do not use an overprotection style more than others [33]. Yaffe Y also confirmed that there is a significant difference in communication patterns between mother-headed households and non-head household ones, but in contrast with our finding considers the more common pattern used by mother-headed households to be an efficient style "authoritative" [34].

The results showed that the higher mothers' education, the less inclined they are to use the child-rearing style "excessive ease". Anton et al, consistent with the present study stated that the family socioeconomic status, especially the mother's education level, and income, is related to the mother-child relationship pattern; mothers with higher education are more likely to use effective relationship models, and on the other hand, mothers with lower education are 65% more likely than mothers with university education to use the inefficient model of excessive ease [23].

The results also showed that increasing education level causes mothers to benefit from the support of friends and others as well because, in the educational process, friends play a major role in supporting the individual, and friendship networks are formed [35]. Abd Hamid consistent with the results of the present study described that the support of friends and neighbors plays a key role in tolerating the challenges and directly can affect the mental health of mother-headed households, then, these mothers prefer to share their problems with friends [36]. Another result of the study showed the children of

divorced mothers are more likely to have externalizing behavioral problems. The researchers believe that children who experience the absence of a father show more behavioral problems than children in normal families [37]. According to Liu et al., children of single-parent families face externalizing behavioral problems included aggressive behavior, withdrawal, and social problems [38]. Daryanani et al., in line with this finding described that children of mother-headed households experience an increase in depressive symptoms and externalizing behavioral problems [39]. On the other hand, Riediger et al., did not find a significant difference in the prevalence of child behavioral problems in single-parent and double-parent adolescents [40].

Another study result showed that children of mothers with very low incomes are more prone to externalizing behavioral problems. Other researchers have also found a statistically significant relationship between the income status of mother-headed households with externalizing behavioral problems of children, and have attributed every \$ 10,000 increase in income to a 0.79 unit decrease in externalizing behavioral problems of children [23]. According to Daryanani research, single-parents' families are far more impoverished than two-parent families due to loss of partner income, lower mothers' education, and discriminatory wages against women, and this poverty affects externalizing behavioral problems of children [39].

According to the final result two parenting styles "excessive ease and overprotection "are effective on children's total behavior problems. Alidosti et al., in line with this finding, concluded that the permissive parenting style is related to the general behavior problems of children [41]. Some researchers believed overprotective parenting style is significantly higher in children with behavioral disorders and leads to both internalizing and externalizing problems [42, 43]. It seems both parenting styles " excessive ease and overprotective" cause different behavioral and emotional problems in children will vary based on the family, cultural, and psychosocial conditions that govern the child's life.

STRENGTHS AND LIMITATIONS

According to the searches, this is the only study that has been done on the relationship between mother-child relationship patterns and child behavioral problems on mother-headed households in Iran, and the findings of the present study can be a basis for future research. The present study has several limitations. Sampling was done by the convenience method and data collection was based

on self-report. On the other hand, many respondents had low levels of literacy that may somewhat decrease the validity of the answers. In addition, generalizing the findings of this study are also questionable to employed head households and higher incomes women, or women who are covered by other charitable public and private organizations.

Conclusion

The findings of this study confirmed the existence of obvious needs and deficiencies in the socio-economic status as well as the knowledge and ability of female-headed households to raise healthy children. If these needs and shortcomings are not properly addressed, adverse health and social development consequences will occur. These findings clearly indicate the need to plan and expand both quantitatively and qualitatively socio-economic and educational support services to improve the living conditions and parenting skills of female-headed households. Further research is also suggested to identify the determinants and types of interventions affecting mother-child relationships, children's behavioral problems, and finally quality of life among this low-income and vulnerable group. Empowerment of women, including in the field of entrepreneurship and family role-playing skills, especially in public education and schools, is one of the proposed strategies.

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Conflict of interest statement

None of the authors has any conflict of interest to declare.

Authors' contributions

MH.K. conceptualized the study project, supervised the implementation process, and edited the manuscript. SS participated in data gathering, data analysis, and the writing of the manuscript. M.MJ contributed to data analysis and the writing of the manuscript. All authors read and approved the final manuscript.

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ORIGINAL ARTICLE

The effect of cognitive behavior therapy on attitude of infertile individuals toward child adoption

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Key words

Infertility • Child adoption • Attitude • Cognitive behavior therapy

Summary

Background. Infertility is one of the most important life-threatening crises that will cause serious psychological problems and serious stressful experiences for couples. Granting the parenting of neglected children can benefit both infertile couples and those children.

Purpose. The study aimed to investigate the effect of Cognitive-Behavioral Counseling (CBT) on the attitude of infertile individuals towards child adoption.

Methods. It is a clinical trial study. Forty samples were determined in each case and control group. Five 90-minute cognitive-behavioral counseling sessions were held for the intervention group. Control group participants were on the waiting list. Data were reported based on frequency distribution, central distribu-

tion, dispersion, Wilcoxon, and paired T-test. The level of significance was set at $p < 0.05$.

Findings. Participants in this study had a mean age of 32.5 years old, the mean years without children was 6.29 years, most of them had higher education. The majority of individuals in the control and intervention groups referred more than once to treat infertility. Based on the current study results, the attitude score of the intervention group before the consultation was 100.74, and it was 112.46 after counseling ($p = 0.046$). Moreover, the score of attitudes toward adoption after counseling in the control group was 97.10 and 112.46 in the intervention group ($p < 0.001$).

Conclusions. CBT has been influential on the attitude of infertile people towards adoption.

Introduction

Infertility is one of the most important life-threatening crises that will cause serious psychological problems and serious stressful experiences for couples. In addition to being deprived of their children, these couples also face other personal, social, and economic problems. In Iran, the prevalence of primary infertility, according to the WHO's clinical, epidemiological and demographic definitions, are 20.2, 12.8, and 9.2%, respectively. In addition, secondary infertility rate is 4.9% [1]. The 12-month prevalence rate of infertility ranges from 3.5 to 16.7% in more developed countries and from 6.9 to 9.3% in the less-developed states, with an estimated overall median prevalence of 9%. The prevalence of primary infertility in 2019 was 20.2% for clinical definition, 12.8% for epidemiological definition, and 9.2% for demographic definitions [2]. The prevalence of infertility varies from region to region, and in some areas, it is reported to be up to 30% [3]. Infertility can have many negative effects on individual and social life. As research shows, sexual dissatisfaction is closely related to issues such as crimes, sexual assaults, psychiatric illness, depression, anger, anxiety, fear, suicidal thoughts and divorce [4]. Infertility is one of the bitter and stressful experiences

of the marital life of couples. Long-term medicinal and therapeutic programs, hazardous diagnostic and therapeutic procedures, planned sexual activity are among these tensions [5, 6]. Family failure, as well as other factors such as parental conflicts, loss of parents, etc., have caused many families to neglect the children in the world, including the Iranian society [7]. Poorly supervised and neglected children are deprived of parental care, effective support, and the benefits of family life [8]. The family-related distress causes these children to be subject to psychological disorders such as depression, anxiety, physical complaints, deterrence, aggression, law-breaking behavior, hostility, arousal, deviance from social norms, destruction of property, and harm to others that will have lasting effects on the child's life [9]. As we know, attitudes represent one's overall assessment of a subject. Even among infertile couples, there is a poor, inefficient attitude towards adoption [10]. The existing legal considerations and the conventional attitude towards the foster child, and issues related to identity and its formation are the most important challenges of these families, and they are considered the most important factors for weak and inefficient attitudes towards adoption [11]. On the other hand, difficult and hardworking treatments, long waiting periods, a sense of loneliness, and rejection

and acceptance of a foster child make these people show high levels of anxiety and physical symptoms, and they have difficulty adapting. This stress and psychological pressure prevent them from thinking reasonably in stressful conditions [12]. Granting the parenting of neglected children under the care of a welfare organization to families who are legally eligible to support neglected children can have benefits both for infertile couples and neglected children [13].

Sometimes couples consider cultural practices, fears of being judged by others, financial implications, and legal (technical) problems as barriers so that they prefer not to have a child or think about new therapies. Factors such as long waiting (2-5 years), increase in financial costs, paperwork and extensive documents and surveys of family, need for fingerprinting, criminal and medical controls, and rigid rules [14], fear of abnormal behavior of the foster child, cultural dissent, fear of some genetic diseases, abnormalities of the foster child, religious opposition, non-similarity of the child to the woman or the man (foster father and foster mother) [15], concern about the eventual adoption of the child (abilities, behavioral and medical problems, etc.) make them unwilling for the practice of adoption [16]. The hope of fertilization [10] and the reason that adoption makes the woman feel that her maternal role is not complete [17] are among the obstacles. Hasanpoor's qualitative study showed that the importance of blood relations, cultural factors, and infertility treatment are among the barriers to adoption in our society. The results show that increasing awareness and enlightenment in the community through the media is essential to minimize the socio-cultural consequences of adoption [18]. Charlottee stated many women are unaware of the adoption process. Most had a positive attitude towards the issue but did not do so [19]. Hajiyan found that Infertile women with a history of unsuccessful ART had high levels of infertility stress and moderate adoption rates. We need to pay more attention to the psychological aspects of infertility and treatment failure. There is a clear need to raise public awareness of adoption and promote "adoption" as a sensible choice for starting a family [20].

The cognitive-behavioral counseling approach is one of the most common approaches to treating sexual and psychiatric disorders, psychological disorders, improved anger control and social skills, and increased adaptability [21].

According to numerous studies, psychotherapy and especially CBT dominate the international guidelines for psychosocial treatments, making it the first-line treatment for many disorders, as noted by the National Institute for Health and Care Excellence's guidelines [2] and American Psychological Association [3]. Therefore, CBT is the gold standard in the psychotherapy field, being included in the significant clinical guidelines based on its rigorous empirical basis [22].

Infertility has multiple injuries in different physical, psychological, mental, and social dimensions in other societies and cultures. In addition, the adoption of a child can be an option for infertile couples to fulfill

their desire for parents; the poor attitude of different communities, despite awareness of adoption, puts couples in a challenge that makes decision-making difficult. It is necessary to increase community awareness and promote adoption as a reasonable choice and the effect of cognitive-behavioral counseling on adoption and marginal infertility issues such as anxiety, Post Traumatic Stress Disorder (PTSD), and infertility-related stress. Knowledge of the positive effect of attitudes toward adoption helps infertile couples think about a foster child. So current study aimed to determine the impact of cognitive-behavioral counseling on the attitude of infertile people towards adoption.

Methods

STUDY DESIGN

This is an interventional study with pretest, posttest design, and control groups to investigate the effect of cognitive-behavioral counseling on the attitude of infertile individuals towards adoption. Participants were Infertile people seeking infertility treatment. The study was performed at Afzalipour Hospital in Kerman, Iran. Afzalipour Hospital is the only governmental infertility treatment center in Kerman province. Sampling and data collection lasted for five months, from 15-10-2019 till 27-3-2020.

SAMPLING

Based on the study population, the type of study and the inclusion criteria, and the 95% confidence interval, and the second type of error 20%, the sample size was estimated to be 31 individuals for each group (control group and intervention group). Sampling was done on even and odd days. Patients who came for treatment on even days were in the intervention group, and patients who came in on odd days were in the control group. Ninety-four persons were eligible. Eleven persons did not have inclusion criteria. 2 persons declined to participate, and one person was excluded for other reasons.

At last, 80 persons participated in study-40 in each group. Nine persons discontinued the survey in the control group because of the extensive time interval between pretest and posttest and pregnancy. In the experimental group, three persons did not participate in 3 counseling sessions due to many meetings and the distance. Two persons discontinued intervention because they got pregnant.

MEASUREMENT SCALE

The data collection tool includes a researcher-made questionnaire of attitude towards adoption. The first part of the questionnaire was related to demographic information. This information included age, education, income, years of infertility, and the frequency of attempts for fertility. A researcher-made questionnaire of attitude towards adoption was used to measure attitude toward adoption. Because the definition of adoption is different in different societies and doing it depends on the culture

and custom of the society and the religious and legal issues governing that society. Therefore, the questionnaire was designed under the beliefs and laws of the Iranian people and different articles and opinions of psychologists and lawyers were also used. The questionnaire was also designed based on individual experience as a midwife, psychologist, and studies. To determine the content validity ratio, we sent the questionnaire to 12 specialists working in infertility health, midwifery, psychology, and health education. All items of the questionnaire had an acceptable CVR greater than 0.80. It was found medium internal consistency (alpha range of 0.70-0.79) and desirable construct validity. The reliability of the questionnaire was confirmed by Cronbach alpha (0.88). The designed questionnaire had 38 questions prepared on a 4-point Likert scale from strongly agree to disagree strongly. Agree got a score of 1, and absolutely opponent got a score of 4. The minimum score of this questionnaire was 38, and the maximum was 152. The cutoff point of the questionnaire was 95, and the mean scores above 95 were considered as positive attitudes and below 95 as negative attitudes.

PROCEDURE

Mental health midwife as a researcher generated the random allocation sequence, enrolled participants, and assigned them to interventions. Participants were infertile individuals seeking infertility treatment. Inclusion criteria were history of primary infertility and lack of history of mental illness, known psychiatric disorder, and hospitalization. Exclusion criteria were getting pregnant while studying and not attending at least two counseling sessions. Since the samples were not all available together, whenever the number of samples reached 10, their intervention started as a group. It took five months until all the samples were available and the intervention was performed. Informed consent was fulfilled. Then pretest form was completed. Then five 90-minute cognitive-behavioral counseling sessions were held for the experimental group. Control group participants were on the waiting list. Post-test was performed in the last counseling session.

INTERVENTION

Both groups' conditions

Participants were asked not to participate in any counseling or educational sessions related to child adoption or study any text about this issue during the study. If anybody acts differently should inform the researcher to exclude her from the study. Participants fill the pretest at the initiation of the first session and the posttest at the end of the last session.

Group one (counseling group): for this group, counseling based on cognitive behavior Beck's CT model was applied. A manual had been prepared based on infertile couples' cognitive and behavioral needs towards the child adoption issue. This manual considered all attitude-related items of the "Attitude towards Child Adoption" questionnaire. These questions are subsets of the main domains of the scale that influence the beliefs, attitudes, and behaviors towards child adoption. The main aim of this counseling approach is the creation and development of a positive attitude towards child adoption. This manual includes five/ 90 minutes' weekly sessions, as shown in (Tab. I) in detail.

Group two (control group)

The control group only attends the ART (assistant reproductive technology) visits in the hospital infertility center during the intervention period. They are on the waiting list for counseling intervention upon their request after the intervention period.

DATA ANALYSIS

SPSS 25 for windows and independent t-test, paired t-test, and Chi-square test were used depending on the case. To investigate and ultimately ensure the ineffectiveness of demographic variables on intervention, the two interventions and control groups were matched in terms of all variables at the beginning of the study. However, the relationship between the two groups and each of the demographic variables was measured by the Chi-square test for more certainty. Shapiro-Wilk and Kolmogorov tests were used to determine the normality of the data. The level of significance was set at $p < 0.05$.

Tab. I. Content of CBT toward child adoption.

| Session | Topic of the meeting | Content |
|---------|---------------------------------------|--|
| First | Introduction and purpose presentation | Pre-test, introduction, purpose of meetings, definition of infertility and its types, childbearing strategies, summary of dysfunctional thoughts and attitudes in adoption and their effects on avoidance adoption behaviors |
| Second | Investigating dysfunctional attitudes | Review previous session, discuss stigmas, tags and views, and where others comment on adoption, Behavioral techniques including: Reducing anxiety, Anger management, Stress management, Stop thinking, Respiratory and muscle relaxation |
| Third | Spirituality | Review of the previous session, the effect of secure attachment to God on quality of life, discussion on the sense of ownership over the adopted child and his legitimacy, some cognitive errors in adoption |
| Forth | Relaxation | Review of the previous session, poverty and luxury in adoption, the topic of genetic and environmental differences in the real child and the adopted child and in the fate of human beings |
| Fifth | Legal procedures | Review of the previous session, legal steps of adoptive adoption in the country, review of behavioral techniques and cognitive errors, conclusion, post-test |

Results

There was no significant difference between the two intervention and control groups regarding the variables of age and years of living without children after marriage, and the two groups were similar.

There was no significant difference between the two groups in the variables of sex, level of education, occupation, income level, the cause of infertility, history of the disease, and the two groups were similar. But there was a significant difference between the two intervention and control groups in the place of residence and the frequency of the infertility treatment. In other words, 94.3 and 71.0% of the samples were residents in the city in the intervention and control groups, and there was a significant difference between the two groups ($p = 0.01$). In the intervention and control groups, 34.6 and 18.5%, respectively, underwent treatment four times or more, and there was a significant difference between the two groups ($p = 0.03$) (Tab. II).

There was no significant difference in the mean score of

attitudes before and after the intervention in the control group.

The mean score of attitudes before the intervention was 100.74 and 98.19 in the intervention and control groups, respectively. After the intervention, the mean score of attitudes was 112.46 and 97.10 in the above groups, respectively. There was a significant difference in the attitude scores before and after the intervention in the intervention group ($p < 0.001$). In other words, the samples had a more positive attitude toward adoption after the intervention. But in the control group, there was no significant difference in the scores before and after the intervention. Also, there was a statistically significant difference between the two intervention and control groups in the attitude score after the study ($p < 0.001$). However, there was no significant difference between the two groups before intervention. The difference in the scores before and after intervention showed that the attitude score increased by 0.29 in the intervention group and decreased by 0.03 in the control group. There was a significant difference between the two groups ($p = 0.002$) (Tab. III).

Tab. II. The demographic information of the units in the intervention and control groups.

| Group Variable | Control group | | Control group | | Statistical test | P-value |
|--|---------------|---------|---------------|---------|------------------|---------|
| | Frequency | Percent | Frequency | Percent | | |
| Sex | | | | | | |
| Female | 18 | 51.4 | 16 | 51.6 | 0.00 | 0.99 |
| Male | 17 | 48.6 | 15 | 48.4 | | |
| Education level | | | | | | |
| High school | 8 | 22.9 | 9 | 29.0 | 0.74 | 0.69 |
| Diploma | 11 | 31.4 | 11 | 35.5 | | |
| Associate degree and higher | 16 | 45.7 | 11 | 35.5 | | |
| Occupation | | | | | | |
| Self-employed | 15 | 42.9 | 13 | 48.1 | 2.98 | 0.23 |
| Employed | 10 | 28.6 | 3 | 11.1 | | |
| Housewife | 10 | 28.6 | 11 | 40.7 | | |
| Income level | | | | | | |
| Lower than one million tomans | 13 | 37.1 | 19 | 61.3 | 4.01 | 0.13 |
| One-two million tomans | 13 | 37.1 | 8 | 25.8 | | |
| Above two million tomans | 9 | 25.7 | 4 | 12.9 | | |
| Residential place | | | | | | |
| City | 33 | 94.3 | 22 | 71.0 | 6.44 | 0.01 |
| Village | 2 | 5.7 | 9 | 29.0 | | |
| Cause of infertility | | | | | | |
| Man-related | 12 | 34.3 | 6 | 19.4 | 3.34 | 0.34 |
| Woman-related | 5 | 14.3 | 8 | 25.8 | | |
| Both | 8 | 22.9 | 5 | 16.1 | | |
| Unknown | 10 | 28.6 | 12 | 38.7 | | |
| History of illness other than infertility* | | | | | | |
| Yes | 3 | 8.6 | 1 | 3.2 | 0.62 | 0.35 |
| No | 32 | 91.4 | 30 | 96.8 | | |
| The frequency of treatment for infertility | | | | | | |
| Once | 8 | 30.8 | 18 | 66.7 | 6.90 | 0.03 |
| Two or three times | 9 | 34.6 | 4 | 14.8 | | |
| Four times and more | 9 | 34.6 | 5 | 18.5 | | |

* Fischer's exact test Chi-square test in other cases.

Tab. III. Mean attitude toward adoption before and after intervention in the control and intervention groups.

| Time Group | Before intervention | | After intervention | | T-paired test | P-value | Mean of difference before and after intervention | | Effect size (mean of difference) |
|------------------|------------------------|----------|--------------------|-------|------------------|---------|--|------|-------------------------------------|
| | Mean | SD | Mean | SD | | | Mean | SD | |
| Intervention | 100.74 | 12.62 | 112.46 | 14.16 | 6.18 | < 0.001 | 0.29 | 0.52 | 0.56 |
| Control | 98.19 | 12.18 | 97.10 | 10.91 | - 1.61 | 0.12 | - 0.03 | 0.18 | -0.17 |
| Statistical test | t = 0.83 | t = 4.89 | | | Z = -3.11 | | | | |
| Effect size | 0.206 | 1.22 | | | 0.82 | | | | |
| P-value | 0.41 | < 0.001 | | | 0.002 | | | | |

SD: Standard deviation; t: Independent t-test; Z: Mann-Whitney U.

Discussion

According to the results of this study, the score of attitudes towards adoption was 100.74 before intervention (counseling) in the intervention group, and in the control group, it was 98.19. That is, both groups had approximately the same attitude before the consultation. Faramarzi's study (2008) was conducted on "the treatment of depression and anxiety of infertile women: cognitive-behavioral counseling and fluocitin." The mean score of anxiety before intervention in the intervention and control groups did not differ significantly, the same as the current study [23]. Based on the current study results, the attitude score of the intervention group before the consultation was 100.74, and it was 112.46 after counseling. This difference was significant. According to Hamzehpour (2014) study, the anxiety score in the intervention group after the consultation reduced from 48.67 to 32.67, which was a considerable difference. It was similar to the present study, and CBT counseling has been influential on the anxiety of infertile women [24]. In this research, the score of attitudes toward adoption after counseling in the control group was 97.10 and 112.46 in the intervention group. After the intervention, the attitude score in the intervention group (who received counseling) was higher than the control group. It was consistent with a previous study with the goal of the effect of CBT on the anxiety of infertile couples [25]. It seems the use of the same counseling method was the reason for consistency. One study with the effect of CBT on women's knowledge, attitude, and sexual self-esteem, found that all the variables improved, and it was aligned with present study results [26]. Results showed that the mean score of attitudes toward adoption decreased in the control group during counseling for the intervention group. Some studies also showed the same results [24, 25]. Although a decrease in the attitude score in the control group was not significant, it is better to study the factors affecting the attitude towards adoption in this group. The reason might be that during this time, the people of the control group faced those who had a foster child and their problems, and the legal path might be a complex process for them. In the intervention group, the number of people with

negative attitudes was 25.7%. After the intervention, those with negative attitudes decreased to 14.4%, and the attitude score of those who had a positive attitude before intervention improved from 74.3 to 85.7%.

A study in 2020 found that cognitive-behavioral therapy altered dysfunctional attitudes and irrational beliefs in infertile women [27]. CBT could also improve the infertile individuals' attitude toward child adoption in this clinical trial.

STUDY LIMITATION

Lack of access to infertile people referring to private treatment centers was the limitation of this research. People who go to governmental centers are usually middle and lower economic levels. Also, most people who come from small towns (cities) for infertility treatment go to governmental centers. Therefore, since the study was conducted in a governmental infertility treatment center, there is no information about clients referred to a private center economically and perhaps socially different.

Conclusions

According to the results, infertile individuals in the intervention group and participated in CBT sessions changed their attitude toward child adoption. They found child adoption as another way of being parents other than going for infertility treatment and looking forward to Assisted reproductive technology (ART), which is a complicated, long, and stressful process. Since adopting a child can have mutual benefits and both a couple has a child and a homeless child is supported and cared for by parents, it is better to talk about adoption in pre-infertility treatment counseling.

Ethical approvals

The study was granted approvals by the Research Ethics Committee (IR.KMU.REC13970114) and the clinical trial code is (IRCT20151103024866N10). Informed consent was obtained from all participants.

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Conflict of interest statement

Authors must fully disclose any existing or potential conflicts of interest of a financial, personal or any other nature that could affect or bias their research. If applicable, authors are also requested to describe the role of the funding source(s) in the study design, data acquisition, analysis and interpretation, and writing of the manuscript. No potential conflicts of interest must also be explicitly stated.

Authors' contributions

The individual contributions of authors to the manuscript should be specified in this section.

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OVERVIEW

Vaccination in the 19th century in Italy and the role of the catholic church in public health: a historical overview

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Key words

Smallpox • History of medicine • Pope Leo XII • Vatican State • Vaccine • Vaccination • Public health ethics

Summary

Using the case of the vaccine against smallpox as an example, this article explores how the attitude and the politics of the Vatican State towards vaccination changed between the 18th and 19th century.

Despite some notable exceptions, the Catholic Church became progressively involved in supporting vaccination in Italy, exerting its temporal and spiritual authority to develop healthcare policies and to convince a population that still considered the vaccine as potentially harmful.

The brief historical overview on vaccine and vaccination shows that during the XIX century the Catholic church and in particular,

the political decision of the Pope, engaged temporal and spiritual power, high authority and persuasive influence to encourage the population, more than anyone the hesitant people, to get vaccine against smallpox.

Although with the due differences determined by the path of time and by the scientific, educational and social advances of modern-day, this view from the past can provide us, with actual COVID pandemic, a reason of deep thinking and also how to face the present COVID-19 pandemic and to prepare for forthcoming future.

Actually, it shows us how the terrible smallpox epidemic was handled and finally overcome, thanks to vaccination.

In the 19th century, medicine was deeply influenced by the introduction of vaccination in Europe. For the first time in history, humanity could face infective mass diseases. However, in the beginning, not everyone shared this optimistic view on the efficacy of vaccination in preventing the spread of infections.

In this article, we evaluate the attitudes and politics adopted by the Vatican State on the vaccination against smallpox.

In the 18th century, the Catholic Church, through his chief Pope Benedetto XIV (1675-1758), indirectly gave its support in the fight against smallpox by promoting vaccinations through homilies at Mass, aimed at convincing people to accept the inoculation. However, in this period the Church generally showed great caution and adhered slowly to the practice of vaccination:

“The Popes are the last to innovate in these things. The slowness of their steps must reflect their age alongside their dignity. If I were an emperor or a king, because of the advantages that I see, the inoculation would now be allowed in my territories but I don’t want to alarm those who are shy and weak” [1].

In the early 19th century, after the discovery of the cowpox vaccine by Edward Jenner (1749-1823) [2], the Vatican State became progressively involved with vaccination [3].

In one of his letters to Jenner, Joseph Marshall, a medical officer who had set up “Jennerian” institutes in Gibraltar

and Malta [4], declared:

“It was not unusual to see in front of the hospital a procession of men, women, and children, during the day of public inoculation, conducted through the streets by a priest carrying a cross” [5].

Not without irony, the author of this letter noted how the population considered the vaccination *“a blessing sent from the Heaven, discovered by one heretic and practiced by another”*.

Even in the clergy, there were different attitudes towards vaccination.

In 1808, the Archbishop of Turin Giacinto della Torre (1747-1814) wrote a pastoral letter to warn against the common belief that considered the inoculation of an animal liquid in a man to be immoral and unnatural:

“Is it not true that men drink milk from cows and eat the meat without considering these substances dangerous in any way? There is, therefore, no risk of contamination with cows using their pus to prevent the spread of smallpox” [6].

In 1809, in Bari, the Superintendent of Calabria Citeriore noticed the negative attitude of the clergy towards vaccination; thus, he promised a reward to those priests who had distinguished themselves in spreading vaccination:

“The Government will always distinguish those priests, who will demonstrate the utmost zeal and commitment to the propagation of the vaccine inoculation. The official praise of their conduct will bring their names to the ear

Fig. 1. The portrait of Pope Benedetto XIV (1675-1758).



of His Majesty, which will be able to distinguish and recompense them with his sovereign magnificence” [7].

In 1810, in Cerignola, Apulia, priests, and physicians worked together in supporting the practice of vaccination, emphasizing their advantages for the population: very often, they personally inoculated the vaccines [8].

The collaboration between clergy and doctors reached its peak in 1822 with the creation of the municipal councils that included priests.

In 1824, Luigi Sacco (1769-1836) was awarded the membership of the Golden Spur (conferred to those who committed to spreading the message of the Church) for his contribution to the mass vaccination that had occurred the same year.

In 1822, the smallpox vaccination became mandatory in the papal territories following the law, promulgated by Pope Pius VII (1742-1823), inspired by Cardinal Consalvi (1757-1824), and supported by Monaldo Leopardi (1776-1847) in the Recanati territories, central Italy, over which the pope had sovereignty. By that time, Leopardi, a philosopher, nobleman, politician, and writer who was one of the main Italian intellectuals of the counter-revolution, had already administered the vaccine to his children, providing a detailed evaluation of its usefulness. Monaldo Leopardi was the father of the famous Italian poet Giacomo Leopardi (1798-1837).

In 1823, after the death of Pius VII (1742-1823), Pope Leo XII (1760-1829) rose to the papal throne: he was nicknamed “the Pope of austerity” as he followed an economic policy aimed to reduce expenses and prevent the speculation in the Vatican State. On 15th of September 1824, after one year of the pontificate, he promulgated a circular that repealed the mandatory vaccination, making it optional (he was the first head of a state in Europe to take such a decision):

“It remains the obligation of Doctors and Surgeons to perform it free of charge [the smallpox vaccination],

to those who wish to fight against it, since this is the treatment and protection of a disease which, like all the others, they are compelled to cure” [9].

Hence, despite making vaccination optional, he prevented doctors from conscientious objection.

The possibility to choose whether to use vaccination or not was also related to economic reasons, as healthcare costs related to it were considerably high. In addition, with this statement, the pope attempted to get along with popular beliefs that were suspicious and skeptical towards vaccination.

Doctor Giacomo Tommasini (1768-1846) was one of the greatest opponents to this papal decision, following the anticlerical attitude showed by Giovanni Rasori (1766-1837), who in his *Rapporto sullo stato dell’Università di Pavia*, 1797, had compared the illicit trade of graduations to the sale of papal indulgences [10].

Giacomo Tommasini, who became director of the vaccine grafting commission of the Dukedom of Parma, Piacenza, and Guastalla, harshly criticized the Vatican’s attitude towards vaccination. In 1836, Tommasini claimed that the choice of Pope Leo XII had caused two smallpox epidemics in 1828 and 1835 and that they could have been prevented if vaccination had remained mandatory [11].

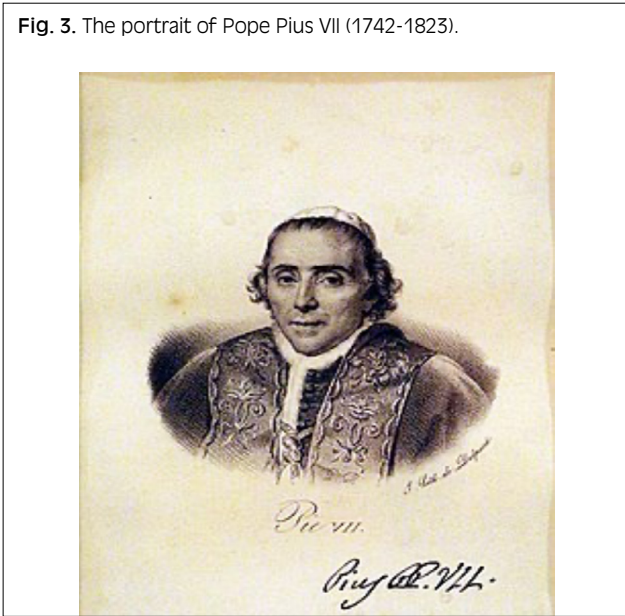
Tommasini examined the cases of smallpox in the Bolognese area between 1820 and 1828, discussing the spread of the epidemic and its manifestation. Specifically, his analysis emphasized that the smallpox epidemic occurring in Bologna in 1828 had caused a tremendous number of victims:

“In the year 1828, the course of the smallpox epidemic had other and more deadly consequences. It is not difficult to find the explanation for this, if we reflect on what we have mentioned above, namely that from the year 1822 to the year 1828 the vaccination was neglected. It is a pity that there is no exact statistic to reproach the unbelievers and the negligent, for which

Fig. 2. Portrait of Edward Jenner (1749-1823).



Fig. 3. The portrait of Pope Pius VII (1742-1823).



it would be possible to demonstrate, clearly and at a glance, how many deformed, how many blind, how many lame and how many deaths were due to the flu pox of that year. In the city of Bologna alone the deaths of smallpox from January to December of the year 1828 were 553. More frightening and exemplary would have been the figure of the sad consequences of having neglected the preventative measure of the Vaccination, if one had considered the massacre of the same epidemic in villages, in small lands, and the free countryside" [12].

The accusation made by Tommasini had some contradictory elements. Vaccination in the papal territory had been mandatory between 1822 and 1824 and optional from 1824 to 1828: if the inoculation of the smallpox vaccine had been neglected, there could be no correlation with the shift from mandatory to optional vaccination. In 1828 the number of deaths in the city of Bologna, compared to the number of people living in the city, remained low; moreover, Alfonso Corradi (1833-1892) mentioned whooping cough and not smallpox as one of the main causes of death [13]. Finally, concerning mortality in the countryside, Tommasini himself referred that vaccine inoculation was often poorly performed:

"And let's say it exactly, as twice we visited the people vaccinated by certain country health officials, of whom we praise the zeal and deplore the ignorance, who - not believing the vaccine matter was good unless the suppuration of the pustules was not in an advanced state - instead of grafting the vaccine pustule, produced abnormal pustules, which sometimes degenerated into sordid ulcers and very difficult healing" [14].

Although the number of rural deaths could not be a direct consequence of optional vaccination, at that time, especially in the abovementioned areas, people frowned upon the vaccination.

In 1819 the Duchess Maria Luigia (1791-1847), ruler of the territories of Parma, Piacenza, and Guastalla, where Giacomo Tommasini held the position of protomedic,

expressly requested the collaboration of the clergy with a decree:

"At the same time and immediately having begun the operations necessary to carry out the vaccination, you will write a circular letter to the Most Illustrious and Reverend Bishops of Parma, Piacenza, Borgo San Donnino, and Abbot of Guastalla, to participate in these My Dispositions, to assure them in My Name of the full confidence that I place in them, so that for their part, and with the voices of persuasion, and with the commandment if necessary, by their subordinate Archpriests, Provosts, Parish Priests, Parish Rectors, etc. they explain to the parishioners the good of these dispositions, and inspire in their obedience to the orders given to them only for their own advantage, to which aim all the aims of My Ordinations tend. These parish priests will also advise the people about the days, hours, and places of vaccination. I know that many of them have lent themselves with true Christian charity in the other periods of vaccination in this State; I, therefore, reserve the right to send some proof of My Sovereign gratitude to any of them, who will be worthily distinguished with this activity" [15].

In addition, the decree considered ten thousand vaccinated individuals as the goal of a vaccination campaign throughout the duchy: *"Calculating approximately 500 per 10,000, that would be forty times that amount, namely 20,000, the vaccinated people of the State, but I would rather believe in less than more. If half of them could be vaccinated in this year it would be a great advantage to the population of My Duchies, and it is My firm intention to bring this to effect"* [16].

Vaccination campaigns in the territories where vaccination was mandatory were so difficult to carry out that the four doctors who had performed more inoculations received a reward: *"The four Doctors or Surgeons, one for each Duchy, and one for the Valtarese region, who will have distinguished themselves more in this operation, and*

Fig. 4. The portrait of Pope Leone XII (1760-1829).



will have vaccinated more individuals (according to the country they had to travel, and the locality) will receive a check, as an extraordinary gratification from My Treasure, for this good duty that they exercised above the others” [17].

In this complex context, Tommasini's attack against the Pope is of particular interest and may have different reasons. In 1828, while holding the teaching chair in Bologna (at the time under papal control), Tommasini was accused of being a Carbonaro by the Vatican; during the legal process Tommasini succeeded in proving his innocence, but this incident led him to move away from the Bolognese territories. Furthermore, his strong friendship with the Italian writer Giacomo Leopardi (DATE), Monaldo's son, may have led Tommasini to clash with the Pope, as he had removed the previous promulgation long supported by Monaldo himself. In conclusion, this brief historical overview shows that throughout the 19th century the Catholic Church employed its temporal and spiritual authority to convince the population to accept inoculation and to develop vaccination politics.

Conflict of interest statement

The Authors declare no conflict of interest.

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Authors' contributions

MM and GR designed the study, conceived and drafted the manuscript; MM, GR, FB revised the manuscript. MM, GR performed a search of the literature, MM and FB complete linguistic revision. All Authors critically revised the manuscript. All Authors have read and approved the latest version of the paper for publication.

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- [6] Pastoral letter of Giacinto della Torre del 26 luglio 1808. “Non è forse vero che gli uomini bevono il latte delle mucche e ne mangiano le carni senza che tali sostanze noccano loro in alcun modo? Non vi è pertanto alcun rischio di contaminarsi con i bovini utilizzando il loro pus per prevenire l'insorgenza del vaiolo”.
- [7] ASBa, Sanità pubblica, 2 1806-1846, fasc 15/1 circolare dell'intendente ai giudici di pace, sindaci e parroci della provincia del 24 febbraio 1809: “Il Governo distinguerà sempre que' sacerdoti, i quali dimostreranno il massimo zelo ed impegno per la propagazione dell'innesto vaccino. Le ufficiali rimostranze di questa loro condotta farà giungere I loro nomi all'orecchio di Sua Maestà, la quale saprà distinguerli e compensarli colla sua sovrana munificenza”.
- [8] Lettera del Sottocomitato di vaccinazione di Cerignola all'intendente del 31 marzo 1810.
- [9] Leone XII, 15 September 1824. “Rimane obbligo a Medici e Chirurghi condotti di eseguirla gratuitamente [la vaccinazione antivaiolosa], a quanti vogliano prevalersene, essendo questa la cura ed il preservativo di una malattia alla quale, come a tutte le altre, essi hanno l'obbligo di riparare.”
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- [12] Tommasini G. Raccolta completa delle opere mediche, Vol. 7. Bologna: Tipografia dall'Olmo e Tocchi 1836, pp. 22-23. “Nell'anno 1828 il corso dell'epidemia vaiuolosa ebbe ben altre e più luttuose conseguenze. Non si stenta a trovare di ciò la spiegazione, se si rifletta a quello che noi abbiamo superiormente accennato, e cioè che dall'anno 1822 all'anno 1828 la vaccinazione fu trasandata. Egli è un peccato, che non si abbia una statistica esatta da rimproverare agl'increduli ed ai neglenti, per la quale chiaramente ed a colpo d'occhio si vedesse, quanti deformati, quanti ciechi, quanti storpi e quanti morti si dovessero all'influenza vaiuolosa di quell'anno. Nella sola città di Bologna I morti di vaiuolo dal gennaio al dicembre dell'anno 1828 sommarono 553. Più spaventosa ed esemplare sarebbe stata la cifra delle triste conseguenze dell'aver neglimentato il preservativo della Vaccinazione, se si fosse tenuto conto della stragge della stessa epidemia ne' villaggi, nelle piccole terre e nella libera campagna”.
- [13] Corradi A. Annali delle epidemie occorse in Italia, Vol. 4. Bologna: Tipografia Gamberini e Parmeggiani 1877, p. 983.
- [14] Tommasini G. Raccolta completa delle opere mediche, Vol. 7. Bologna: Tipografia dall'Olmo e Tocchi 1836, p. 22. “E diciamo esattamente perchè due volte ci siamo trovati nel caso di visitare I vaccinati di certi uffiziali di Sanità di campagna, de' quali lodiamo lo zelo e deploriamo l'ignoranza, che non credendo buona la materia vacina se la suppurazione delle pustole non era bene inoltrata, invece d'innestare la pustola vaccina, producevano pustole anomali, che qualche volta degeneravano in ulcere sordide e di guarigione difficilissima”.
- [15] Sovereign disposal regarding vaccination 1819, 31 July 1819, pp. 4-5. “Contemporaneamente e subito incominciate le operazioni necessarie per eseguire la vaccinazione, ella vorrà scrivere una lettera circolare agli Illustrissimi e Reverendissimi Signori Vescovi di Parma, Piacenza, Borgo San Donnino, e Abate di Guastalla, per partecipar loro queste Mie Disposizioni, per assicurarli in Nome Mio della piena confidenza che in essi ripongo, ed affinché dal canto loro, e colle voci della persuasione, e col comandamento se fia duopo, dai loro subordinati Arcipreti, Preposti, Parrochi, Rettori ecc. delle Parrocchie facciano spiegare a' Parrocchiani il bene di esse, ed ispirino in essi l'ubbidienza agli ordini dati a solo loro vantaggio, al quale scopo tendono tutte le mire delle Mie Ordinazioni. Per essi Parrochi si potrà anche far avere cognizione dei giorni, delle ore, e dei

luoghi della vaccinazione. So che molti di essi si sono prestati con vera carità cristiana nelle altre epoche della vaccinazione in questo Stato; mi riservo quindi di far pervenire ad alcuno di loro, che si sarà sotto questo rapporto meritevolmente distinto, qualche prova della Mia Sovrana gratitudine”.

- [16] Sovereign disposal regarding vaccination 1819, 31 July 1819 pp. 2-3. “Calcolando approssimativamente a 500 per 10.000, sarebbero quaranta volte tanto, ossia 20.000 I vaccinandi dello Stato, ma crederei piuttosto in meno che di più. Se in quest’anno si potesse vaccinarne la metà sarebbe un gran vantaggio alla

popolazione de’ Miei Ducati, ed è Mia ferma intenzione di portare ciò ad effetto”.

- [17] Sovereign disposal regarding vaccination 1819, 31 July 1819 p. 4. “I quattro Medici o Chirurghi, uno per ogni Ducato, ed uno per il Valtarese, che si saranno maggiormente distinti in questa operazione, ed avranno vaccinati più individui (proporzione fatta per paese da percorrere, e della località) riceveranno un assegno, come gratificazione straordinaria per una volta dal Mio Tesoro, per questa loro bene esercitata incombenza al di sopra degli altri”.

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ORIGINAL ARTICLE

Association between ABO and RH blood groups and Hepatitis B virus infection among young Nigerian adults

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Key words

Hepatitis B Virus • Blood groups • ABO • Rh antigen • Adolescents • Nigeria

Summary

Background. Several diseases are reported to be associated with ABO/Rh blood groups. Data on the association between ABO and Rh D blood group antigens in the Nigerian population is sparse. This study aimed at determining the prevalence of Hepatitis B Virus (HBV) infection as well as its association with ABO and Rh D antigens among young Nigerian adults.

Methods. Whole blood was collected from 496 students and screened for the presence of HBsAg using an immuno-chromatographic technique. The ABO and Rh D antigen status of participants were also determined using standard techniques.

Results. In this study, the prevalence of HBV infection was 10/496 (2.10%). Of all factors assessed, only age of participants was identified as a risk factor ($P < 0.05$) for HBV seropositivity. Over half

257/496 (51.5%) of subjects were of the blood group O type, while 18/496 (3.6%) were of the AB blood type which was the least in occurrence. Rh D negative blood group was observed among 24/496 (4.8%) subjects. Those with the B blood type were observed to have an insignificantly ($P > 0.05$) higher prevalence of HBV infection. However, with respect to Rh D antigen alone, participants negative for the antigen were observed to have a five times higher risk of acquiring HBV infection than those positive for it ($OR = 5.273$, $95\% CI = 1.056, 26.321$, $P > 0.05$). Combining the ABO and Rh blood group systems, an association ($OR = 20.174$; $P > 0.05$) was found to exist between B Rh D negative status and HBV infection.

Conclusion. Possession of B antigen without Rh D antigen is associated with increased risk of acquiring HBV infection.

Introduction

Amongst several other blood group systems, the ABO and Rh blood group systems stand out as the most important in medicine today. The phenotypes of the ABO blood group system, A, B, AB and O, are determined by the presence or absence of one or both of A and B antigens on host red blood cell membrane. The Rh blood group system is highly pleomorphic containing about forty four different antigens, and is the second most important system to the ABO [1]. Of all the pleomorphic forms, the presence or absence of the Rh D antigen on red blood cell of the host is the most significant [1]. The presence or absence of ABO and Rh antigens on an individual's red blood cell is genetically mediated [2, 3]. HBV is the leading cause of liver disease worldwide, accounting for over 360 million cases of chronic hepatitis and 620,000 deaths per year [4]. HBV infection is hyper-endemic in Sub-Sahara Africa (SSA) and a major cause of chronic liver disease [5].

The distributions of ABO and Rh antigens have been extensively researched and their frequencies observed to vary considerably with respect to ethnic and geographical differences [1]. Apart from being resident on red blood cell membrane, studies have shown that the ABO

antigens are heavily distributed on the surfaces of human cells including the epithelium, sensory cells, platelets, leucocytes, saliva, seminal fluid, gastric secretion [6, 7]. Reports indicate that blood groups can serve as receptors for some microorganisms, facilitating the spread and establishment of infectious diseases [8]. This underlines the clinical relevance of blood group antigens in several other diseases besides transfusion and transplantation disorders. Studies have reported an association between ABO antigens and risk for the development of infectious diseases, [9] including hepatitis B virus associated hepatocellular carcinoma [10].

Literature is awash of studies exploring the relationship between ABO/Rh blood groups systems with infectious and non-infectious disease, but little is known about the correlation between these variables and HBV infection. Conflicting reports exists on the role of ABO and Rh antigens on susceptibility to HBV infection, with many of these reports showing a geographical and racial bias [11]. To the best of our knowledge, only one study [12], conducted in 1992 has evaluated the relationship between ABO blood group and HBV infection in Nigeria. This study [12], focused on blood donors only. Data on the relationship between Rh D antigen and HBV infection in Nigeria is missing. Knowledge of the association of various blood group types and diseases amongst

different groups in a population can give useful direction for the articulation and implementation of individualized approaches to management and prevention of diseases. Against this background, this study aimed at determining the prevalence as well as the association if any, between HBV infection and ABO and Rh blood group types among young Nigerian adolescents.

Methods

STUDY POPULATION

The study was conducted among undergraduate students of Edo University Iyamho, Edo State, Nigeria. Established in 2016, the University presently has student strength of about 3500 distributed across six different faculties. A total of 496 students were enrolled for this study consisting of 302 females and 194 males. The age range of the participants was 18-25 years. The students were drawn from all faculties/college in the University.

SAMPLE SIZE DETERMINATION

The sample size was determined using the formula $n = Z^2 Pq/d^2$, where:

n = sample size

Z = Standard normal deviate = 1.96 at 95% confidence limit

p = prevalence of HBV in a previous Nigerian study = 12.5% = 0.125 [13].

q = 1- P ; = 1-0.125 = 0.875

d = error margin = 0.05

Computing the value above will give

$N = (1.96)^2 \times 0.125 \times 0.875 / (0.05)^2 = 168$.

Thus a sample size of 168 persons was obtained. However, to make room for non-responses and improperly filled and /or unreturned questionnaires, the sample size was increased to 496.

ETHICAL CLEARANCE

Approval was sought and obtained from the Ethical Research Committee of Edo University Iyamho, Edo State, Nigeria. Informed consent was obtained from all consenting participants before commencement of collection of blood. Inclusion criteria was been registered as a student of Edo State University, Uzairue, Edo State, Nigeria.

SAMPLE COLLECTION AND PROCESSING

Using a simple random sampling technique, a total of four hundred and ninety six (496) students were recruited for this study. Four milliliters of blood was collected from each consenting student and dispensed in an Ethylene-diamine Tetra acetic Acid (EDTA) container. Plasma obtained from the collected blood specimens were used for the serological detection of Hepatitis B surface antigen (HBsAg) using the immuno-chromatographic kits (Skytec Rapid Diagnostics USA), as previously described [14]. In brief, 20 μ l of each participant's serum was placed on the adsorbent portion of the Skytec Rapid Test Strip that had been removed from its foil and placed

on a flat surface. This was allowed to stand for 5 minutes after which it was observed for the emergence of bands at strategic positions. The emergence of a single band at the control portion of strip indicated a negative result, while the appearance of a band on the control portion and another on the test region of strip was indicative of a positive result.

ABO AND Rh D BLOOD GROUP DETECTION

The slide agglutination technique as previously described was used to determine the ABO and Rh blood groups [15]. Briefly, a drop of each participant's blood was placed on three separate areas on a clean white tile. Each drop of blood was mixed with a drop of commercially prepared antisera A, B, and D, and observed for agglutination. Each mixture (blood plus antisera) was viewed microscopically to confirm agglutination.

STATISTICAL ANALYSIS

The data obtained were analyzed using Chisquare (χ^2) or Fischer's exact test as appropriate and odd ratio analysis using the statistical software INSTAT®.

Result

The seroprevalence of HBV among study participants was 10/496 (2.01%). Age was identified as a risk factor ($P < 0.05$) for HBV seropositivity, with participants within the age group of 24-26 years having the highest risk of infection. Although male participants had a higher prevalence of HBV than female, the difference failed to reach statistically significant proportion ($P > 0.05$). With respect to marital status and religion, single students as well as those of the Moslem faith were observed to have a higher prevalence of HBV infection, albeit the difference was statistically insignificant ($P > 0.05$). Similarly, student's faculty/college did not significantly affect the prevalence of HBV infection in this study ($P > 0.05$) (Tab. I).

Over half 257/496 (51.5%) of the total number of study subjects were of the blood group O type. The distribution of A, B and AB blood types were 132/496 (26.6%), 89/496 (17.9%) and 18/496 (3.6%) respectively. Study participants with the B blood type had the highest prevalence 24/496 (4.5%) of HBV infection. No infection was recorded among participants of the AB blood type. Generally, the prevalence of HBV infection did not differ significantly ($P > 0.05$) with respect to ABO blood type. The absence of the Rh D antigen on red blood cell of study subjects was found to be associated with HBV seropositivity (Rh Negative vs. Rh Positive: 2/24 (8.33%) vs. 8/472 (1.69%); OR = 5.273, 95% CI = 1.056, 26.321) albeit, it failed to reach statistical significance ($P > 0.05$) (Tab. II).

A combination of ABO and Rh D blood groups revealed that only blood group B Rh D negative status was associated (OR = 20.714 95%CI = 0.800, 536.26; $P > 0.05$) with higher sero-prevalence of HBV infection (Tab. III).

Tab. I. Prevalence of Hepatitis B virus infection among study participants.

| Variables | N (%) | N. HBsAg positive (%) | OR | 95% CI | P value |
|--|------------|-----------------------|--------|----------------|---------|
| Age (years) | | | | | |
| 15-17 | 67 (13.5) | 0 (0.0) | | | 0.039 |
| 18-20 | 190 (38.3) | 3 (1.58) | | | |
| 21-23 | 138 (27.8) | 2 (1.45) | | | |
| 24-26 | 101 (20.4) | 5 (4.95) | | | |
| Gender | | | | | |
| Male | 175 (35.3) | 4 (2.28) | 1.228 | 0.342, 4.413 | 0.7473 |
| Female | 321 (64.7) | 6 (1.87) | | | |
| Marital status | | | | | |
| Single | 483 (97.4) | 10 (2.07) | 0.5987 | 0.0333, 10.761 | 1.000 |
| Married | 13 (2.6) | 0 (0.0) | | | |
| Religion | | | | | |
| Islam | 92 (18.5) | 2 (2.17) | 1.100 | 0.229, 5/270 | 1.000 |
| Christianity | 404 (81.5) | 8 (1.98) | | | |
| Faculty/college | | | | | |
| College of Medicine | 228 (45.9) | 5 (2.19) | | | 0.5891 |
| Faculty of Engineering | 57 (11.5) | 2 (3.51) | | | |
| Faculty of Arts Management and Social Sciences | 58 (11.7) | 0 (0.0) | | | |
| Faculty of Law | 93 (18.8) | 1 (1.08) | | | |
| Faculty of Science | 60 (12.1) | 2 (3.33) | | | |

N: number of subjects; OR: odd ratio; CI: confidence interval; Test statistics used: Chisquare (χ^2) or Fischer's exact test.

Tab. II. Prevalence of Hepatitis B virus infection with respect to ABO and Rh blood type.

| Variables | N. (%) | N. HBsAg positive (%) | OR | 95% CI | P value |
|--------------------------|------------|-----------------------|-------|---------------|---------|
| Abo blood type | | | | | |
| O | 257 (51.8) | 4 (0.78) | | | 0.3105 |
| A | 132 (26.7) | 2 (1.52) | | | |
| B | 89 (17.9) | 4 (4.50) | | | |
| AB | 18 (3.6) | 0 (0.00) | | | |
| Rhesus blood type | | | | | |
| Negative | 24 (4.8) | 2 (8.33) | 5.273 | 1.056, 26.321 | 0.079 |
| Positive | 472 (95.2) | 8 (1.69) | | | |

N: number of subjects; OR: odd ratio; CI: confidence interval; Test statistics used: Chisquare (χ^2) or Fischer's exact test.

Tab. III. Prevalence of Hepatitis B virus infection with respect to ABO and Rh Blood grouping.

| Blood group | N | No. HBsAg positive (%) | OR | 95% CI | P value |
|-------------|-----|------------------------|--------|---------------|---------|
| A + | 127 | 2 (1.57) | 0.578 | 0.026, 12.638 | 1.000 |
| A - | 5 | 0(0.0) | ND | ND | ND |
| B + | 84 | 2 (2.38) | 0.879 | 0.040, 19.275 | 1.000 |
| B- | 5 | 2(40.0) | 20.714 | 0.800, 536.26 | 0.059 |
| AB + | 18 | 0(0.0) | ND | ND | ND |
| O + | 243 | 4 (1.65) | 0.545 | 0.028, 10.623 | 1.000 |
| O - | 14 | 0 (0.0) | 1 | 1 | |

N: number of subjects; ND: not done; Test statistics used: Fischer's exact test.

Discussion

There is paucity of data on the prevalence and associated risk factors for HBV infection among young Nigerians. Although reports abound on the association of ABO and Rh blood group systems with disease, none have specifically focused on the relations between the blood group systems and HBV infection among young adults

in Nigeria. Against this background this study was conducted.

The finding of a HBV prevalence of 2.1% is consistent with a value of 3/300 (1.5%) recorded in an earlier Nigerian study [16]. Our finding is however at sharp variance with 37/800 (4.6%) and 47/407 (11.5%) reported in other African studies respectively [17, 18]. The observed variation in result may be due to

differences in geographical location of studies as the studies by Ekouevi *et al.*, 2015 [17], and Tesfa *et al.*, 2021 [18], were conducted in Togo and Ethiopia respectively. Students within the age group of 24-26 years had a significantly higher risk of being infected by HBV while younger participants in the age group of 15-17 years recorded no HBV infection. This observation is at variance with findings from a previous Nigerian study where undergraduate students less than 18 years were reported to have a significantly higher risk of HBV seropositivity than older ones [13]. It is however in agreement with a Togolese one [17]. Nigeria commenced her universal HBV immunization program in 2004 [19]. Although, the HBV vaccination history of our study participants were not noted at time of research, it is possible that students in the age category of 15-17 years are better beneficiaries of the young Nigerian HBV vaccination program in Nigeria. This may have accounted for the zero prevalence of HBV infection observed among them. In this study, gender, religion and faculty/college of participants were not found to significantly affect the prevalence of HBV infection. Findings from other studies [13, 16], have supported our observations.

The distribution of ABO blood types among study participants was O 257/496 (51.8%), A 132/496 (26.6%), B 89/496 (17.9%) and AB 18/496 (3.6%). A similar pattern has been reported by other African studies [1, 20]. One Asian study [21] however, documented blood group B as the most predominant blood type followed by O. while others [22, 23, 24] reported blood group A as the most common among their study populations. Of all participants examined in this study, only 4.8 percent were found to lack the rhesus D antigen. A Rh D negative prevalence of 6%, 7.2% have been reported by studies from Nigeria [25] and Ethiopia [26] respectively. Asia and Africa are generally known to have a low number of Rh D negative individuals [27]. Blood group types are inherited and its frequencies vary from one population to another [25]. This may explain the observed variation in blood types in the aforementioned studies.

Studies have reported an association between certain diseases and the ABO/Rh blood group systems. In this study, the prevalence of HBV was observed to be highest among participants with B blood type, followed by blood type A. Participants with blood type AB had no incidence of HBV infection. A similar trend had been reported by an earlier study [28]. However, findings from a meta-analysis study of thirty-eight articles showed the contrary with blood group B individuals reported to have the lowest risk for HBV [11]. The variation in result could be due to several reasons. Firstly, the study by Jing and his colleagues [11], focused on a disproportionately higher number of non-African studies, with only seven of them being from the African continent, out of which just two were from Nigerian. Again all thirty articles analyzed by Jing and his colleagues [11] focused on either blood donors or patients from hospital settings in contrast to our study population which comprised of young undergraduate students. Other studies [29, 30]

also had a different finding, with blood group A donors reported to have the highest prevalence of HBV infection. Reports have shown that blood antigens may serve as receptors for bacteria, parasites and viruses, leading to colonization and invasion of host or evasion of its immune system [31]. It is interesting to note that the preferences for histo blood group antigens by some microorganisms including *norovirus* and *Helicobacter pylori* are influenced by specific genotypes and subtypes [31, 32]. As the genotypes of HBV are geographically diverse [33]. It is possible that the variation in these reports could be attributed to differences in preferences of histo-blood group antigens by predominant HBV genotypes in these regions. Further investigations are however, needed to verify this.

Participants with blood type AB had the least prevalence of HBV infection in this study. Some studies [12, 28] have reported similar findings. The reason for this is unclear. Perhaps, the small size of samples of blood group AB tested may be responsible for this finding, or the co-existence of histo -antigens A and B on host cells may represent a resistance factor for HBV infection. This will definitely require further studies to verify. Generally, the prevalence of HBV was not significantly affected by ABO blood group system. This is contrasting to an earlier report [15].

The finding of a higher prevalence of HBV among Rh D negative subjects in this study has been previously reported by an Indian study [28]. Indeed, subjects that tested negative to the Rh D antigen in our study were observed to have a five times higher risk of acquiring HBV than their Rh positive counterparts in this study. It is however at variance a report elsewhere [15]. Basically, three molecular mechanisms have been reported for development of Rh D negativity namely, total deletion of the Rh D gene, (RHD), the presence of pseudo Rh D gene (RHD_s) (inactive) in association with ce allele in the RHCE, and the presence of hybrid gene, with the latter two mechanisms leading to the production of a non-functional Rh protein [3]. Interestingly, the expression of these forms has been reported to vary vastly with respect to race, location and tribe [3]. Genetic variations in human populations plus environmental factors contribute to susceptibility to infectious diseases [34]. Perhaps this could explain the variation in observations earlier reported. Generally however, the prevalence of HBV was not significantly affected by Rh status. This is in line with findings from other studies [28, 30].

Combination of the ABO and Rh D blood group systems, revealed an association between HBV sero-positivity and B Rh D antigen negative blood group. Indeed, a twenty times higher risk (OR = 20.714) for HBV sero-positivity was observed among participants with B Rh D negative blood group status. Interestingly, no such association (OR = 0.879) was found amongst subjects with B and Rh antigens. Findings from some studies points to the protective effect of Rh D antigen against Hepatitis B virus infection [20, 35]. Also, studies have reported a generally lower health status among persons who lack the Rh D antigen [36, 37]. Differences in blood

group antigen expression can increase or decrease host susceptibility to many infections [31]. Thus the observed pattern of result in this study may be as result of the concomitant effect of the expression of B antigen and the lack of Rh D antigen on their red blood cell of host. This definitely requires further study to substantiate. The gold standard for diagnosis of hepatitis B virus infection is the detection of HBV nucleic acid in blood or liver [38]. This study focused on the detection of HBsAg in blood serologically. This is a limitation in this study.

Conclusion

Generally, the prevalence of HBV infection was 2.01% among study subjects. Age was identified as a risk factor for HBV seropositivity. Subjects with Blood group antigen B but lacking the Rh D antigen were more at risk of acquiring HBV infection. These findings may prove valuable to health managers and planners in articulating and implementing HBV infection control strategies.

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Conflict of interest statement

Authors have no conflict of interest to declare.

Disclosure statement

The authors report no conflict of interest.

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Author's contribution

All authors took part in the study design, generated and analyzed data and substantively took part in the drafting of manuscript.

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ORIGINAL ARTICLE

Assessing influenza vaccination coverage and predictors in persons living with HIV/AIDS in Louisiana, June 2002-June 2013

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Key words

Influenza • Vaccination • HIV

Summary

Background. Despite the burden of disease and increased risk of influenza-associated morbidity and mortality among PLWHA, influenza vaccination has been understudied in this population.

Methods. We built an 11-year cohort of HIV-infected adults from medical records of PLWHA seeking care within the Louisiana State University medical system from June 2002-June 2013. Influenza vaccination uptake among PLWHA was calculated overall and for each medical facility for each influenza season. Linear regression was used to assess influenza vaccination uptake over time, both overall and by facility. Data were restricted to the final influenza season (2012-13) to assess predictors of PLWHA vaccination. Individuals were nested within medical facilities in order

to assess the amount of variability in influenza vaccination rates across medical facilities.

Results. Influenza vaccination uptake among PLWHA increased over the study period ($p < 0.01$). The overall proportion of PLWHA vaccinated during the 2012-13 influenza season was 33.7%. 37.9% of the variability in the model occurred at the facility-level.

Conclusions. Although there was an increase in influenza vaccination within the PLWHA cohort over the course of the study, vaccination rates remained low overall. Special efforts must be made to increase vaccination uptake among PLWHA, with particular focus on those within the population who are likely to be at highest risk. The substantial variability at the facility-level indicates that there are unmeasured facility-level factors that contribute significantly to PLWHA vaccination.

Background

Vaccine preventable diseases represent a significant yet avoidable burden on the United States (US) population. Influenza afflicts 5-20% of the US population in a given year [1]. For most of the population, infection with the influenza virus does not cause severe illness or lead to significant complications. However, for others there are significant sequelae associated with influenza, including hospitalization and death. It is estimated that 200,000 people are hospitalized due to influenza-associated complications and between 3,000 and 49,000 influenza-associated deaths occur per year in the United States, with the majority of morbidity and mortality experienced by the very young, the very old, and those with comorbid conditions, including persons living with HIV/AIDS (PLWHA) [2, 3].

The PLWHA population is of particular interest in Louisiana, with the metropolitan statistical areas (MSAs) of New Orleans (27.0 cases/100,000 persons) and Baton Rouge (26.9 cases/100,000 persons) ranking 4th and 5th in newly diagnosed HIV infections in the US in 2017 [4]. Nationally, the incidence of HIV infection has decreased in recent years, but there were still approximately 1.1 million people in the US living with HIV at the end of 2017, representing a significant portion of the population [4].

PLWHA are at increased risk for influenza-associated morbidity and mortality due to their immunocompromised status [5-11]. The influenza vaccine has been shown to be safe and effective in the prevention of influenza-associated illness and complications [6, 12-18]. As a result, influenza vaccination has been recommended in PLWHA since the early 1990s by the Advisory Committee on Immunization Practices (ACIP) and the United States Public Health Services (USPHS) and current guidelines recommend annual influenza vaccination for all PLWHA, regardless of immune system status [19-21].

Despite these factors, there are few studies that have attempted to quantify influenza vaccination uptake among PLWHA. The first study of influenza vaccination uptake in PLWHA was conducted in the early 1990s and revealed a vaccination rate of approximately 30% in PLWHA [22, 23]. Subsequent studies have shown uptake of influenza vaccination varies between 26.4% and 50.9% in the PLWHA population, with one study showing an influenza vaccination uptake of 55% and 57% in women with HIV/AIDS during the 2006-07 and 2007-08 influenza seasons, respectively [24-28]. Of the US studies that reported vaccination uptake among PLWHA, few describe predictors of influenza vaccination in PLWHA. Within this limited literature, predictors of influenza vaccination uptake in PLWHA are inconsistent.

Furthermore, those studies that evaluate predictors of influenza vaccination only do so at the individual level. Undoubtedly, there are higher level factors that also influence vaccination rates, including institutional policies and provider practices. The influences of institutional policies and provider practices on influenza vaccination uptake are demonstrable across a diverse body of literature [29-42]. While we cannot directly measure specific policies and practices, we are able to assess the influence of medical facility on vaccination uptake among PLWHA. Medical facilities are likely to vary both in the institutional practices that they implement and the beliefs and practices of the providers that they employ. The absence of analyses accounting for medical facility and other second level factors presents a significant gap in the literature.

The goals of this study are to (1) quantify influenza vaccination uptake among PLWHA, (2) analyze trends in PLWHA vaccination uptake over time, (3) assess the variability of PLWHA vaccination between medical facilities, and (4) determine what factors predict PLWHA vaccination.

Methods

STUDY DESIGN

We assembled an 11-year cohort of HIV-infected adults from electronic medical records of individuals seeking care within the Louisiana State University (LSU) medical system from June 2002 through June of 2013. The LSU medical system included seven medical centers in southern Louisiana, including Bogalusa (Bogalusa Medical Center [BMC]), Baton Rouge (Earl K Long Medical Center [EKL]), Independence (Lallie Kemp Regional Medical Center [LAK]), Houma (L.J. Chabert Medical Center [LJC]), New Orleans (Medical Center New Orleans/Interim LSU Public Hospital [MCL]), Lafayette (University Medical Center [UMC]), and Lake Charles W.O. Regional Medical Center [WOM]). Each of these medical centers provided primary care and specialty HIV care to PLWHA during the study period.

STUDY POPULATION

Patients included in this cohort had an HIV/AIDS ICD-9 diagnosis code (V098 or 042), were aged 18 years or older, and had a minimum of two visits to LSU medical centers during the study period. In yearly analysis, patients were required to be in care, which is defined as having a minimum of two visits during the preceding calendar year. These criteria resulted in a total sample size of 12,001, with a total of 4,586 PLWHA in care during the 2012-13 influenza season.

DATA SOURCE

During the study period, the LSU medical system used three different medical record systems. From 2002-2006, LSU medical centers used paper-based records. In 2006, these records were migrated into the newly developed electronic records system, Clinical Inquiry

(CLIQ). CLIQ was used to maintain medical records until 2012, when LSU medical centers began using the Epic system. All of the medical records in these systems were migrated to the HarmonIQ data warehouse, which was used to form the cohort used in this study.

OUTCOME

The outcome of this study was influenza vaccination status, which was defined as receipt of an influenza vaccine during a given influenza season (October 1st through March 31st). Patients were considered to have received an influenza vaccination if an influenza vaccination was documented in their medical records or was self-reported by the patient and documented by the provider. Prior to 2006, patients were not routinely asked whether they had received influenza vaccination in locations outside of the LSU medical system. From 2006-2012, under the new CLIQ system, providers were expected to either administer an influenza vaccination or to document receipt of an influenza vaccination in another location or refusal of an influenza vaccination. The post-2012 Epic system also allowed providers to document an administered vaccine or report of vaccination in a different setting.

Influenza vaccination status was dichotomized into a yes/no variable for each influenza season. The proportion of PLWHA who received an influenza vaccination was calculated by restricting the sample to PLWHA who were in care during the calendar year and dividing those with a reported vaccination by those without.

INDEPENDENT VARIABLES

LSU medical facility served as a second level unit in which individuals are nested. Select characteristics of included medical facilities are available in Tab I. Medical facility information was obtained from the 2011 LSU Healthcare Services Division (HCSO) Annual Report, which was the final published annual report by the organization (43). Individuals were assigned to a medical facility based on the medical facility where they had the most encounters over the years, apart from 2012-13. For that year, patients were assigned to a medical facility based on the medical facility they had the most encounters from January 2012 through June 2013. Encounters could be inpatient or outpatient visits. A complete list of independent variables can be found in Tab II, and includes demographics, healthcare related variables, cluster of differentiation four (CD4) counts, and conditions at increased risk for influenza-associated morbidity and mortality. Demographics considered for analysis included age, sex, and race. Age was recorded at last visit during the 2012 calendar year and was divided into three categories, aged 18-49 years, aged 50-64 years, and aged 65 years and older, based on age groups the Centers for Disease Control and Prevention (CDC) uses to report influenza surveillance data. Potential responses for sex included male or female. Due to the dominance of Black and White races in Southern Louisiana, race was categorized into racial/ethnic minority (Hispanic ethnicity, Black, and races other than White) and Whites.

Tab. I. Characteristics of medical facilities in the LSU Healthcare Network in Southern Louisiana.

| Facility Code | Location | Estimated Economic Impact (in Millions) | Full Time Employees | Medical Residents | Licensed Beds | Inpatient Admissions | Inpatient Days | Outpatient Encounters | Emergency Department Encounters |
|---------------|------------------|---|---------------------|-------------------|---------------|----------------------|----------------|-----------------------|---------------------------------|
| BMC | Bogalusa, LA | \$ 124.52 | 608 | 21 | 98 | 2,573 | 10,015 | 118,946 | 27,843 |
| EKL | Baton Rouge, LA | \$ 282.25 | 1,078 | 191 | 165 | 4,884 | 18,525 | 194,553 | 46,720 |
| LAK | Independence, LA | \$ 78.87 | 405 | 8 | 25 | 1,122 | 4,273 | 81,554 | 27,371 |
| LJC | Houma, LA | \$ 200.60 | 934 | 46 | 156 | 3,943 | 15,378 | 175,403 | 41,950 |
| MCL | New Orleans, LA | \$ 718.94 | 2,240 | 895 | 390 | 11,090 | 56,876 | 271,664 | 53,462 |
| UMC | Lafayette, LA | \$ 215.80 | 916 | 70 | 150 | 4,188 | 18,417 | 182,256 | 44,562 |
| WOM | Lake Charles, LA | \$ 87.72 | 396 | N/A | 74 | 938 | 3,782 | 94,598 | 27,211 |

BMC: Bogalusa Medical Center; EKL: Earl K. Long Hospital Center; LAK: Lallie Kemp Regional Medical Center; LJC: L.J. Chabert Medical Center; MCL: Interim LSU Public Hospital; UMC: University Medical Center; WOM: W.O. Regional Medical Center. Medical facility characteristics are based on the LSU Health Annual Report, which was last published in 2011.

A sizable portion of individuals had missing values for race (7.9%). These individuals were included in analysis as “unknown races” and compared against the racial/ethnic minority and White categories.

Healthcare related variables included insurance status, number of years in care, and number of encounters from January 2012 through June 2013. Insurance status was categorized into three groups: those with insurance (private, Medicare, and Medicaid), those receiving free care (LSU policy per state law designated that those with an income less than 200% of the federal poverty limit are eligible to receive free care at the public hospitals) or grants to cover their HIV management, and those without insurance or who were labeled as uncollectable debt (individuals from whom the medical center did not anticipate recouping money expended for care). Number of years in care was calculated by subtracting the patient’s date of HIV/AIDS diagnosis from the date of last visit and dividing the resulting number by 365. The number of encounters an individual had from January 2012 through June 2013 was measured by summing the total number of inpatient and outpatient encounters from any medical facility in the LSU medical system.

The last lab value available for a patient’s CD4 count was considered his or her CD4 count for the purposes of analysis. The CD4 counts were categorized based on HIV infection staging (CD4+ T-lymphocyte counts of > 500 cells/μL, 200-499 cells/μL, and < 200 cells/μL). A substantial proportion of the population was missing CD4 counts (18.8%). These patients were grouped into an unknown CD4 category and compared against those without missing CD4 values.

Comorbid conditions considered to be high risk for influenza-associated morbidity and mortality included chronic conditions such as diabetes status (type 1 and type 2), kidney disease (chronic kidney disease, nephritic syndrome, renal transplantation, hemodialysis, end stage renal disease), heart disease (heart failure, hypertensive heart disease, pulmonary heart disease,

heart valve disorders, arrhythmias, congenital heart defects, stroke), liver disease (cirrhosis, jaundice, viral hepatitis, hemochromatosis, Reye’s syndrome, Wilson’s disease), chronic lung disease (bronchitis, chronic bronchitis, emphysema, COPD, asthma, bronchiectasis), and all cancers. If a patient was diagnosed with any of these conditions, it was assumed from that point on that they were afflicted with the condition. If a patient had a diagnosis code for any of these conditions, they were considered to have at least one comorbid condition.

STATISTICAL ANALYSIS

PLWHA influenza vaccination uptake was calculated for each influenza season during the study period. Trends in influenza vaccination uptake were assessed using linear regression models, with vaccination uptake set as the dependent variable and influenza season as the independent variable. Regressions were performed for each medical facility, enabling a comparison in vaccination uptake between medical facilities. P-values of these models were used to assess the significance of these trends over time.

Data were restricted to the most recent available influenza season to assess the variability of influenza vaccination uptake among PLWHA between medical facilities and determine what factors predict PLWHA vaccination. Additionally, patients had to be in care to be considered for analysis. This resulted in a sample size of 4,586 for analysis.

In order to account for the differences in influenza vaccination status between medical facilities, a multilevel model with patients nested within medical facility was constructed. The multilevel models used in this study were random-intercept, which allowed the assessment of variability between facilities. A series of multilevel models, with each predictor variable individually, medical facility (2nd level variable), and vaccination status were used to generate unadjusted

ORs. To obtain adjusted ORs, vaccination status was regressed on all potential predictors in a full multilevel model. Medical facility was set as the second level unit of analysis. A crude intraclass correlation coefficient (ICC) was obtained from the full model. Predictors were eliminated from the model based on a threshold p-value of 0.05. When all the remaining predictors had p-values less than or equal to 0.05, adjusted ORs and an intraclass correlation coefficient (ICC) were obtained.

Inclusion of unknown values as additional comparison groups of a categorical variable can potentially bias the results of the analysis (44). In order to assess whether bias was present and the magnitude of the potential bias, a sensitivity analysis restricted to individuals with complete records was conducted. Removing those with missing values reduced the analytic sample size from 4519 to 3391 individuals. To obtain adjusted measures for the sensitivity analysis, vaccination status was regressed on all potential predictors in a full multilevel model. Predictors were eliminated from the model based on a threshold p-value of 0.05. When all the remaining predictors had p-values less than or equal to 0.05, adjusted ORs and an ICC were obtained.

All analyses were performed using SAS 9.4. This study was approved by the LSUHSC IRB (IRB#10178).

Results

Table I describes the characteristics of medical facilities included in this analysis. Although none of these data were included as predictors in the multilevel model and their statistical impact was not evaluated, they provide important context and relevant descriptions of included facilities. Estimated economic impact ranged from \$78.87 million in LAK to \$718.94 million in MCL. All other facility-related factors, such as number of full time employees (range: 396-2,240), number of medical residents (range: 0-895), number of licensed beds (range: 25-390), number of inpatient admissions (range: 938-11,090) and inpatient days (range: 3,782-56,876), number of outpatient encounters (range: 81,554-271,664), and emergency department encounters (27,211-53,462), correlated to the estimated economic impact of the medical facility. Facilities in urban areas, such as EKL in Baton Rouge (\$282.25 million) and MCL in New Orleans (\$718.94 million) had the highest economic impacts.

From a qualitative perspective, economic impact and all other corresponding factors did not appear to correlate to increased influenza vaccination uptake within facilities. For instance, MCL, the facility that serves the largest population, has the largest economic impact, the largest number of full time employees and medical residents, and so on, had an influenza vaccination uptake of just 10.6% among PLWHA during the 2012-13 influenza season. The two most successful facilities, LJC (PLWHA vaccination uptake: 74.7%) and WOM (PLWHA vaccination uptake: 58.8%) had the second and fourth lowest economic impacts of the facilities included in this study.

Fig. 1. The proportion of in care PLWHA adults reporting receipt of an influenza vaccination by year and facility, Southern Louisiana, June 2002 to June 2013.

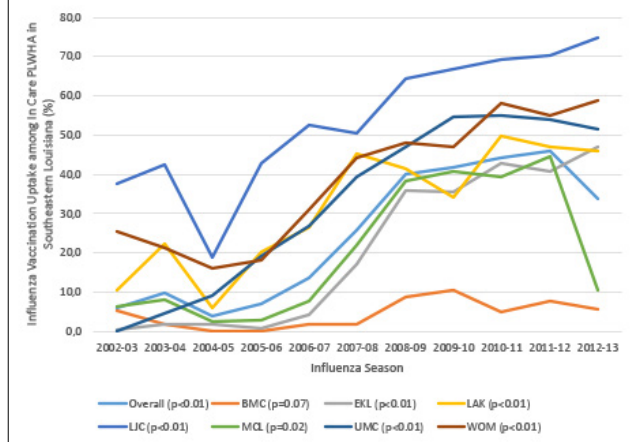


Figure 1 shows influenza vaccination uptake among PLWHA from the 2002-03 through the 2012-13 influenza seasons. Results are presented for overall influenza vaccination uptake and vaccination uptake by medical facility. With the exception of BMC (7.4% increase in influenza vaccination uptake), influenza vaccination uptake among PLWHA increased significantly from baseline over the study period within all medical facilities (EKL, 11,650.0% increase; LAK, 343.2% increase; LJC, 97.6% increase; MCL, 68.2% increase; UMC, 25,650.0% increase; WOM, 129.6% increase). Overall, PLWHA influenza vaccination uptake increased over the study period (471.2% increase), with a substantial increase in the 2006-07 and 2007-08 influenza seasons, stable rates until the 2011-12 influenza season, and substantial decrease in the 2012-13 influenza season. The decrease between the 2011-12 and 2012-13 influenza seasons was fueled primarily by a 76.3% decrease in influenza vaccination in MCL, the largest medical center in the LSU healthcare network. The proportion of PLWHA receiving influenza vaccination in LSU medical facilities followed the same general trend as the overall proportion of PLWHA, except for the 2012-13 influenza season. While the overall proportion of PLWHA receiving influenza vaccination decreased from the 2011-12 to the 2012-13 influenza seasons, EKL, LJC, and WOM all experienced increases of between 6.3-15.0% in PLWHA influenza vaccination uptake.

Table II shows the overall distribution of vaccination status, demographics, healthcare related variables, CD4 counts, and comorbid conditions at increased risk for influenza-associated morbidity and mortality as well as the relationship between the independent variables and vaccination status. The proportion of PLWHA who received an influenza vaccination during the 2012-13 influenza season was 33.7%. The majority of PLWHA were served by medical facilities in two major-metropolitan areas (Baton Rouge, LA and New Orleans, LA), MCL (40.0%), and EKL (29.4%). The majority of the population sample was aged 18-49 years (56.3%),

Tab. II. Characteristics of in care PLWHA in Southern Louisiana 2012-13, by vaccination status (n = 4586).

| Study Variables | Overall (n = 4586) n (%) | Vaccinated (n = 1547) n (%) | Unvaccinated (n = 3039) n (%) | p-value* |
|---|--------------------------------|-----------------------------------|-------------------------------------|----------------|
| Outcome | | | | |
| Vaccination | | | | |
| Vaccinated | 1547 (33.7) | N/A | N/A | N/A |
| Unvaccinated | 3039 (66.3) | | | |
| 2nd Level Variable | | | | |
| Medical Facility | | | | |
| MCL | 1834 (40.0) | 195 (10.6) | 1639 (89.4) | < 0.01 |
| BMC | 139 (3.0) | 8 (5.8) | 131 (94.2) | |
| EKL | 1345 (29.4) | 632 (47.0) | 713 (53.0) | |
| LAK | 230 (5.0) | 106 (46.1) | 124 (53.9) | |
| LJC | 277 (6.1) | 207 (74.7) | 70 (25.3) | |
| UMC | 624 (13.6) | 322 (51.6) | 302 (48.4) | |
| WOM | 131 (2.9) | 77 (58.8) | 54 (41.2) | |
| Predictors | | | | |
| Insurance Status | | | | |
| Uncollectable Debt/Uninsured | 1390 (30.7) | 247 (17.8) | 1143 (82.2) | < 0.01 |
| Free Care/Grant | 1092 (24.1) | 463 (42.4) | 629 (57.6) | |
| Insured | 2042 (45.1) | 824 (40.4) | 1218 (59.7) | |
| Sex | | | | |
| Female | 2004 (43.7) | 659 (32.9) | 1345 (67.1) | 0.28 |
| Male | 2582 (56.3) | 888 (34.4) | 1694 (65.6) | |
| Age | | | | |
| Aged 18-49 Years | 2581 (56.3) | 832 (32.2) | 1749 (67.8) | 0.05 |
| Aged 50-64 Years | 1748 (38.1) | 623 (35.6) | 1125 (64.36) | |
| Ages 65 Years and Older | 257 (5.6) | 92 (35.8) | 165 (64.2) | |
| Race | | | | |
| Non-White | 3236 (70.6) | 1098 (33.9) | 2138 (66.1) | < 0.01 |
| White | 986 (21.5) | 387 (39.3) | 599 (60.8) | |
| Unknown | 363 (7.9) | 62 (17.1) | 301 (82.9) | |
| Comorbid Conditions | | | | |
| No | 1759 (38.4) | 523 (29.7) | 1236 (70.3) | < 0.01 |
| Yes | 2827 (61.6) | 1024 (36.2) | 1803 (63.8) | |
| CD4 | | | | |
| < 200 | 736 (16.1) | 216 (29.4) | 520 (70.65) | < 0.01 |
| 200-499 | 1540 (33.6) | 534 (34.7) | 1006 (65.3) | |
| 500+ | 1449 (31.6) | 583 (40.2) | 866 (59.8) | |
| Unknown | 861 (18.8) | 214 (24.9) | 647 (75.2) | |
| Study Variables | Mean (SD) | | | p-value |
| Years in Care | 6.33 (4.02) | 6.58 (3.90) | 6.21 (4.08) | 0.05 |
| Encounters from January 2012-June 2013 | 15.01 (12.38) | 16.52 (11.37) | 14.24 (12.79) | < 0.01 |

n: population; N/A: not applicable; BMC: Bogalusa Medical Center; EKL: Earl K. Long Hospital Center; LAK: Lallie Kemp Regional Medical Center; LJC: L.J. Chabert Medical Center; MCL: Interim LSU Public Hospital; UMC: University Medical Center; WOM: W.O. Regional Medical Center. * Chi-squared tests used to calculate p-value for categorical variables and t-test used to calculate p-value for continuous variables.

male (56.3%), racial and ethnic minority (70.6%), insured (45.1%) or received free care or had care that was covered by a grant (24.1%), had at least one comorbid condition (61.6%), and had CD4 counts above 200 (65.2%). The mean number of years in care was 6.33 years (SD = 4.02) and the mean number of encounters from January 2012 through June 2013 was 15.01 (SD = 12.38). All potential predictors, including demographics, healthcare related variables, CD4 count, and conditions at increased risk for influenza-associated morbidity and mortality, with the exception of sex, demonstrated an unadjusted relationship with vaccination status ($p \leq 0.05$). Table III shows the unadjusted and adjusted ICCs, the unadjusted relationship between each of the predictors

and vaccination status in a multilevel model, and adjusted relationship between significant predictors and vaccination status in a multilevel model. The unadjusted model had an ICC of 0.377, indicating that 37.7% of the total variability in influenza vaccination uptake was between medical facilities. Even after accounting for significant individual-level predictors of vaccination status and compositional differences in these predictors across medical facilities, the ICC remained high, at 0.379. This result indicates that 37.9% of the total variability in influenza vaccination uptake was between medical facilities. Insurance status, sex, CD4 count, and number of encounters from January 2012 through June 2013

Tab. III. Unadjusted and adjusted relationships between predictive variables and vaccination status among in care PLWHA in Southern Louisiana, 2012-13 (n = 4519).

| Predictors | Unadjusted* OR (95% CI) | Adjusted** OR (95% CI) | Adjusted Sensitivity Analysis*** OR (95% CI) |
|--|----------------------------|---------------------------|--|
| Insurance Status | | | |
| Uncollectable Debt/Uninsured | Reference | Reference | Reference |
| Free Care/Grant | 1.46 (1.18-1.80) | 1.24 (0.99-1.54) | 1.20 (0.92-1.55) |
| Insured | 1.54 (1.27-1.86) | 1.34 (1.11-1.64) | 1.42 (1.13-1.78) |
| Sex | | | |
| Female | Reference | Reference | Reference |
| Male | 1.23 (1.07-1.42) | 1.21 (1.04-1.40) | 1.29 (1.09-1.52) |
| Age | | | |
| Aged 18-49 Years | Reference | N/A | N/A |
| Aged 50-64 Years | 1.18 (1.02-1.37) | | |
| Aged 65 Years and Older | 1.01 (0.75-1.36) | | |
| Race | | | |
| Racial and Ethnic Minority | Reference | N/A | N/A |
| White | 1.11 (0.93-1.33) | | |
| Unknown | 0.80 (0.58-1.11) | | |
| Comorbid Conditions | | | |
| No | Reference | N/A | N/A |
| Yes | 1.26 (1.09-1.46) | | |
| CD4 | | | |
| < 200 | Reference | Reference | Reference |
| 200-499 | 1.35 (1.09-1.67) | 1.41 (1.13-1.75) | 1.42 (1.13-1.78) |
| 500+ | 1.61 (1.30-1.99) | 1.70 (1.37-2.11) | 1.66 (1.32-2.08) |
| Unknown | 0.60 (0.47-0.77) | 0.66 (0.51-0.85) | Excluded |
| Years in Care[#] | 1.05 (1.03-1.06) | N/A | N/A |
| Number of Encounters from January 2012- June 2013[#] | 1.03 (1.02-1.04) | 1.03 (1.02-1.04) | 1.03 (1.02-1.04) |
| ICC | 0.377* | 0.379** | 0.395*** |

n: population; N/A: not applicable; OR: odds ratio; CI: confidence interval; ICC: intraclass correlation coefficient. Bolded values are significant at $p \leq 0.05$.
[#] ORs calculated as one unit offsets from the mean. * Model includes all potential predictors. ** Model includes insurance status, sex, CD4 count, and number of encounters from January 2012-June 2013. *** Model uses only complete cases (n = 3391) and includes insurance status, sex, CD4 count, and number of encounters from January 2012-June 2013.

remained significant predictors of vaccination status in the final model. Those who were insured (OR = 1.34, 95% CI [1.11, 1.64]) and who had free care or care covered by a grant (OR = 1.24, 95% CI [0.99, 1.54]) were more likely to receive an influenza vaccination than those who were uninsured. Males (OR = 1.21, [1.04, 1.40]) were more likely than females to receive an influenza vaccination. Those with CD4 counts higher than 200 were more likely to receive influenza vaccination (OR₂₀₀₋₄₉₉ = 1.41, 95% CI [1.13, 1.75]; OR₅₀₀₊ = 1.70, 95% CI [1.37, 2.11]), while those with unknown CD4 counts were less likely to receive an influenza vaccination (OR_{Unknown} = 0.66, 95% CI [0.51, 0.85]). Additionally, those with greater numbers of encounters from January 2012-June 2013 were more likely to receive an influenza vaccination (OR = 1.03, 95% CI [1.02, 1.04]).

The results of the sensitivity analysis are presented in Table III. The adjusted model in the sensitivity analysis contained the same predictors as the adjusted model in the primary analysis. The ORs describing the relationship between the predictors and the outcome did not differ substantially between the two models. The ICC in the sensitivity analysis (0.395) was slightly higher than the ICC in the primary analysis (0.379).

Discussion

Despite the safety and effectiveness of the influenza vaccine in PLWHA, the increased risk of influenza-associated morbidity and mortality in PLWHA, and the recommendation that PLWHA receive the influenza vaccine, influenza vaccination uptake among PLWHA was low across both facilities and influenza season. Annual influenza vaccination uptake among PLWHA seeking care within the LSU healthcare network (4.1-46.0%) was drastically lower than the recommended vaccination goal of 90% for those with high risk conditions [45]. However, the overall proportions of PLWHA receiving an influenza vaccination from 2007-08 through 2012-13 (25.8-46.0%) in the cohort were similar to those quantified in previous literature [24-28]. The increase in influenza vaccination uptake beginning in 2006-07 and extending through the end of the study period was likely attributable to Healthcare Effectiveness Programs implemented by HCSD. In 2006, HCSD built and implemented CLIQ, a hybrid system that combined medical guidelines, patient medical records, and clinical decision support tools to provide providers with real-time information on the patient. Multiple guidelines were built into the system, reminding providers to address

certain healthcare needs, including vaccination. HCSD also began implementing competitions among clinical leads and their teams within LSU medical facilities in an effort to improve quality metrics. Those that excelled in the Healthcare Effectiveness programs or showed drastic improvement in a particular area received awards from HCSD.

The 76.3% drop in influenza vaccination in MCL from the 2011-12 to 2012-13 influenza season is a particularly interesting result. Through data validation, we have ensured that this was not a data tracking error and that the drop in vaccination uptake is a true result. One possible explanation for the drop in vaccination proportions is the switch to the Epic healthcare records system. The Epic system contained many more areas of focus than the CLIQ system. It is possible that other portions of the HCSD Healthcare Effectiveness Program were prioritized over influenza vaccination, leading to lower vaccination proportions overall and specifically in MCL.

The adjusted, multilevel model showed that those with insurance or free care or care covered by a grant, those of male sex, those of CD4 counts higher than 200, and those with more encounters from January 2012 through June 2013 are more likely to receive the influenza vaccine. The limited research on the predictors of influenza vaccination in PLWHA provides an inconsistent profile of those who receive influenza vaccinations. Across studies, number of visits is predictive of influenza vaccination [24, 25, 27, 28]. Insurance status, increased CD4 count, and male sex have all been identified in one or more studies as significant predictors of influenza vaccination [24, 25, 27, 28]. Predictors found significant in other studies, including age and race, were found to be non-significant among PLWHA in the LSU healthcare system [24, 25, 28].

Insurance status, sex, CD4 count, and number of encounters logically correlate with higher vaccination rates. An increased number of visits indicates that a patient is more engaged in care, potentially has additional risk factors that would indicate influenza vaccination, and has an increased opportunity to receive a provider recommendation, which has been shown to be predictive of influenza vaccination across studies [38, 39, 41, 42]. Those who are insured or receive free care or care covered by a grant are more likely to have access to medical care, visit the medical facility with regularity, receive a provider recommendation, and receive an influenza vaccine as a result. Men were more likely than women to receive a vaccination in our sample. This may be due to unmeasured confounders such as income, education, employment, and other socio-economic or demographic factors that typically correlate with gender. Those with higher CD4 counts were more likely to receive an influenza vaccination, despite the fact that those with lower CD4 or unknown counts are more likely to experience influenza-associated morbidity and mortality [8, 46, 47]. Lower or unknown CD4 counts potentially indicate increased non-adherence to HIV-related care and preventive care in general, which would include influenza vaccination.

The multilevel model indicated that there was a large amount of unexplained variance (37.9%) in vaccination uptake across medical facilities. The large proportion of unexplained variance at the facility-level suggests that there are unmeasured factors at the facility-level that are contributing to the overall difference in vaccination rates among PLWHA. The qualitative characteristics of the medical facilities do not seem to offer any clear patterns that would contribute to the different influenza vaccination uptake between facilities. As such, it is likely that differing institutional policies and provider beliefs and practices between the facilities either promote or inhibit influenza vaccination uptake. Although we cannot measure these institutional policies and provider practices and beliefs, we can make inferences based on what we know about the programs. All of the hospitals in the LSU health system were managed by HCSD and used the same EHR. This would indicate that tactics such as standing orders, electronic alerts, quality improvement programs, and others would be the same between the hospitals. However, there is no way to tell if each of the programs initiated by HCSD were implemented and prioritized to the same degree. Also, there are efforts that could have been undertaken by each of the hospitals, such as making efforts to reduce out-of-pocket costs to patients, sending patient reminders, piloting incentive programs within the PLWHA population, and providing assessment and feedback to providers. Additionally, there are factors that likely varied with respect to providers, such as knowing how to bill for vaccinations, lack of time with patients, prioritization of other health conditions over the influenza vaccine, and not consistently recommending the influenza vaccine. In any case, the amount of variation occurring at the facility-level is substantial, indicating that understanding what is occurring at these higher levels is absolutely essential to understanding differences in influenza vaccination uptake among PLWHA.

The adjusted sensitivity analysis did not reveal any substantial differences from the primary analysis. This suggests that inclusion of the “unknown” categories in the race/ethnicity and CD4 count variables did not bias the adjusted measures produced by the adjusted multilevel model. Therefore, we elected to keep the “unknown” categories in order to maintain a larger sample size.

LIMITATIONS

This study is subject to several limitations. Outcome assessment was based on patient medical records. Although these medical records allowed providers to indicate whether a patient had received a vaccination in a location outside of the medical facility, there is no guarantee that providers consistently input this information, and the degree of this inconsistency cannot be quantified. This would result in individuals being misclassified as unvaccinated, which would artificially suppress the proportion of individuals who received influenza vaccination. These effects are minimized because the LSU medical facilities were the source of

primary care for most patients and the patients included in this study were classified as in care. The combination of these factors reduces the likelihood that patients would receive influenza vaccination in settings other than LSU medical facilities. In any case, the estimates in this paper provide a conservative estimate of the overall influenza vaccination rates in the HIV population.

The use of medical records limited the number of potential predictive variables included in the multilevel model. Notably, certain demographic and socioeconomic variables, such as income, education, and employment, among others, were not recorded in the medical records but have been shown to influence influenza vaccination among non-PLWHA adults [40, 48-52]. Furthermore, reasons why influenza vaccination was not received were not recorded or captured in the medical records. Negative attitudes and beliefs and structural barriers influence an individual's choice to receive an influenza vaccination but were unable to be assessed given the data source [50, 53, 54].

There were clear differences in the proportion of PLWHA who received influenza vaccination by medical facility. These differences are likely due to unmeasured institutional policies and provider beliefs and practices. Due to the limitations of the data, the unmeasured factors could not be identified and their influence could not be quantified.

The demographic composition of the cohort used in this study was primarily racial/ethnic minority, with the large majority of racial and ethnic minorities being Black. These demographics, combined with the use of medical records, may indicate that this cohort is not generalizable to the rest of the United States, particularly of White Hispanics and those who are not in care.

STRENGTHS

This study uses a large cohort of HIV-infected individuals ($n = 12,001$) to assess influenza vaccination uptake among PLWHA over time, to assess predictors of influenza vaccination, and to assess facility-level variability in influenza vaccination. The results of this study provide the most up-to-date analysis of the predictors and influenza vaccination uptake in the PLWHA population and was the first study to assess the influence of medical facility on influenza vaccination among PLWHA.

Conclusions

Despite the recommendation that PLWHA should universally receive the influenza vaccine, the proportion of PLWHA who received the vaccine remained low over the course of this 11-year period. Moreover, those PLWHA who were not receiving the influenza vaccine, including those with low or unknown CD4 counts, those who are uninsured, and those with fewer numbers of encounters are those who are more likely to be at risk of influenza-associated morbidity and mortality. Special efforts must be made to increase influenza vaccination

rates in the PLWHA population, particularly among those who are at highest risk. There was also clear variation by medical facility in this study, even though all facilities were managed by the same entity. This indicates a need for universal standards for PLWHA influenza vaccination across medical facilities and a method to evaluate these standards must be developed.

There is significant room for further research on these topics, particularly as it relates to the barriers and facilitators of influenza vaccination in PLWHA. Medical records cannot be used to ascertain the reasons why individuals are not being vaccinated, whether it be negative attitudes and beliefs regarding the influenza vaccine, structural barriers to vaccination, or other reasons. The high variability at the facility-level indicates that institutional policies and provider beliefs and practices influences individual PLWHA influenza vaccine uptake. Future research should be dedicated to identifying these higher level factors. Identifying barriers to influenza vaccination is the key to increasing overall influenza vaccination rates within the PLWHA population.

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Conflict of interest statement

None of the authors report any conflict of interest.

Authors' contributions

PM conceptualized, designed, and implemented this study. He supervised the establishment of the PLWHA cohort, performed all data analyses, and authored the manuscript. AR aided in study design and provided feedback on the analyses and manuscript. SB advised on the multilevel analyses conducted in this manuscript. She also provided feedback on the manuscript. JC assisted in establishing the cohort of PLWHA seeking care at LSU hospitals. EP and SSB aided in study design and provided feedback on the analyses and manuscript.

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ORIGINAL ARTICLE

Effect of epidemic management and control plan on COVID-19 mortality in Iran: an interrupted time series analysis

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Key words

COVID-19 • Control Measures • Iran • Mortality

Summary

Background. Globally, several measures have been taken to decrease COVID-19 mortality. However, the effectiveness of preventive measures on the mortality related to COVID-19 has not been fully assessed. Thus, the present study aimed the present study aimed to assess the success of COVID-19 epidemic management and control plan on the mortality associated with COVID-19 in Iran from February 19, 2020, to February 5, 2021.

Methods. In the current quasi experimental study an interrupted time series analysis of daily collected data on confirmed deaths of COVID-19 occurred in Iran and in the world, were performed using Newey ordinary least squares regression-based methods.

Results. In Iran, the trend of new deaths increased significantly

every day until 24 November 2020 according to pre-intervention slope of [(OR 1.14, 95% CI 0.96 - 1.32,); $P < 0.001$]. The occurrence of new deaths had a decreasing trend after November 24, 2020, with a coefficient of [(OR -5.12, 95% CI -6.04 - -4.20), $P < 0.001$]. But in the global level daily new deaths was increasing before [(OR 18.66, 95% CI 14.41-2292; $P < 0.001$)] and after the 24 November 2020 [(OR 57.14, 95% CI 20.80 - 93.49); $P: 0.002$].

Conclusions. Iranian COVID-19 epidemic management and control plan effectively reduced the mortality associated to COVID-19. Therefore, it is essential to continue these measures to prevent the increase in the number of deaths.

Introduction

The number of deaths from COVID-19 continues to increase universally, and the first COVID-19 death was formally reported in Iran on February 19 2020 [1]. On March 1, the Ministry of Health and Medical Education (MOHME) stated 135 new deaths [2]. On March 20 (Nowruz; The first day of the Iranian New Year), 149 deaths were reported. On April 4 (The day after the Iranian New Year holidays), daily new deaths had increased to 158 [2]. On June 14, daily deaths touched over 100, with 107 deaths reported [2]. This reduction is stated to be due to a social distancing started formally by the Iranian government in late March 2020 of to March 2020 [3]. On June 29, MOHME reported a new record figure of deaths in a day, with 162 deaths [2]. On July 7, the number of fatalities jumped by 200 deaths [2]. On October 19, 2020, Iran topped the list with 337 new deaths [2]. October 28 On November 16, another rise of 486 deaths was reported [2]. According to some mathematical models, the number of daily deaths in the country in December was predicted to reach more than 800 per day [4]. To deal with this terrible increase in the number of deaths from the disease, on November 10 Nov, the COVID-19 epidemic management and control plan was implemented by the MOHME in a family-oriented manner [5]. The plan's goal was to break the transmission chain and reduce deaths from COVID-19

disease with the help of non-governmental organizations (NGOs) and through supportive coverage of high-risk groups in the community [5]. As of November 21, over 1.4 million out of 3 million families in Tehran have undergone screening [5]. The plan is designed in three phases of care, support, and monitoring [5]. In the support phase, to cut the transmission chain and reduce the contact of infected people, through which, 40 centers in Tehran receive COVID-19 patients who cannot quarantine at home [5]. Also, from the beginning of December 2020, the government completed the plan by intensifying social distancing measures [5]. In this plan, the status of cities across the country is divided into three categories: yellow, orange, and red, based on the number of patients admitted whose disease was confirmed by PCR [5]. Restrictions were then placed on long-distance travel, closure of offices and unnecessary jobs depending on the situation in each city [5]. At February 5, 2021 Iran in terms of the number of deaths due to COVID-19, is ranked 11th after the United States, Brazil, Mexico, India, the United Kingdom, Italy, France ,Russia Germany and Spain [2]. The effectiveness of the control measures implemented in Iran on COVID-19 mortality has not been fully investigated. This is essential to improve ongoing health decisions and responses to similar pandemics in the future. The present study aimed to explore the efficacy of preventive measures undertaken by the Iranian government aimed to investigate the

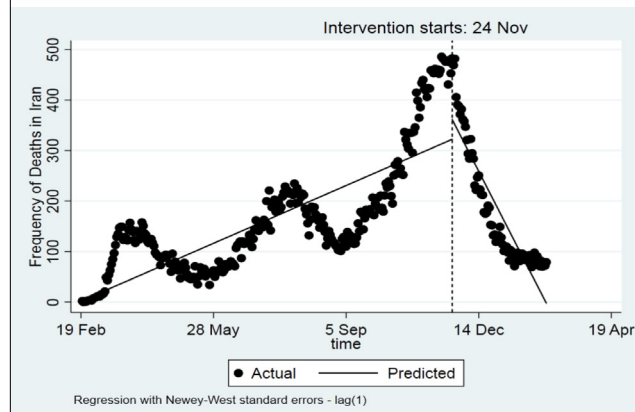
effectiveness of preventative measures undertaken by the Iranian government to reduce the mortality related to COVID-19 among the Iranian population from February 19, 2020 to February 5, 2021.

Methods

We did an interrupted time series analysis (ITS) of daily collected data on confirmed deaths of COVID-19 occurred in Iran and in the world, from February 19, 2020, to February 5, 2021. The dataset which is available at (<https://ourworldindata.org/coronavirus>) was used in the current study. The data included 351 observations of the death occurred in Iran and the world. Although COVID-19 epidemic management and control plan started formally in November 10, 2020, Due to the Incubation period of this infection, November 24, 2020, considered as the starting time of preventive measures in the analysis. Findings from the Princess Diamond cruise ship shows that deaths occurred about 14 days after the time which the Index case was identified [6]. Hence, it is rational that one assesses the COVID-19 mortality with a two-week delay in this case. So, in the current analysis deaths occurred before November 24, 2020, were considered as control period, while deaths occurred after November 24, 2020, were considered as the intervention period in Iran. However, the starting date of the COVID-19 epidemic management and control plan was November 10, 2020, in the current analysis, November 24, 2020 was considered as time of intervention start. This is also in accordance with the average incubation period of the SARS-CoV-2 which has been reported to be 5.1 days [7]. Segmented regression model and ITS analysis using Newey ordinary least squares regression-based methods were used. The standard ITS regression model was as follows [8, 9]: $[Y_t = \beta_0 + \beta_1 T_t + X_t + \beta_3 X_t T_t + e]$.

Y_t is the aggregated number of deaths that occurred at each time point t , T_t is the time since the first day of the study, X_t is representing the intervention (pre-intervention periods 0, otherwise 1), and $X_t T_t$ is an interaction term. The β_0 represents the intercept. β_1 is the slope of the trend of deaths before the start of the intervention. β_2 represents the change in number of deaths in the period after the start of the intervention. β_3 represents the difference between pre-intervention and post-intervention slopes of the trend of deaths. A

Fig. 1. Segmented regression model new deaths of COVID-19 in Iran since February 19, 2020 to February 5, 2021 using the Newey-West standard errors.



significant β_2 shows an effect immediately after the intervention, while a significant β_3 means an effect over the time [10, 11]. In order to attribute the observed change in the number of deaths before and after the implementation of the Iranian COVID-19 epidemic management and control plan, the correlation between the number of daily deaths due to COVID-19 in Iran and the world was examined in two-time stages before and after November 24, 2020. All analyzes were done using Stata Corp. 2017. h Station, TX: StataCorp LLC (USA).

Results

The Median (Interquartile range) of registered cases during the understudied period in Iran was 133(362-83) cases per day. The minimum and maximum number of deaths during this period was 0 and 486 deaths per day. The highest number of deaths in Iran was recorded in November and early December 2020.

Figure 1 shows the trend of COVID-19 deaths from February 19, 2020, to February 5, 2021, in Iran. The starting point of the deaths of COVID-19 was estimated at 3.11 and the trend of new deaths increase significantly every day until November 24 2020 according to pre intervention slope of [(OR 1.14, 95% CI 0.96 - 1.32); $P < 0.001$]. The occurrence of new deaths had a decreasing trend after 24 November 2020 with a coefficient of [(OR -5.12, 95% CI -6.04 - -4.20); $P < 0.001$] (Tab. I).

Tab. I. Estimated coefficients of segmented regression model for new deaths of COVID-19 in Iran since February 19, 2020 to February 5, 2021.

| Regression with Newey-West Standard Errors Maximum Lag: 1 Number of Observation = 351 F (3, 347) = 97.41, P < 0.001 | | | | | | |
|---|--------------|----------------|--------|---------|-------------------------|-------|
| New cases | Coefficients | Standard error | t | P | 95% confidence interval | |
| Intercept | 3.11 | 10.84 | 0.29 | 0.77 | -18.22 | 24.44 |
| Pre intervention slope | 1.14 | 0.08 | 12.79 | < 0.001 | 0.96 | 1.32 |
| Chang in intercept | 39.13 | 25.50 | 1.53 | 0.12 | -11.03 | 89.30 |
| Chang in slope(interaction) | -6.26 | 0.47 | -13.09 | < 0.001 | -7.21 | -5.32 |
| Post intervention linear trend | -5.12 | 0.46 | -10.92 | < 0.001 | -6.04 | -4.20 |

Fig. 2. Segmented regression model new deaths of COVID-19 in the world since February 19, 2020 to February 5, 2021 with Newey-West standard errors.

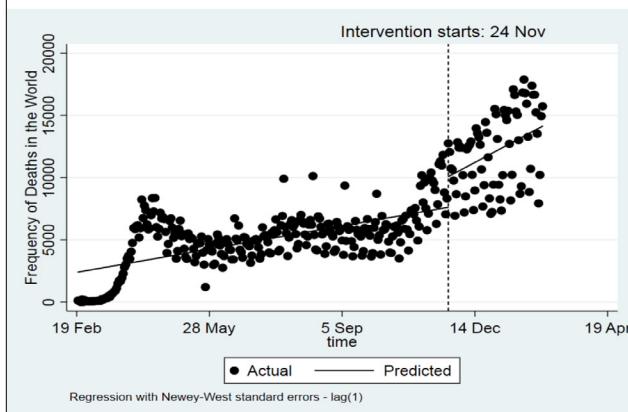


Figure 2 shows the trend of COVID-19 deaths from February 19, 2020, to February 5, 2021, in the world. The starting point of the new deaths of COVID-19 was estimated at (2405.19), and the trend of daily new deaths was increasing before [(OR 18.66, 95% CI 14.41-22.92); $P < 0.001$] and after the 24 November 2020 [(OR 57.14, 95% CI 20.80-93.490); $P: 0.002$] (Tab. II). Figure 3 demonstrates that there was a significant and positive correlation ($r: 0.31, p < 0.001$) between number of new deaths of COVID-19 that occurred in the world and Iran since February 19, 2020, to November 24 2020. On the other hand, Figure 4 shows a significant but reverse Correlation between number of new deaths of COVID-19 that occurred in the world and Iran since November 24 2020 to February 5, 2021 ($r: -0.27, P: 0.01$).

Discussion

RespondAny government must respond proactively in front of a pandemic, including the COVID-19 pandemic. The response, in this case, must include making policies to provide adequate personal protective equipment [12] and quick implementation of preventive measures such as lockdown, effective quarantine, social distancing, and screening, along with patient management and treatment [13, 14]. However, Iranian government has focused on gentle and without coercion measures to control the pandemic, rather than mandatory quarantine

Fig. 3. Correlation between the I the number of new COVID-19 happened in the world and Iran from February 19, 2020, to November 24 2020.

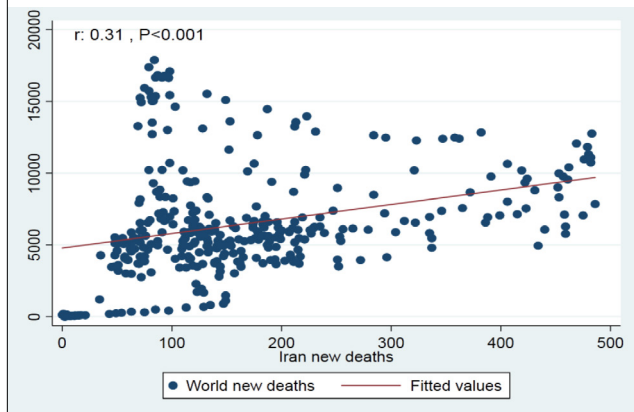
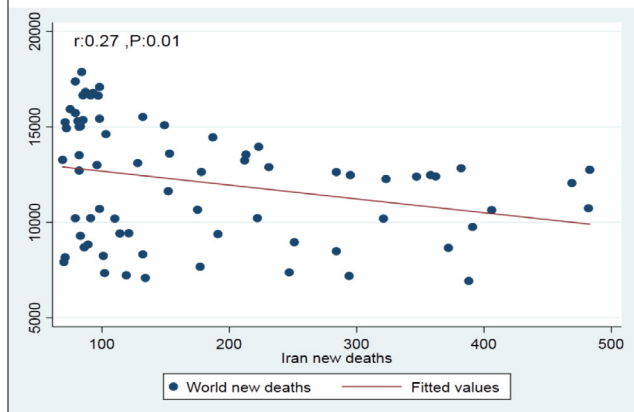


Fig. 4. Correlation between the number of new deaths of COVID-19 occurred in the world and Iran from November 24 2020 to February 5, 2021.



or lockdown [3]. In fact, for the Iranian government, which has been under the most severe economic sanctions in recent years, it is not even possible to implement a strict social distance program, let alone the government wants to enforce a complete lockdown or so-called stay-at-home policies, like what is done in some European countries [15].

From the early days of the COVID-19 pandemic, In Iran, a significant reduction in the number of new deaths due to COVID-19 has been observed in 2 weeks after the implementation of social distancing in the 4th

Tab. II. Estimated coefficients of segmented regression model for new death of COVID-19 in the world since February 19, 2020 to February 5, 2021.

| Regression with Newey-West Standard Errors Maximum Lag: 1 Number of Observation = 351 F (3, 347) = 105.16, P < 0.001 | | | | | | |
|--|--------------|----------------|------|---------|---------------------------|---------|
| New cases | Coefficients | Standard Error | t | P > t | [95% confidence interval] | |
| Intercept | 2405.19 | 372.56 | 6.46 | < 0.001 | 1672.42 | 3137.96 |
| Pre intervention slope | 18.66 | 2.16 | 8.63 | < 0.001 | 14.41 | 22.92 |
| Chang in intercept | 2462.09 | 714.63 | 3.45 | < 0.001 | 1056.54 | 3867.65 |
| Chang in slope (interaction) | 38.48 | 18.60 | 2.07 | 0.03 | 1.88 | 75.08 |
| Post intervention linear trend | 57.14 | 18.47 | 3.09 | 0.002 | 20.80 | 93.49 |

week of March 2020 [3]. Unfortunately, Relying on the success achieved in the previous step, due to economic constraints, Iran has decided to implement a kind of smart distancing instead of a rigid social distancing program, ring spite of health experts concerns and warning about the consequences of such a decision [3]. In fact, the smart distancing allows the Iranian society to gradually return to normal condition, and many jobs are to be resumed steadily [3]. Consequently, about a month after the reopening of schools and universities, the number of deaths due to COVID-19 reached (415). The present study results showed that Iranian COVID-19 epidemic management and control plan, which started on November 10, 2020, significantly reduced the number of COVID-19 deaths in Iran. The direct correlation between the number of deaths that occurred in Iran and the world before November 24, 2020, and the inverse correlation between the two after the date mentioned can also be a proof and confirmation of the results obtained (Figs. 3,4). In fact, these figures show that before the mentioned date, the number of daily deaths in Iran has increased along with the number of deaths in the world, but after that date, while the number of deaths in the world has continued to increase, the number of deaths in Iran has decreased. Despite the economic and psychological impacts of the COVID-19 epidemic management and control plan and other preventive measures [15, 16], their role in containing the pandemic is undeniable. Some studies with ITS analysis approach reports significant effects of control measures on the COVID-19 mortality [3, 16-19]. A study on 149 countries found that social distance measure reduced in 13% the COVID-19 morbidity [16]. Figueiredo et al. [17] reported a daily decrease of 7.88% in deaths, after the implementation of preventive policies in China. Siedner et al. [18], in the United States also showed a daily reduction in COVID-19 epidemic growth after the implementation of social distancing. Ghanbari et al. [3, 19] and also Alimohamadi et al reported a significant effect of preventive policies on COVID-19 mortality in Iran. One thing to note is that such success has been achieved without severe restrictions heavy fines. Another point is that this success was achieved despite the limited number of COVID-19 diagnostic tests (which also has economic reasons). Iran as a country with more than 84 million population, currently, is ranked 121th in the world and 6th (Last) in Persian Gulf region in terms of the number of tests per one million (with 112,305 tests /1 milion population and more than 9 million tests population since the beginning of the pandemic [2]. However, COVID-19 mortality rate has been reported to be negatively associated with COVID-19 test number [20]. The current study had some limitations; during the study period, some variables such as people knowledge, attitude and practice about the disease, the criteria for the confirmed deaths. The accuracy of the diagnostic tests as well as the people's compliance to health principles (such as using face masks, avoid attending gatherings and crowded places, etc), may be altered and this could affect the effectiveness of the

preventive measures. Nevertheless, controlling the role of above-mentioned variables was not possible due to unavailability of data.

Conclusions

The Iranian COVID-19 epidemic management and control strategy reduced the mortality associated with COVID-19. Therefore, it is essential to continue these measures, in order to prevent the increase in the number of deaths.

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Ethical Statement

There is no ethical consideration of this study.

Conflict of interest statement

The authors declare that there is no conflict of interests.

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Authors' contribution

YA and MS formulated the research questions, methodology, formal analysis, prepare drafts of the manuscript, review and editing. All authors have read and approved the final version of the manuscript.

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LETTER TO THE EDITORS

RTS,S/AS01 Malaria Vaccine - The Next Step for a Developing Country

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Key words

RTS S/AS01 • Malaria • Plasmodium • Developing countries • Endemic

Malaria is a curable, yet deadly parasitic infection caused by Plasmodium species. It is responsible for one child's death every two minutes globally and is accredited to be the second most prevalent disease in Pakistan [1].

Due to this high morbidity and mortality rate, medical researchers worldwide have been working towards the development of a malarial vaccine since the 1960s [2]. Till now, none of these vaccines were able to complete the clinical development phase. However, recently, RTS,S/AS01, a pre-erythrocytic vaccine (PEV), developed by GSK laboratories, became the first malaria vaccine against *P. falciparum* to do so [3].

The pilot program was launched by WHO in Ghana, Kenya, and Malawi in January 2016, which showed promising results, with about a 30% reduction in severe malarial cases [3].

The vaccine has been declared safe, feasible, efficient, and cost-effective by WHO and widespread use of this vaccine, among the children of Sub-Saharan Africa, was approved by WHO on 6th October 2021 [3].

It is administered as an intramuscular injection in 4 doses in children from the age of 5 months. An additional dose may be added before the malarial season [3].

In Pakistan, almost 60% of locals live in malaria endemic areas [1].

As a result, the death toll stands to 50,000 deaths each year attributed to either the infection directly or its complications [1].

It's imperative to take into account that the most vulnerable of these are infants, children, and expectant women from the at-risk population in Pakistan [1].

In a developing country such as Pakistan it is rather difficult to repress malarial outbreaks because of chaotic urbanization and habitation, sinking sanitary conditions, environmental hazards e.g., monsoon rains and floods [1].

In addition to this, it is fair to highlight Pakistan as a fertile state, therefore the majority of the population co-exists with this fatal infection.

The efforts to roll back malaria have been in vain due to inadequate care given at both federal and provincial levels [1].

There is a heterogeneous distribution of the major

Plasmodium species in Pakistan, mainly *P. vivax* (75% malaria cases) and *P. falciparum* (25% cases) [1].

A six-fold increase in *P. falciparum* cases in the last decade was reported by the National Malaria Control program [4].

The affected population also fails to seek relevant treatment in time or tends to self-medicate, resulting in complications.

It may be contributed by the lack of knowledge regarding the disease severity and the rising antimalarial drug resistance in Pakistan [5].

This can be a significant burden on the economy.

A number of initiatives are required to reduce the intolerable burden of malaria.

Investment and development of public-private partnerships, cost-effectiveness, efficient delivery methods, and approval by liable regulatory authorities are some of the approaches to ensure vaccine efficacy.

Due to the crippling statistics discussed above, Pakistan becomes a strong candidate for the WHO RTS malaria vaccine administration.

A successful vaccine trial along with well-planned training of staff, accessibility of vaccines to the general masses especially those who are highly prone, adequate monitoring, and continuous encouragement of individuals to participate can contribute immensely in medical research data needed to restrain the disease.

Compliance with all the necessary precautionary measures coupled with a groundbreaking vaccination trial could give hope to developing countries, who would be able to include this in their EPI schedule and turn this long-deferred dream of malarial elimination, into a reality.

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ORIGINAL ARTICLE

Eleven-Year surveillance of methicillin-resistant *Staphylococcus aureus* infections at an Academic Health Centre

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Key words

Staphylococcus aureus • Infection • Methicillin-Resistant

Summary

Introduction. Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important human pathogen associated with nosocomial and community infections. There is a continual focus on the epidemiology of this public health threat owing to the increase in its spread and rapid development of resistance.

Aim. We aimed to demonstrate the time trend of antibiotic resistance by describing the epidemiology of MRSA infections at an academic health centre.

Methodology. We retrospectively reviewed cases during an 11-year period (from January 2009 to December 2019) with positive cultures for MRSA from various clinical sites in King Fahad Hospital of the University, to understand their clinical and microbiological profiles. Screening and colonisation samples were excluded.

Results. A total of 1338 MRSA isolates were identified, with an increasing trend from 5.2% to 14.5% during 2009-2019. Skin and soft tissue samples were the most common source (52.4%) of MRSA infections. Vancomycin activity remained stable against MRSA, and only one isolate showed resistance to linezolid (< 1%). A significant reduction in susceptibility to clindamycin ($p = 0.003$), trimethoprim-sulfamethoxazole ($p = 0.001$), and rifampin ($p < 0.0001$) was detected over the study period.

Conclusions. MRSA infections still represent a significant burden on healthcare systems. Our data support the need for constant local and regional surveillance to devise relevant protocols to manage MRSA infections. Empirical therapy needs to consider the changing antimicrobial susceptibility trends among MRSA isolates.

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of community-acquired and hospital-acquired infections worldwide [1, 2]. MRSA was first identified more than five decades ago and has since undergone epidemiologic expansion and rapid evolutionary changes, causing a wide range of infections potentially leading to sepsis and death [1, 3]. The first MRSA outbreak was described in the 1960s [4]. The Centers for Disease Control and Prevention (CDC) categorised MRSA as a 'serious threat' [1]. MRSA infections represent a major challenge to hospitals because of increased morbidity, mortality, hospital stays, and costs, as well as the emergence and spread of clones that show decreased susceptibility to a wide range of antimicrobial agents [1, 3, 5]. The increasing resistance to multiple antimicrobial agents, including glycopeptides and oxazolidinones, among MRSA strains is a healthcare concern worldwide, causing considerable difficulty in the management of staphylococcal infections [3, 6, 7]. In Saudi Arabia, the prevalence of MRSA varies among different regions [8-10]. A pooled estimation study from 2002 to 2012 showed that the prevalence of MRSA in Saudi Arabia was 35.6% [11]. A retrospective review in the western

region of Saudi Arabia from 2009 to 2010 showed that the most common infections caused by MRSA were skin and soft tissue infections (87.3 %) [10]. Moreover, in another study, a greater proportion of community-acquired MRSA infections was recovered from skin and soft tissue specimens (76%) than healthcare-associated infections (58.7%) [12]. The rates of resistance to rifampin, trimethoprim-sulfamethoxazole, erythromycin, and clindamycin were variable in several studies [10, 12, 13]. However, most MRSA isolates were shown to be susceptible to vancomycin and linezolid [10, 13]. Surveillance of MRSA infections in both healthcare systems and the community is important because of the continuously changing epidemiologic and susceptibility profiles.

We aimed in this study to describe the epidemiology of MRSA infections, the antimicrobial susceptibility patterns, and to demonstrate the time trend of resistance to three agents (sulfamethoxazole-trimethoprim, clindamycin, and rifampin) in pathogenic MRSA isolates.

Methods

STUDY SETTINGS

This was a retrospective, cross-sectional study at King Fahad Hospital of the University (KFHU) Al-Khobar, a

550-bed secondary care and academic training facility. Culture-positive MRSA samples representing infections, obtained from various sites between January 2009 and December 2019 in patients of all age groups, were included. Cases with clinically significant isolates were identified by reviewing electronic charts individually, eliminating screening samples for colonisation sites. Patients' data (sex, age, and location of patients when specimens were collected) and microbiological results from the laboratory information system were analyzed for the included cases. Routine testing of MRSA isolates in the laboratory was performed using the VITEK 2 automated system (bioMérieux Inc., Durham, NC, USA) between 2009 and 2016 and the VITEK MS (bioMérieux Inc.) between 2017 and 2019. Cefoxitin 30 µg discs on Muller-Hinton agar (SPML, Dammam, Saudi Arabia) were used to screen for MRSA, followed by susceptibility testing using the VITEK 2 automated system throughout the study period. The results were interpreted based on the Clinical & Laboratory Standards Institute (CLSI) breakpoints [14]. Any discrepancy between the cefoxitin inducer test and VITEK 2 system was resolved by molecular testing (GeneXpert MRSA). Patients with repeated MRSA positive culture result within 6-month period were excluded in the analysis.

STATISTICAL ANALYSIS

Statistical analysis was performed using version 23.0 of the Statistical Package for Social Sciences (IBM Corp., Armonk, NY, USA). The Pearson chi-square test was applied to measure the proportion difference, and a p -value < 0.05 was considered statistically significant.

Results

DEMOGRAPHIC PROFILE

A total of 1338 MRSA isolates were included during the study period, of which 138 (10.3%) were from the intensive care unit (ICU). Demographic data of the patients are summarised in Table I. Over the 11-year study period, there was an increase in the absolute number of MRSA cases from 5.2% in 2009 to 14.5% in 2019. In 2010, there was a reduction in MRSA cases (4.8%) compared to the other years. A large proportion of the patients ($n = 324$, 24.2%) were aged < 1-9 years, with an overall female to male ratio of 1:1.17. Figure 1 illustrates the number of MRSA cases per sex over the study period, and Figure 2 highlights the age trend of MRSA over the years.

DISTRIBUTION OF MRSA IN DIFFERENT CLINICAL SAMPLES

Skin and soft tissue specimens were found to be the major source of MRSA cases (52.4%; $n = 702$) in the cohort, followed by lower respiratory specimens (15.1%; $n = 203$). Lower respiratory specimens were the dominant source of MRSA infections in the ICU (71.7%; $n = 99$). Table II shows the distribution of MRSA among the different types of clinical specimens.

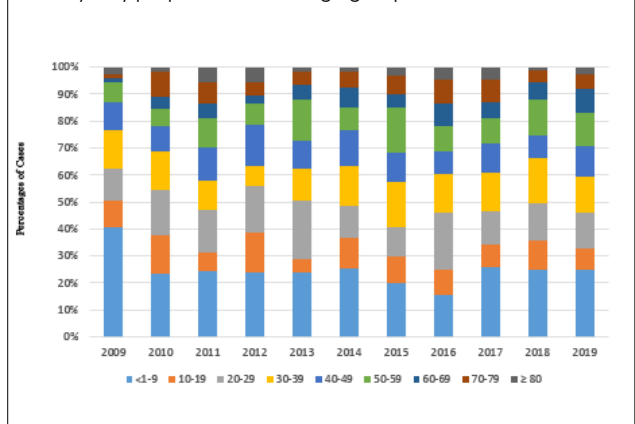
Tab. I. Demographic characteristics of MRSA cases, 2009-2019.

| | | Number | % |
|-------------|--------------------|--------|------|
| Year | 2009 | 69 | 5.2 |
| | 2010 | 64 | 4.8 |
| | 2011 | 74 | 5.5 |
| | 2012 | 104 | 7.8 |
| | 2013 | 117 | 8.7 |
| | 2014 | 115 | 8.6 |
| | 2015 | 120 | 9.0 |
| | 2016 | 124 | 9.3 |
| | 2017 | 179 | 13.4 |
| | 2018 | 178 | 13.3 |
| | 2019 | 194 | 14.5 |
| Gender | Male | 722 | 54.0 |
| | Female | 616 | 46.0 |
| Nationality | Saudi | 1270 | 94.9 |
| | Non-Saudi | 65 | 4.9 |
| | Data not available | 3 | 0.2 |
| Age | < 1-9 | 324 | 24.2 |
| | 10-19 | 130 | 9.7 |
| | 20-29 | 198 | 14.8 |
| | 30-39 | 186 | 13.9 |
| | 40-49 | 144 | 10.7 |
| | 50-59 | 150 | 11.2 |
| | 60-69 | 80 | 5.9 |
| | 70-79 | 84 | 6.3 |
| | ≥ 80 | 42 | 3.1 |

Fig. 1. Gender distribution of MRSA cases, 2009-2019.



Fig. 2. Age trend of MRSA cases over 2009-2019. The columns show yearly proportions (%) of age groups.



Tab. II. Distribution of MRSA cases among the type of clinical specimen.

| Type of specimen | Number | % |
|-------------------------|--------|------|
| Skin and soft tissue | 702 | 52.4 |
| Lower respiratory tract | 203 | 15.1 |
| Ear samples | 158 | 11.8 |
| Blood | 92 | 6.9 |
| Ophthalmic | 59 | 4.4 |
| Tissue biopsies | 50 | 3.7 |
| Urine | 23 | 1.7 |
| Peritoneal Fluid | 9 | 0.7 |
| Tracheostomy | 9 | 0.7 |
| Umbilical cord | 4 | 0.3 |
| Bile | 3 | 0.2 |
| Pleural Fluid | 3 | 0.2 |
| CSF | 2 | 0.1 |
| Synovial Fluid | 2 | 0.1 |
| Others | 19 | 1.4 |

ANTIBIOTIC SUSCEPTIBILITY PATTERN

Overall, the MRSA isolates were highly susceptible to glycopeptides, oxazolidinone, and rifampin (Tab. III). In contrast, moderate susceptibility was noted for lincosamides and sulfonamides, and low sensitivity rates were noted for macrolides. The linezolid-resistant strain was isolated from an 80-year-old Filipino male patient who presented with a left forearm abscess. Confirmatory linezolid E-test was performed for this strain, which showed a minimal inhibitory concentration (MIC) > 256 µg/mL. This isolate was also resistant to clindamycin and chloramphenicol but retained susceptibility to sulphonamides. Moreover, the resistance rate to erythromycin (31.7%) was high, followed by that to clindamycin (26.4%). Of the 137 erythromycin-resistant MRSA isolates, 81%, 32.8%, and 8% were also resistant to clindamycin, trimethoprim-sulfamethoxazole, and rifampin, respectively. There was a significant reduction in clindamycin ($p = 0.003$), trimethoprim-sulfamethoxazole ($p = 0.001$), and rifampin ($p < 0.0001$) susceptibility over the years. However, no significant difference was noted in the susceptibility to erythromycin over time ($p = 0.167$) (Fig. 3).

Discussion

The global epidemiology of MRSA infection in community and healthcare settings has evolved rapidly in recent years [1-3]. In Saudi Arabia, the prevalence of MRSA varies widely, ranging from 2 to 38% [11, 15, 16]. In our study, MRSA isolate numbers showed an increasing trend from 5.2% in 2009 to 14.5% in 2019. Approximately 24% of MRSA isolates in this study were from patients aged < 1-9 years. In the United States and Canada, the clinical epidemiology and molecular characteristics of MRSA infections in the paediatric age group changed dramatically between 2000 and 2010. This was owing to an epidemic of community-

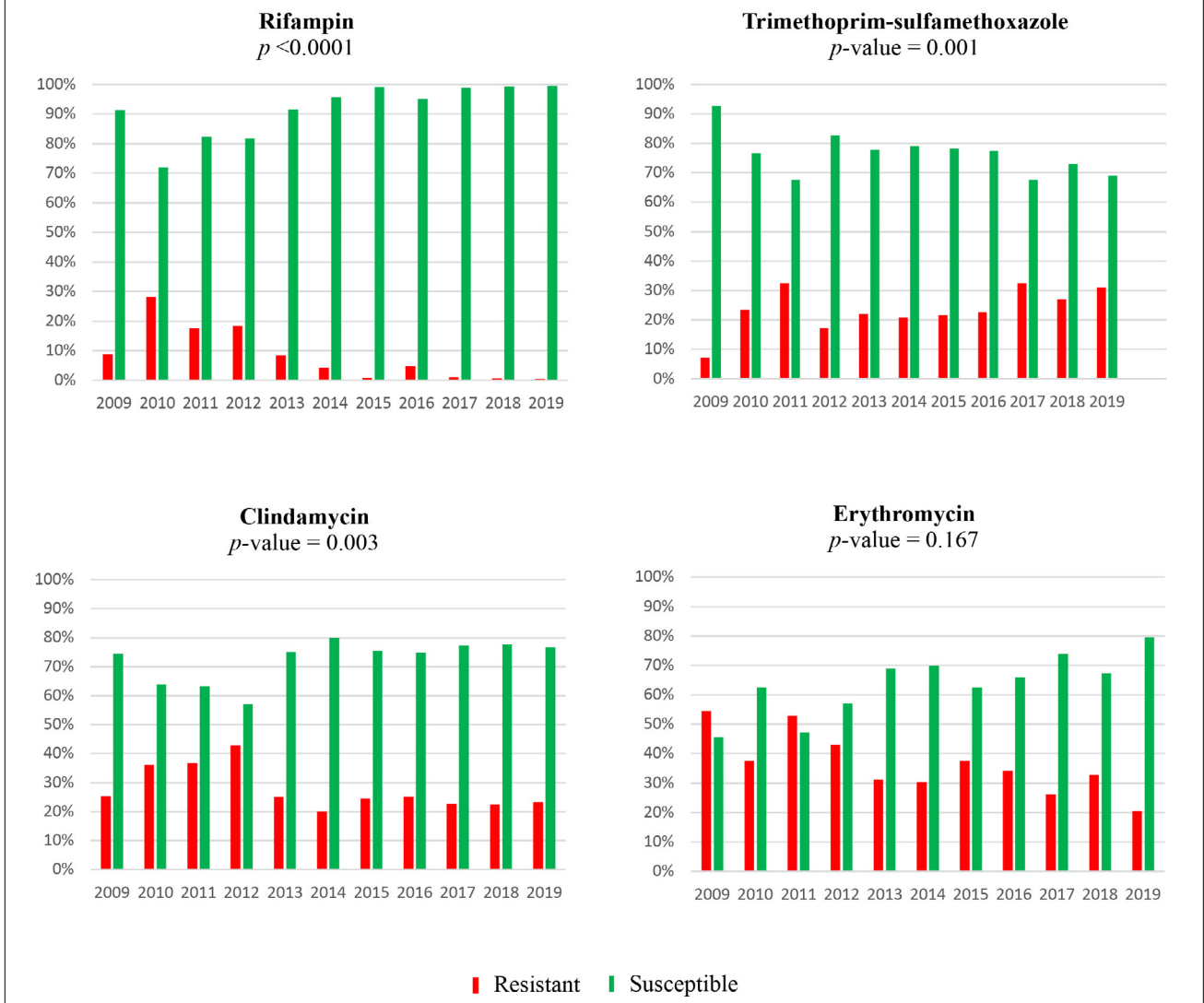
Tab. III. Antimicrobial susceptibility among MRSA isolates during 2009-2019

| Antibiotic | Number | % |
|-------------------------------|--------|------|
| Vancomycin | 1338 | 100 |
| Linezolid | 1337 | 99.9 |
| Rifampin | 1256 | 93.9 |
| Trimethoprim-sulfamethoxazole | 1006 | 75.2 |
| Clindamycin* | 888 | 73.6 |
| Erythromycin* | 295 | 68.3 |

* Reported based on the site of infection

associated MRSA skin and soft tissue infections (SSTIs) and the introduction of the USA300 pulsed-field gel electrophoresis typing of MRSA in the health care and community settings [17]. MRSA was previously shown to be distributed differently in different age groups. In two local studies, MRSA isolates were found in the extreme age groups of patients who were ≥ 60 and ≤ 5 and ≤ 1 years old [13, 18]. Another study showed that patients aged 56 years and older had the highest prevalence of MRSA [10]. In the United States, one study found a trend of declining age over a 10-year period of observation, while another study at the same time showed that greatest increase in MRSA rate was in people aged ≤ 17 years [13, 19]. These observations clearly indicate the variations based on geographical location. Regarding gender distribution, 54% of the isolates were recovered from male patients, while 46% were from females. Other studies have also shown that MRSA isolates were recovered relatively more from males than females in Saudi Arabia [18, 20, 21].

Skin and soft tissue infections were the most common infections caused by MRSA in the present study, in concordance with the established evidence from a number of studies [10, 22-24]. In a US study conducted between 1996 and 2006, Frei et al. discovered 58,942 MRSA infection cases (9.6%) from clinical infections in the skin and soft tissue of paediatric patients [22]. As stated by the CDC, 33% of humans have *S. aureus* in their nose and approximately 2 in every 100 have MRSA. One of the main limitations of this study was that the screening and colonization samples were excluded. Despite the fact that many people are MRSA nasal carriers, the majority do not develop serious MRSA infections [25]. However, nasal and skin carriage of *S. aureus* have been reported as a potential source of infected skin and soft tissue [26, 27]. In our study, lower respiratory samples were the most common site of MRSA in the ICU, in contrast to that in other studies where blood stream infections were the most common site of ICU-related MRSA infections [28, 29]. MRSA infections of the skin and soft tissues, as well as pneumonia, may cause bloodstream infections and are linked to higher mortality rates, higher hospital costs, and longer hospital stays than infections caused by methicillin-susceptible *S. aureus* isolates [21, 30, 31]. In the current study, 6.9 % of MRSA isolates originated from the blood. MRSA bacteraemia is a serious, life-threatening infection with an estimated mortality rate of

Fig. 3. Trend of susceptibility among MRSA isolates during 2009-2019.

20-40% [32, 33]. According to the 2014 World Health Organization Antimicrobial Resistance Report, MRSA represents a widely variable proportion (20-80%) of cases of staphylococcal bacteraemia [34].

Several antimicrobial therapies are available for the treatment of MRSA infections. However, numerous publications, including the 2019 antibiotic resistance threats report by the CDC, demonstrate that MRSA has become resistant to many first-line antibiotics [2, 3, 25]. In the current study, all MRSA isolates were susceptible to vancomycin. Similar results have been reported in several other local studies [10, 23, 24]. Several countries have reported clinical strains of *S. aureus* with reduced susceptibility to vancomycin after the appearance of the first case in Japan [35-37]. In 2010, the first detected MRSA strain (D958) with reduced susceptibility to vancomycin was reported in Saudi Arabia [38]. While MRSA with reduced vancomycin susceptibility has not been identified at our institution, the unique ability of *S. aureus* to acquire resistance necessitates the use of surveillance programs to combat this problem. In

the present study, in line with previous studies, one MRSA strain (0.1%) was reported to be resistant to linezolid [13, 39, 40]. The phenotype exhibited by the strain is suggestive of the rare *cfr* methyltransferase mechanism that confers resistance to erythromycin, clindamycin, chloramphenicol, and linezolid; however, this is uncertain since the isolate was not available for molecular characterisation at the time of the study. Staphylococcal resistance to linezolid is uncommon and is usually mediated by the G2576T point mutation related to the 23S rRNA binding site DOMAIN V [41]. Regarding the other antimicrobial agents, a significant reduction in the susceptibility to clindamycin, trimethoprim-sulfamethoxazole, and rifampin was noted over the years. A recently published large global surveillance study showed that these antimicrobial agents exhibited increased resistance over time, which is consistent with our findings [42]. Variations observed in the susceptibility of MRSA isolates over the years and the geographical variation and diversity in susceptibility

patterns necessitate continuous local and regional surveillance in order to devise comprehensive protocols. Although MRSA is traditionally classified as healthcare-associated (HA-MRSA) and community-associated (CA-MRSA), this classification also overlaps at the molecular and epidemiological levels [43]. Thus, the Disease Control and Prevention Active Bacterial Core (CDC-ABC) Surveillance System recommends subdividing HA-MRSA based on the setting of onset: hospital or community [44]. A limitation of our study is that we were unable to retrospectively differentiate between community- and hospital-acquired MRSA infections. A published study from Saudi Arabia showed an increasing proportion of community-acquired MRSA infections from 41.7% in 1999 to 66.6% in 2002, and reduced nosocomial MRSA infection from 33% in 1999 to 19% in 2003 [12]. According to a cross-sectional study published by KFHU from January 2010 to September 2011, SCCmec type IV was the most frequently found genotype in a total of 106 MRSA isolates from infection and carrier colonisation sites. This shows that most strains were of community origin [45].

Conclusions

With the help of the present study, we inferred that skin and soft tissue are the primary sources of MRSA at King Fahad Hospital of the University (KFHU) in Al-Khobar, Saudi Arabia. Throughout the 11-year study period, the trend of MRSA infections has increased with the emergence of new strains that showed resistance to one or more antibiotic classes. These findings highlight the need for continuous surveillance to understand microbial infections, their antibiotic resistance patterns, and to identify the emergence of new strains for successful management and control.

Ethical approval

Ethical approval for this study was obtained from the Institutional Review Board of Imam Abdulrahman Bin Faisal University (IRB-PGS-2020-01-368).

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Consent for publication

Not applicable.

Availability of data and material

Data available on request from the authors.

Conflict of interest statement

No conflict of interest to disclose that is relevant to this study.

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Authors' contributions

A.A. and S.A.L. conceived of the presented idea conceptualization. A.A. and A.M.A. designed the investigational methodology. S.A.M., Q.A. and S.A.L. performed the collection and formal analysis of the data. S.A.M. wrote the manuscript. A.A. and A.M.A. supervised the project administration. All authors reviewed and approved the final manuscript.

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CASE REPORT

Clinical characterization and whole genome sequence-based typing of two cases of endophthalmitis due to *Listeria monocytogenes*

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Key words

Listeriosis • Endophthalmitis • Surveillance • Whole-genome sequencing • Virulence

Summary

Endophthalmitis due to Listeria monocytogenes is a rare form of listeriosis. Here, we report two cases that occurred in patients with different medical history, a 46-years-old woman with no comorbidities and an elderly man with several comorbidities. There was no history of trauma or surgery in either patient suggesting an endog-

enous origin. Despite antibiotic treatment, both patients showed poor visual acuity outcomes. Subtyping clinical isolates using whole genome sequencing could allow to characterise Listeria monocytogenes strains involved in rare clinical manifestation, such as in unusual anatomical sites, even in immunocompetent patients.

Introduction

Listeria monocytogenes (*Lm*) is a major foodborne pathogen that can cause a number of life-threatening clinical syndromes, most frequently sepsis and meningitis, particularly in immunocompromised patients [1, 2]. Endophthalmitis is a serious intraocular infection of the vitreous cavity resulting from exogenous or endogenous spread of microorganisms into the eye and is an exceedingly rare form of listeriosis [3-6]. Indeed, since the publication of the first case in 1967 [7], less than 50 cases have been reported, almost all after the year 2000 in Europe or North America [6]. Although rare, *Lm* endophthalmitis deserves attention and was recently included in the case definition of invasive listeriosis by the European Centre for Disease Prevention and Control (ECDC) [8]. Notification of invasive listeriosis has been mandatory in Italy since 1990, and in 2018 the national rate (0.29 per 100,000 inhabitants) was lower than in most European Union countries [9]. In the Lombardy Region (more than one-sixth of the Italian population), where the national mandatory notification system has been integrated since 2005 with a laboratory-based network, a significantly higher incidence (0.75 per 100,000 inhabitants) was observed in the same year [10]. Starting from January 2019, all *Listeria monocytogenes* isolates have been analysed by whole-genome sequencing (WGS), in collaboration with the Istituto Superiore di Sanità (ISS). To date, a total of 1,070 cases of invasive listeriosis were recorded by the Regional Reference Laboratory (RRL), and only two cases (referred to as case A and case B) of endophthalmitis (0.2%) were detected in the period 2018-2019. The aim of this study was to report the two

cases of endophthalmitis and characterized the clinical isolates by using WGS data.

Case Report

Since the clinical record was not available, information on case A was only provided by the epidemiological investigation form. A 46-year-old woman presented to a hospital emergency room (ER) in Brescia in September 2018 with photophobia, pain in the left eye, and nausea. She reported having initial symptoms of redness and a slightly blurred vision a few days before. There was no history of previous trauma, infection, or surgery. Her medical history was unremarkable. She was initially treated for an anterior uveitis with ophthalmic drops of steroids and antibiotics for one week, but a worsening of symptoms, with pulsating pain, reduced vision, and increasing ocular pressure (> 21 mmHg) was reported. Both blood and aqueous humour cultures were performed. After 24 hours, *Lm* was identified in both blood culture and aqueous humour by VITEK MS system (Biomérieux, Marcy l'Étoile, France). Antimicrobial susceptibility testing was performed by E-test on Mueller-Hinton Fastidious Agar (Biomérieux, Marcy l'Étoile, France) and showed resistance to erythromycin and trimethoprim/sulfamethoxazole. The woman decided to leave the hospital against the medical advice ten days after admission. After ten months, the ocular inflammation was resolved, but reduced vision and photophobia persisted. The second case was represented by an 85-year-old man presented to an ER in Milan in January 2019, reporting pain in his left eye, occurring one week after an episode of non-

Tab. I. Clinical and molecular characteristics of case A and case B.

| Case | Age/Sex | Underlying medical conditions | Ocular symptoms | Blood culture | Other positive cultures | Serotype | Lineage | Sequence Type/Clonal Complex | Virulence |
|------|---------|--|--|---------------|-------------------------|----------|---------|------------------------------|--------------------------------|
| A | 46/F | None | Photophobia, pain, redness, blurred vision | Positive | Aqueous humor | 1/2a | II | ST20/CC20 | LIPI-1, LIPI-2 |
| B | 85/M | Renal insufficiency, hypertension, type 2 diabetes | Pain, palpebral edema, blurred vision | Positive | Vitreous humor | 4b | I | ST4/CC4 | LIPI-1, LIPI-2, LIPI-3, LIPI-4 |

febrile gastroenteritis. The patient suffered from chronic renal failure and other comorbidities (hypertension, mild type 2 diabetes mellitus, and right eye glaucoma). His medical history was also significant for a grade 9 prostate adenocarcinoma. He was dismissed from the ER with steroids and antibiotic eye drops (dexamethasone-netilmicin and cyclopentolate) to be administered in both eyes. Four days later, due to the worsening of his left eyesight, the patient came back to the ER. The presence of periorbital oedema and hyperaemia was observed, and his vision was limited to light perception and hand movement. An increase in the intraocular pressure (30 mmHg) and a retinal detachment in the left eye were detected. Systemic antimicrobial therapy with ceftriaxone and eye drops (ampicillin, vancomycin, voriconazole, moxifloxacin and tobramycin) were prescribed. A vitrectomy of the left eye and blood culture were performed. After less than 24 hours, both vitreous humour and blood culture tested positive for *Lm*, which was identified by using VITEK MS system (Biomerieux, Marcy l'Étoile, France). Antimicrobial susceptibility testing showed no resistance to all tested antibiotics. On this basis, ampicillin (2 g q4h) and cotrimoxazole (15 mg/kg q6h) were added to ceftriaxone. The antibiotic therapy was administered for 7 weeks, totally. After one month, the patient was discharged from the hospital. No visual improvement was observed.

As required by the national surveillance system, the clinical isolates of *Lm* from the two patients were referred to the RRL for molecular subtyping. The isolates were typed with WGS, as requested by. DNA was extracted from pure cultures using the GenElute Bacterial Genomic DNA kit (Sigma-Aldrich, St. Louis, MO, USA), spectrophotometrically quantified and controlled for quality. Purified DNA was then processed with the Nextera XT sample preparation kit (Illumina, Inc., San Diego, California, USA) and genomic libraries were sequenced on the Illumina MiSeq platform (Illumina, Inc., San Diego, California, USA) with 2 x 250 base pairs paired end runs. Lineage, Sequence Type (ST), Clonal Complex (CC) and virulence information were obtained from the genome sequence using the *Listeria* database hosted by the Institut Pasteur, France [11]. Conventional serotyping was performed at the ISS in Rome, using *Listeria* antisera (Denka Seiken Co., Ltd., Tokyo, Japan). The strain recovered from patient A was classified as serotype 1/2a, lineage II, ST20, CC20. Patient B's strain resulted serotype 4b, lineage I, ST4, CC4. Both strains harboured the two major *Listeria* pathogenicity islands (LIPI) LIPI-1 and LIPI-2. Isolate B carried also LIPI-3 and LIPI-4. Clinical characterization and

WGS-based typing results are listed in Table I.

Discussion

Listeria monocytogenes is an extremely rare and serious cause of endophthalmitis, often with a poor outcome. It spreads mostly by hematogenous dissemination, although it is not easy to attribute the source of infection, as in the cases reported in this study [5, 12]. Considering that the present cases were not related to surgical procedures or trauma, it can be hypothesized that *Lm* has entered the eye from the bloodstream, following the ingestion of contaminated food. This hypothesis could be supported by the observation of an episode of gastroenteritis in patient B one week prior to the onset of the visual problem. A comparison between our cases and those reported in the literature shows that symptoms, age of the patient, and course of the disease observed here are in line with previous studies. Indeed, in the literature, a wide range of age (24-88 years) and different clinical and immunological conditions were described [3, 5, 6]. Moreover, *Lm* endophthalmitis may occur both in immunocompetent (such as case A) and immunocompromised patients (such as case B), [3, 6]. In correspondence with the previous findings, in both cases the final visual outcome was poor [3-6]. Regarding case A, the outcome could also be influenced by the poor ocular penetration of several antimicrobials [6, 12]. Interestingly, the resistance to trimethoprim/sulfamethoxazole was also observed in a recently published case of *Lm* endophthalmitis [12]. WGS-based typing revealed that isolate A belongs to ST20 and CC20, which appear to be rare, frequently isolated from the environment [13] and, remarkably, previously associated with eye infections [11]. Although this strain resulted clinically relevant in an immunocompetent subject, CC20 has not been previously described as a hypervirulent clone [11, 13]. Moreover, no other isolate with this ST has been recorded in the RRL database to date. The isolate B belonged to ST4 and CC4, typically associated with clinical cases [11, 14] and, remarkably, previously isolated from a case of endophthalmitis occurred in Austria in 2018 [15]. CC4 is reported to be a hypervirulent clone, strongly associated with central nervous system (CNS) infection due to the presence of LIPI-4, which is the first factor specifically implicated in *Lm* elective tropisms for the CNS [11, 14, 15]. Since the

optic nerve is considered part of the CNS, its involvement in ocular form of listeriosis is not surprising. Strain B also harboured LIP-3, only detected in lineage I strains, which can enhance the haemolytic and cytotoxic activity of *Lm* [13, 14].

WGS is a powerful tool for the characterization of *Lm*, as it allows an exceptional subtyping resolution by using the complete genome to determine molecular characteristics of the circulating strains, even in unusual anatomical sites and in not-at-risk subjects. The unexpected finding of a strain not previously classified as hypervirulent in an immunocompetent subject represents a further confirmation of the versatile nature and unpredictability of *Lm*.

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Conflict of interest statement

The authors declare no conflict of interest.

Author contributions

Conceptualization and study design, MG, ET and MP; molecular subtyping analysis, MG, SB, GC, AL and CF; data collection and clinical investigation, MT, NC and NM; data analysis, MG, SB, GC, AL, MT, NC and CF; writing—original draft preparation, MG, SB, GC, MT and MP; writing—review and editing, NM, AA, GZ and ET; supervision, ET, MP and MC; All authors have read and agreed to the published version of the manuscript.

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Usefulness of the SF-36 Health Survey questionnaire in screening for health-related quality of life among parents of children with cancer: Latent profile analysis

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Key words

Cancer • Cut-off points • Parents • Quality of life • SF-36 Health survey

Summary

Background. Poor health-related quality of life (HRQOL) of parents of children with cancer as their main caregivers can adversely affect child's HRQOL. Short Form-36 Health Survey (SF-36) is a widely used instrument to measure HRQOL. However, there are no clearly defined cut-off points for screening for parents with poor HRQOL. This study aimed to find appropriate cut-off points for the SF-36 questionnaire in a sample of parents of children with cancer using latent profile analysis to add another possibility to use it.

Methods. In this cross-sectional study, a number of 108 couples (108 mothers and 108 fathers), who had children with cancer, were selected by simple random sampling method from the patients' files. The study was conducted at two settings, pediatric hematology/oncology wards of BESAT hospital (a hospital related to Hamadan University of Medical Sciences, Iran) in 2017. Latent

Profile analysis (LPA) method was used to determine appropriate cut-off points for the SF-36 questionnaire. Data was analyzed by Mplus and R3.3.0 software.

Results. Based on the results, scores ≤ 44 , 45-63 and ≥ 64 for mental health, and scores ≤ 43 , 44-59 and ≥ 60 for physical health classes indicate weak, medium, and good, respectively. These cut-off points showed acceptable accuracy in classification of individuals. For the total quality of life, correct classification rates were 88%, 65% and 53% for each class respectively. For mental health (physical health), they were 79 (63), 50 (62) and 52 (63) for each class respectively.

Conclusions. The cut-off points for the classes identified here can be useful in screening parents of children with cancer in clinical setting to provide clinical interventions to protect vulnerable parents from negative outcomes.

Background

Childhood cancer is an important cause of death in Asia, Central and South America, North Africa, and the Middle East [1]. According to the World Health Organization (WHO), each year about 300,000 new cases are diagnosed with cancer among children aged 0-19 years [2] and the estimated age-standardized incidence rates for all types of cancer ranges from 2.3 to 23.6 per 100,000 children worldwide (both sexes, ages 0-19) [3]. While, a higher incidence rate of cancer has been reported in developed countries (less than 40 per 100,000 children), the incidence of rate of cancer has been reported to be increased dramatically in developing countries including Iran [4]. In Iran, cancer related deaths rank first (14.2%, 23,300 cancer deaths) and only about 10,000 Iranian children were diagnosed with cancer during 2002-2012 [5]. In recent decades, because of remarkable progresses made in cancer treatment, the life expectancy and survival rates increase and cancer has become a chronic disease rather than an incurable disease [6]. It has been reported that the overall survival rate of children's cancer has increased from about 10% to approximately 90% over the last 40 years [7]. Extended

remission periods have increased the number of children and families that need adjusting to daily living problems. Parents are the primary support system for children with cancer and they experience reduced health-related quality of life (HRQOL) remarkably compared with parents of healthy children, since diagnosis of cancer and during the treatment [8-10]. HRQOL is defined as the perceived health status and daily living with any changes in physical and mental health, and social functioning [11]. It has been reported by studies that HROQL of parents (of children with cancer) is associated with a variety of the factors including higher levels of education, age of child, time elapsed since cancer diagnosis, type of treatment, or treatment intensity, etc. [11-13]. However, there is not a consensus among the studies in associated factors. Higher HRQOL of parents (who have children with cancer) and parental adjustment can positively affect child's treatment, and even the outcome of treatment [12]. Therefore, it is crucial to investigate HRQOL of parents among different areas, preferably using a valid and robust questionnaire in this area. Short Form-36 Health Survey (SF-36) questionnaire is one of the most widely used questionnaire in studies not only for measuring HRQOL in parents of children

suffering from cancer [13-15], but also for assessing the health status of adults aged 18 and older [16-18] and comparing HRQOL in different cultural groups within a country [17], as well as assessing HRQOL of individual patients with various diseases in clinical settings [15, 19, 20]. The SF-36 questionnaire is a psychometrically sound, relatively brief, and a simple instrument that is frequently used in health studies [17] that is available in many languages and has been psychometrically validated [16, 21]. The Persian version of the SF-36 questionnaire (used in this study) has also been psychometrically validated in Iran as well. Scores are calibrated so that 50 is the mean score or norm [22]. In some studies, it is only stated that a lower score indicates poorer health [15, 23]. In some others, score 50 has been reported as a distinction point between the lower and upper score of health [23, 24].

Parents of children with cancer are considered as main caregivers especially when their children receive the treatment at home. The required time and effort needed to care for a child with cancer, along with the financial/logistical issues created by treatment, expose parents to extensive stress which may have implications for parents' HRQOL. Healthcare systems should understand diminishing of HRQOL in parents having a child with cancer to manage its implications more effectively. By screening for parents, one can achieve early detection and reveal the risk factors affecting HRQOL to help health care professionals to provide intervention strategies to promote HRQOL of parents of children with cancer. This in turn can substantially improve quality of life of children with cancer. This highlights the need for separating parents with different levels of HRQOL and determining suitable cut-offs using appropriate statistical methods to identify parents with poor HRQOL. To our knowledge, despite the widely use of this questionnaire, the cut-off point of this scale is not clearly defined. Understanding and interpretation of results based on unique cut-off points might help identifying individuals at the potential risk for poor HRQOL in some conditions like comparison of HRQOL of caregivers or individual patients with various diseases or different cultural groups. Moreover, cut-off points can be used in clinical practice to screen HRQOL of parents of children with cancer.

The purpose of the present study was to find appropriate cut-off points for the SF-36 questionnaire in a sample of parents of children with cancer applying latent profile Analysis (LPA) in order to adding another possibility to use it. We also investigated the potential impact of demographic characteristics to see if they are related to HRQOL in our sample of parents of children with cancer.

Methods

DESIGN

The present cross-sectional study was conducted at two settings, pediatric hematology/oncology wards of a

large and central university hospital (BESAT hospital) in 2017. This hospital is the only university hospital with pediatric and clinic departments in Hamadan, Iran. Pediatric hematology ward has 14 active beds, 14 staffs and 3 doctors. In this ward, services such as chemotherapy, blood and bone marrow sampling are provided.

POPULATION AND SAMPLE

The children diagnosed with cancer were selected by simple random sampling from the patients' medical records. Inclusion criteria were: (1) passing at least three months since the child's diagnosis of cancer; (2) not having a diagnosed physical or psychological illness in the parents that might effect on HRQOL (examples are depression, migraine, and physical chronic diseases); (3) being only one child with cancer in the family; and (4) both parents are alive. The sample size was estimated 112 couples (112 mothers and 112 fathers) with type I error of 0.05 and 90% power. Of the 112 couples invited, one did not respond to the invitation, one did not complete the questionnaire correctly, and two could not come back to the hospital within the study timeframe. Therefore, the sample size was reduced to 108 couples (the response rate was 96.43%).

DATA COLLECTION AND USED VARIABLES

Data was collected between May and October 2017. The data collection tools were demographic information including gender, age and education level of parents, the number of children in the family, gender, age and rank of birth of the child with cancer, and SF-36 questionnaires. The SF-36 questionnaire is a generic instrument for assessing the perceived HRQOL and daily functioning that are used internationally [25]. This questionnaire consists of 36 items and eight subscales, summarized in two summary domains: the physical (PCS) and mental component summary (MCS) measures or domains [26]. Its eight subscales include: physical functioning (PF, 10 items), role-physical functioning (RP, 4 items), bodily pain (BP, 2 items), general health perception (GH, 5 items), vitality (VT, 4 items), social functioning (SF, 2 items), role-emotional functioning (RE, 3 items), and mental health (MH, 5 items). One item asks about change in health status [22]. All items in each subscale are scored so that a high score defines a more desirable HRQOL. Then, the scores transfer linearly so that the lowest and highest scores in each subscale and total scores of PCS and MCS are set between 0 (worst HRQOL) and 100 (best HRQOL) [25, 27]. Scores are calibrated so that 50 is the average score or norm [25]. The PCS domain consists of physical functioning, bodily pain, general health perception and role-physical functioning subscales. The MCS domain consists of role-emotional functioning, vitality, social functioning and mental health subscales [28]. The score of each summary domain is the sum of these four subscales [26, 27]. In SF-36 questionnaire, usually the total score is not given and only the mean score of subscales and each summery domain are calculated

and compared with the 50 [24, 26]. The PCS and MCS domains were constructed to simplify the analysis of the outcomes by reducing the number of subscale scores, increasing the reliability and improving the validity of scores in distinguishing between physical and mental health outcomes [26, 29].

Montazeri et al. translated the SF-36 in Persian and assessed the psychometric property of the questionnaire in a sample of 4000 healthy adults. In Montazeri et al. study, Cronbach's alpha computed to assess internal consistency was between 0.77 and 0.90 for subscales [24]. In another study, internal reliability of the SF-36 was investigated and Cronbach's alpha values were determined as 0.90 for PCS and 0.87 for MCS [27]. In current study Cronbach's alpha values were between 0.70 and 0.83 for subscales, 0.70 for the PCS and 0.84 for the MCS domains indicating an appropriate internal consistency of the SF-36.

PROCEDURES

One of or both parents of a child were met in pediatric hematology/oncology wards of hospital when they brought their child for chemotherapy, visiting by the doctor, or follow up testing. After explaining the goals of the study, the questionnaires were given to a parent who was accompanied by her/his child and were asked to bring the completed questionnaire back at the next visiting time. Each questionnaire for mothers and fathers of the same child was put in separate envelopes. There was no name on the filled questionnaires and the questionnaire data was collected anonymously. The expected time to complete the questionnaire was about 45 minutes per person.

DATA ANALYSIS

Data was analyzed using Mplus 6.0 [30] and DiagTest3Grp package of R 3.3.0 [31]. Demographic characteristics of the participants were summarized using descriptive statistics and interpreted with ordinal logistic regression. Latent profile Model (LPM) [32] was used to find the cut-off points for the SF-36 questionnaire. P-value < 0.05 was considered to be statistically significant.

2-5-1 LPM. In the present study, several goodness of fit criteria were utilized, including:

- Akaike Information Criteria (AIC) [33];
- Bayesian Information Criteria (BIC) [34];
- Sample size adjusted Bayesian Information Criteria (SSABIC) [35].

The model with the lowest value of AIC, BIC, SSABIC is the most parsimonious model. The Lo-Mendel-Rubin Adjusted Likelihood Ratio Test (LMRT) and the Entropy criterion were also utilized to determine the number of latent classes as well as the accuracy of classification of individuals [36]. The LMRT is a statistical test to compare nested normal mixture distribution model with different number of classes (comparing a model with k classes and $k-1$ classes) [36, 37]. The entropy criterion

determines the accuracy of individual classification and its higher values indicate a better fit with the values greater than 0.80 indicating high discriminating ability of the latent classes [32, 36].

Determination of cut-off points. Optimal cut-off points for obtained optimal number of classes were determined using the volume under the ROC surface (VUS) [38], as well as, the extended Youden index [39]. Then using these criteria, the posterior memberships of individuals to each class obtained from LPM were used as a gold standard. Let D_1, D_2, \dots, D_K be the K classes (in order) of the quality of life (QOL) and also let $c_1 = c_2, \dots, c_{K-1} (c_1 < c_2 < \dots < c_{K-1})$ be the $K-1$ cut-off points creating the K ordinal classes for the HRQOL for the parents participated in the study. Then the VUS can be calculated using $F_i (i = 1, 2, \dots, K)$ which is the cumulative distribution of HRQOL for each class. For a complete description of calculating VUS for three class or more see [31]. The values of VUS equal 1 mean perfect cut-off points. The Youden index takes its values between 0 (inadequate pointer) and 1 (perfect pointer). A complete description about calculating the extended Youden index for more than two diagnosed classes can be found in [34].

Results

DESCRIPTIVE STATISTICS OF DEMOGRAPHIC VARIABLES AND HEALTH RELATED QUALITY OF LIFE

More than half of the children was male (55.5%). The mean age of children was 10.5 ± 1.06 years. More than half of the children aged 5-8 years (59.3%), followed by 8-11 (27.7%), and 11-14 years (13%). More than half of the children were the first-born child (51.6%), followed by the second (28.7%), the third (13%) and the fourth child and more (6.5%) in the family. The most frequent cancer type was acute lymphocytic leukemia (69.4%), followed by lymphoma (10.1%), chronic lymphocytic leukemia (7.4%), sarcoma (4.6%), Wilms tumor (3.8%), and eye neoplasm (2.8%). The mean time since diagnosis of cancer in children was 12.4 ± 16.5 (95% CI: 72-3) months. The mean of age was 35.37 ± 11.7 for mothers and was 41.29 ± 7.4 for fathers. Most of the fathers were high school graduate (70.4%), 13.9% of fathers and 11.4% of mothers had a university degree, and 15.7% of fathers and 21.3% of mothers were primary school graduates or undergraduate.

The mean scores of the PCS and MCS domains were 54.91 ± 12.98 and 53.39 ± 11.67 for mothers, respectively and were 57.69 ± 10.45 and 52.82 ± 11.25 for fathers, respectively. Also, the mean score of total HRQOL were 55.26 ± 9.48 and 54.15 ± 11.04 for fathers and mothers, respectively.

CHOOSING THE OPTIMAL NUMBER OF LATENT CLASSES USING LPA

An LPA with one- to four-latent classes was performed on the eight subscales of the SF-36 questionnaire.

Tab. I. Fit indices from the latent profile analysis.

| Number of latent class | AIC | BIC | Sample-size adjusted BIC ($n^* = (n + 2)/24$) | Entropy | LRT test | p-value |
|------------------------|-----------|-----------|--|---------|----------|---------|
| C = 1 | 15395.590 | 15449.595 | 15398.893 | | | |
| C = 2 | 15232.682 | 15317.064 | 15237.843 | 0.898 | 177.245 | < 0.001 |
| C = 3 | 15090.496 | 15205.256 | 15097.515 | 0.942 | 156.941 | < 0.001 |
| C = 4 | 15072.051 | 15217.188 | 15080.928 | 0.906 | 35.707 | 0.154 |

C: Class; AIC: Akaike Information Criteria; BIC: Bayesian Information Criteria; LRT test: Lo-Mendel-Rubin adjusted test

Table I shows the results. According to the criteria listed in this table, the three-latent classes' solution was the best, so that the smallest AIC, BIC, and SSABIC were obtained when the number of three classes was used (considering four classes did not improve the results significantly). Based on the LMRT test, fitting a LPM with three classes is significantly better than a LPM with two classes ($p < 0.001$) for capturing the heterogeneity of observed responses on the eight subscales, while fitting a LPM with four classes did not improve the results significantly ($P = 0.154$). Moreover, the obtained entropy for the three latent classes' model (0.942) indicates a very well discrimination of the classes using the eight subscales (Tab. I).

Figure 2 illustrates the mean scores of the eight subscales of the SF-36 questionnaire for the three identified classes. One of the three classes included 11.1% of parents characterized by low scores on the six subscales including the physical functioning, pain, general health, energy, emotional well-being and social functioning subscales and high scores on the two subscales of role limitations due to physical health and emotional problems. The second class represents the moderate HRQOL (included 80% of parents) and the third class represents the good HRQOL (included

9% of parents) (Fig. 1). The mean scores of the total HRQOL and the two summary domains for the three identified classes as well as the total sample were provided in Figure 1.

OPTIMAL CUT-OFF POINTS FOR TOTAL QOL

The estimated cut-off points using generalized Youden index were 47.53 and 59.04 with Youden index 0.46 (95% CI: 0.36-0.57) and correct classification proportions of 87%, 47% and 58%, for weak, moderate and good QOL, respectively. The estimated cut-off points using ROC surface were 46.78 and 62.43 with VUS 0.58 (95% CI: 0.46-0.71) and correct classification proportions were 88%, 65% and 53%, respectively. Therefore, score ≤ 47 , 48-61 and ≥ 62 indicating weak, medium, and good QOL, respectively.

OPTIMAL CUT-OFF POINTS FOR MENTAL HEALTH

The estimated cut-off points using generalized Youden index were 45.64 and 61.30 with Youden index 0.38 (95% CI: 0.27-0.49) and correct classification proportions of 81%, 58% and 37%, for weak, moderate and good mental health, respectively. The estimated cut-off points using ROC surface were 43.29 and 58.63 with

Fig. 1. The mean scores of the physical and mental health summary domains, and the total health related quality of life for each identified class.

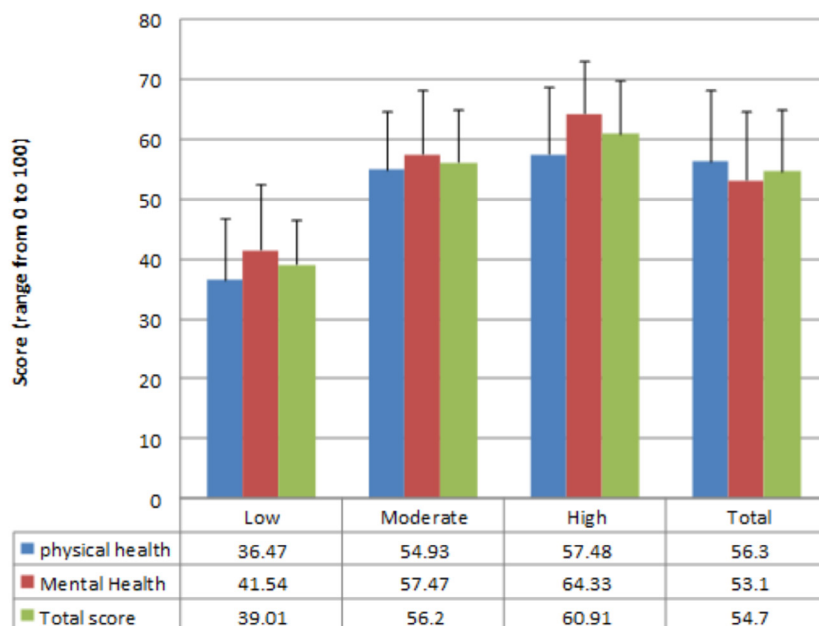
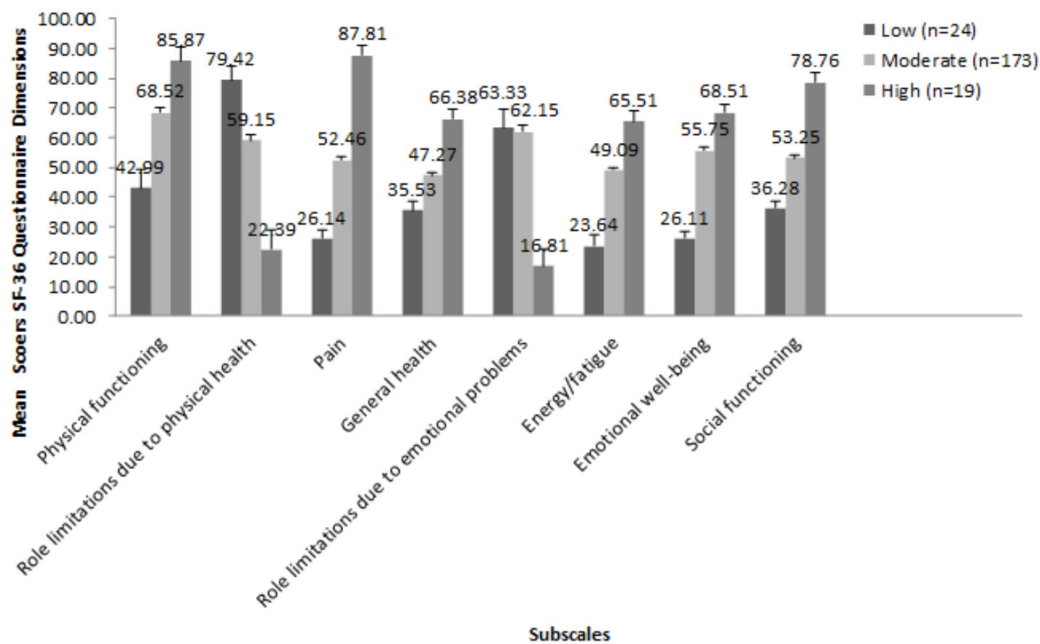


Fig. 2. Latent Profile Analysis on the eight subscales of the SF-36 questionnaires.

VUS 0.46 (95% CI: 0.34-0.56) and correct classification proportions were 79%, 50% and 52%, respectively. Therefore, based on the results score ≤ 44 , 45-63 and ≥ 64 indicating weak, medium, and good mental health, respectively.

OPTIMAL CUT-OFF POINTS FOR PHYSICAL HEALTH

The estimated cut-off points using generalized Youden index were 49.40 and 58.83 with Youden index 0.41 (95% CI: 0.31-0.52) and correct classification proportions of 76, 33 and 73%, for weak, moderate and good physical health, respectively. The estimated cut-off points using ROC surface were 43.29 and 58.63 with VUS 0.56 (95% CI: 0.45-0.64) and correct classification proportions were 63%, 62% and 63%, respectively. Therefore, based on the results score ≤ 43 , 44-59 and ≥ 60 indicating weak, medium, and good physical health, respectively (Fig. 3). Figure 4 illustrates the correct classification proportions for the two subscales and total HRQOL.

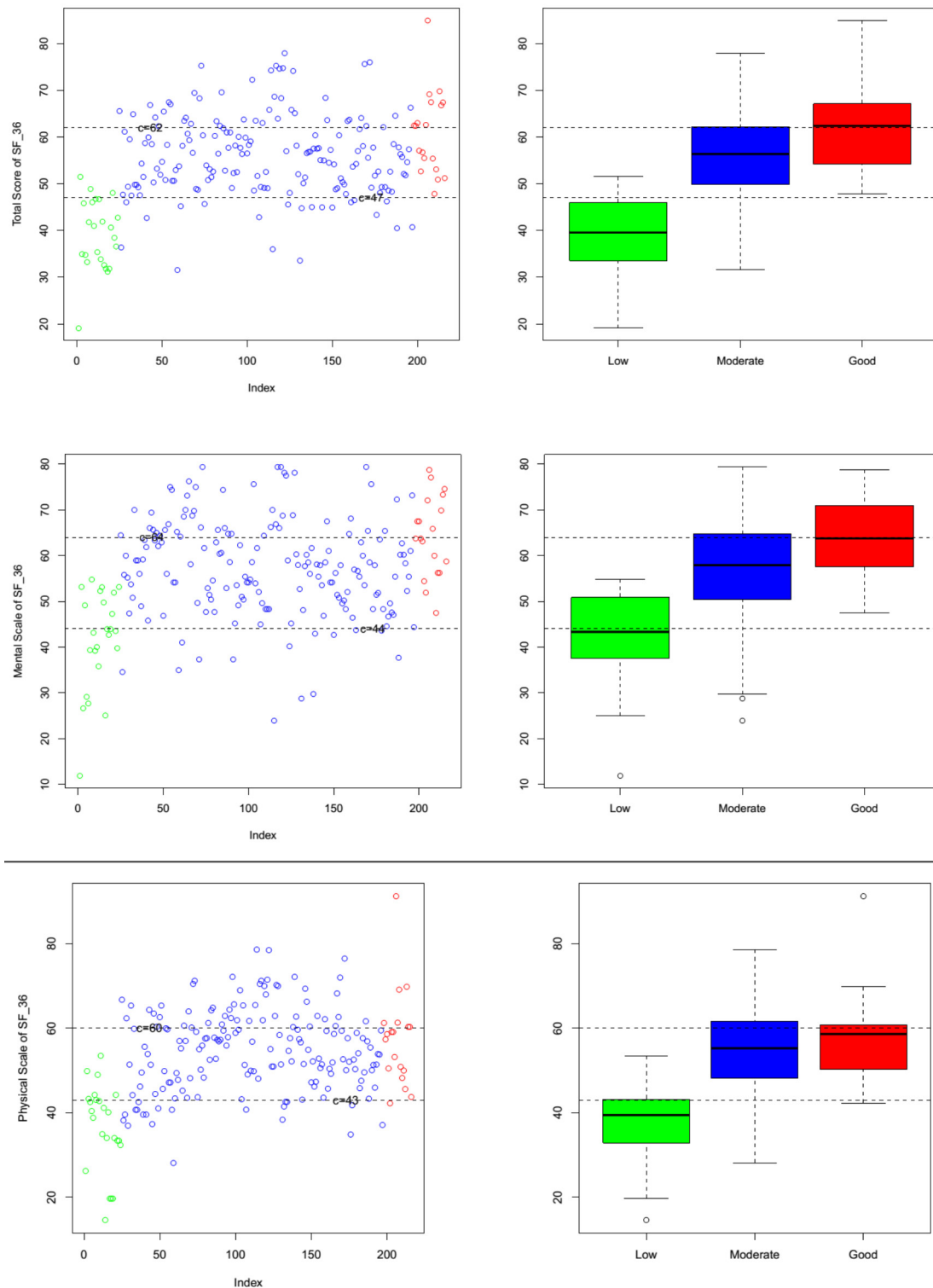
Results of Fitting ordinal Logistic regression to investigate associated factors

The relative frequency of demographic characteristics of the study units for the three identified HRQOL latent classes was provided in Table II. For example, 62.5% of weak class was mothers. The potential effect of these demographic variables including age of parent, age and gender of child, gender of parent, parent's education level and birth rank was investigated on the three identified latent classes of HRQOL using ordinal logistic regression. Results were shown in Table III. According to Table III, none of the demographic variables had a significant association with the three identifies classes of HRQOL (P-value > 0.05).

Discussion

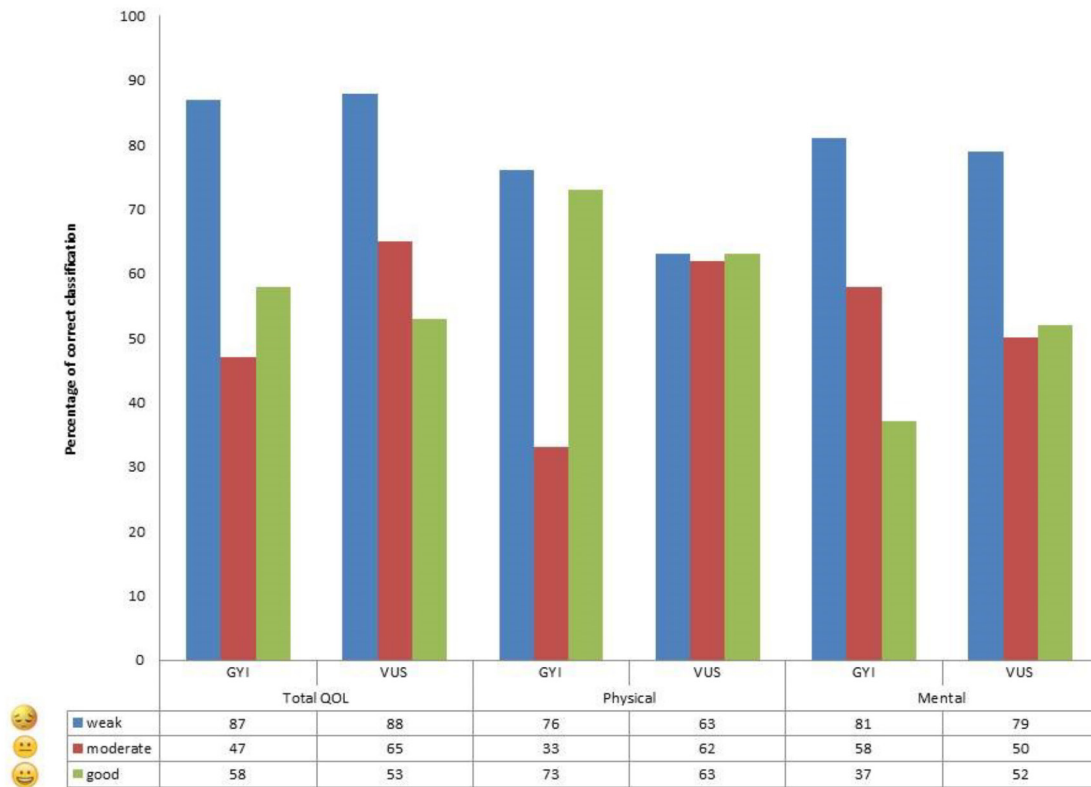
SF-36 is one of the useful tools for screening HRQOL. The expanded utility of this questionnaire to classify HRQOL of parents of children with cancer including three classes of good, moderate, and weak, in both PCS and MCS domains, and total HRQOL can add one more feature to its ability to use. Current study was conducted to determine cut-off points for SF-36 using LPA aiming at screen subjects with poor HRQOL. To our knowledge, some other studies have used other methodologies to determine cut-off points, but all of them have identified only two classes [40-43] and no study has identified cutoff points of SF-36 in parents of children with cancer. LPA methodology is a suitable and powerful statistical technique that can search for the best number of classes of subjects and captures the heterogeneity between individuals to allocate them to the classes [32]. In the present study, the results of LPA suggested that the SF-36 can be used to screen parents of children with cancer with low HRQOL. The optimal cut-off points (thresholds) were ≤ 43 to ≥ 60 on the PCS domain, ≤ 44 to ≥ 64 on the MCS domain and ≤ 47 to ≥ 62 on the total scale and had fair to good correct classification proportions (88, 65 and 53% for the three classes respectively). The determined cut-points were especially successful in identifying parents of children with cancer with low HRQOL (over 80% correct classification) indicating the usefulness of SF-36 in screening for subjects with poor HRQOL (those who may need urgent appropriate interventions). We also determined a two-class cutoff point (threshold) to compare our used method with similar studies which determined a two-class threshold for the SF-36 [40-42]. With a threshold of 47, the sensitivity, specificity and the

Fig. 3. Scatter plots and box plots of SF-36 Health Survey Questionnaire (the optimal cut-points indicated in dashed lines). Weak, moderate and good QOL classes colored in green, blue and red, respectively.



area under the ROC curve were obtained 87, 90, and 91 % respectively in parents of children with cancer which achieved greater or comparable performance compared with similar studies with different methodologies. This research improved the utility of SF-36 as a widely used

questionnaire and provided remarkable scope for further validation and secondary analyses of existing datasets. Our findings related to association between demographic characteristics and HRQOL did not indicate any significant relationship between the three

Fig. 4. The percentage of correct classification based on generalized Yuden index (GYI) and volume under ROC Surface (VUS).

identified classes of HRQOL of parents of a child with cancer and their demographic characteristics, such as gender, age and education level, as well as the number of children, gender and age of child and time since diagnosis of cancer in children. Our findings were in line with previous studies [13, 14, 44, 45], but contradicted with some other studies. In a study conducted in Korea, the gender of child with cancer was shown to have a potential influence on maternal adjustment and mental health. The authors concluded that this finding might be related to Korean culture that the first son is expected to take care of his parents during their aging period [12]. In other studies, the higher education level was associated with low HRQOL in parents of children with cancer [13, 46]. The authors stated that these parents wanted to be involved in the medical decision-making [46], or might like to look for information about their child's cancer and be familiar with risks that their children face. This preference might increase stress and have negative impact on their HRQOL [13].

Strengths and Limitations. There were some limitations in the present study. One primary limitation was the lack of a "gold-standard" questionnaire in general to measure HRQOL to validate the SF-36 domains in studies trying to determine cut-off points for the SF-36 questionnaire. So, we were unable to validate our results. Second limitation was the lack of enough

Tab. II. The relative frequency of demographic characteristics of study units in the three identified HRQOL latent classes.

| Variable | Weak (n = 24) | Moderate (n = 173) | Good (n = 19) |
|-----------------------------|------------------|-----------------------|------------------|
| Parent | | | |
| Father | 37.5 | 50.9 | 57.9 |
| Mother | 62.5 | 49.1 | 42.1 |
| Age of parent | | | |
| < 35 | 20.8 | 31.2 | 31.6 |
| 35-45 | 50 | 56.1 | 31.6 |
| 45-50 | 29.2 | 12.7 | 36.8 |
| Education of parents | | | |
| Undergraduate | 100 | 86.7 | 78.9 |
| Graduate | 0 | 13.3 | 21.1 |
| Number of child | | | |
| < 3 | 50 | 72.8 | 63.2 |
| ≥ 3 | 50 | 27.2 | 36.8 |
| Gender of child | | | |
| Female | 33.3 | 45.7 | 47.4 |
| Male | 66.7 | 54.3 | 52.6 |
| Age of child | | | |
| 8-11 | 41.7 | 61.3 | 57.9 |
| 11-14 | 41.7 | 27.7 | 15.8 |
| 14-18 | 17.6 | 11 | 26.3 |
| Rank of child | | | |
| < 3 | 62.5 | 84.4 | 68.4 |
| ≥ 3 | 37.5 | 15.6 | 31.6 |

* Ref stands for the reference category

Tab. III. Comparison of the three classes: testing equality for latent class predictors with multiple ordinal logistic regressions.

| Variable | Odds Ratio | 95% CI | P-value |
|------------------------|------------|--------------|---------|
| Gender | | | |
| Male | 1.85 | (0.84, 4.09) | 0.129 |
| Female (Ref*) | 1 | - | - |
| Age | | | |
| < 35 | 1.31 | (0.33, 5.24) | 0.705 |
| 35-45 | 0.72 | (0.23, 2.24) | 0.579 |
| 45-50 (Ref) | 1 | - | - |
| Education | | | |
| Undergraduate | 0.39 | (0.14, 1.11) | 0.078 |
| Graduate (Ref) | 1 | - | - |
| Number of child | | | |
| <3 | 1.42 | (0.51, 3.96) | 0.504 |
| ≥ 3 (Ref) | 1 | - | - |
| Sex of child | | | |
| Female | 1.37 | (0.68, 2.75) | 0.379 |
| Male (Ref) | 1 | - | - |
| Age of child | | | |
| 8-11 | 0.56 | (0.18, 1.79) | 0.331 |
| 11-14 | 0.34 | (0.10, 1.13) | 0.077 |
| 14-18 (Ref) | 1 | - | - |
| Rank of child | | | |
| < 3 | 0.99 | (0.28, 3.42) | 0.982 |
| ≥ 3 (Ref) | 1 | - | - |
| Time since diagnosis | 1.01 | (0.98,1.03) | 0.527 |

* Ref stands for the reference category.

samples to show the heterogeneity of subjects in terms of HRQOL. It is suggested to conduct large scale studies to determine cut-off points in different diseases. Third limitation was the use of self-report to assess HRQOL, which increased susceptibility to recall as well as social desirability bias and may result in an underestimation of HRQOL. Consequently, the HRQOL levels should be interpreted with caution. Fourth, in the present study, no information was gathered about the relapse or treatment protocol in children with cancer, because the participants were parents. Despite these limitations, this analytic study may have a number of strength and implications for healthcare policy. First, here LPA was used to determine cut-off points which have several advantages over other techniques like hierarchical/k-means clustering. This is due to the fact that LPA is a model-based method, so maximum likelihood estimates are used to classify cases based on their posterior probability of class membership [47]. Second cut-off points were provided for both components of the questionnaire and the whole questionnaire (total quality of life) which add another possibility to use the SF-36 questionnaire.

Conclusions

The current study determined cut-off points for SF-36 using LPA method to classify HRQOL of parents of

children with cancer in the good, moderate, and weak classes, on both PCS and MCS subscales, and total HRQOL. The optimal cut-off points (two and three classes) obtained by LPA can be used in clinical settings to screen parents of children with cancer with low HRQOL. Nevertheless, further validations using larger datasets and gold standard are recommended for future studies. We also investigated the association between demographic characteristics and the HRQOL. None of demographic variables was significantly associated with the ordinal outcome of HRQOL.

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Ethics approval and consent to participate

This study Compliance with ethical standards and was approved by the Institutional Review Board of the Hamadan University of Medical Sciences [approval NO. 950 221 669]. This study was compliance with ethical standards [Ethical NO. was IR.UMSHA.REC.1395.52]. Written informed consent was obtained from all participants and the purpose of the study was explained. It is also important to note that the results of the study were anonymously reported to comply with the ethical criteria.

Consent for publication

The article presented has been confirmed by all authors for publication.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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None.

Conflict of interest statement

The authors declare that they have no competing interests

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Authors' contributions

LT conceived the idea. LT and NS performed content analysis, interpreted the results and participated and revised the draft of manuscript. AF designed study, and abstracted the data. AS participated in design study and in whole project. FC supervised the whole project, participated in initial study design, participated in study implementation and drafted the manuscript.

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ORIGINAL ARTICLE

Emerging multimorbidity patterns and their links with selected health outcomes in a working-age population group

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Key words

Latent class analysis • Multimorbidity • Self-rated health • Quality of life • Primary care.

Summary

Background. The study aims to identify recurrent multimorbidity pattern among individuals in the age-group 15-64 years. Further, the study examines the association of these identified patterns with sociodemographic variables and selected health outcomes.

Methods. The study utilized data on 2912 individuals in the age-group 15-64 years collected under the burden of diseases study among patients attending public health care settings of Odisha. A latent class analysis was used to identify commonly occurring disease clusters.

Results. The findings suggested that 2.4% of the individuals were multimorbid. Two latent disease clusters were identified, low co-morbidity and Hypertension-Diabetes-Arthritis. Findings

highlighted that age, belonging to a non-aboriginal ethnicity and urban area increased the risk of being in the 'Hypertension-Diabetes-Arthritis' group. Furthermore, 50% of the individual in the 'Hypertension-Diabetes-Arthritis' group reported poor quality of life, whereas 30% reported poor self-rated health compared to only 11% by their counterparts. Additionally, the mean health score reported by the individuals in the 'Hypertension-Diabetes-Arthritis' group was 39.9 compared to 46.9 by their counterparts.

Conclusions. The study findings hint towards increasing burden of multimorbidity among the working age population, which depicts a shift in causation of diseases as a result of which preventive measures also need to be taken much prior.

Introduction

Multimorbidity is defined as the coexistence of two or more chronic conditions [1]. With the rise of chronic non-communicable diseases (NCDs) and increased life expectancy, multimorbidity is becoming a norm rather than the exception. In low- and middle-income countries (LMICs) such as India, the impact of these changes are more explicit due to changes in the lifestyle and environmental exposures which contribute to NCDs (such as an increase in obesity and physical inactivity) along with aging [1]. But the healthcare system is still oriented towards treatment for single conditions and acute diseases. Even the treatment guidelines are based on particular conditions rather than holistic treatment of multiple co-morbid conditions. Consequently, patients with multimorbidity need to often visit multiple healthcare providers, which increases the treatment burden, leads to low patient satisfaction and poor health outcomes [2-4].

A global multi-country study has reported the prevalence of multimorbidity to be high (ranging from 45-71%) across LMICs [5]. In another study, covering 28 LMICs, the mean world standardized multimorbidity prevalence for LMICs was 7.8%, among population aged ≥ 18 years [6]. Prevalence of multimorbidity varied from 4.5% to 83.0% in South Asia [7, 8]. Community-based studies from India such as the WHO SAGE survey conducted in 2007-2010

among those aged ≥ 18 years, reported a prevalence of 20% [9]. Another study conducted among rural elderly reported a prevalence of 60% [10]. In primary care settings the prevalence of multimorbidity increased from 6% among 18-29 year olds to 44% among those aged ≥ 70 years [11]. In all the studies multimorbidity increased with age. Of note, those with multimorbidity were reported to have higher mortality as compared to those with single morbidity [8]. Although most studies have focused on older patients, multimorbidity is more prevalent in absolute terms in those aged under 65 years. However, the impact of multimorbidity in those aged between 15-64 years is under-researched, and we know little about the clinical and socio-demographic characteristics of the working age population with multimorbidity, their patterns of health and social care use, and the potential changes that could be made to services to manage these patients better.

In another study, the number of people with multimorbidity and the prevalence of multimorbidity seems to have increased in recent years [6, 11]. Recent studies examining comorbidity patterns in non-centenarian populations using correlation analysis [12, 13] and latent class analysis revealed that diseases are not independent and tend to compound and interact. Seven comorbidity classes emerged from the data in a study of a large representative sample of Danish adults [14]. While 59% were classified as having no or just one condition, the other six classes had a very high

prevalence of multimorbidity. The most prevalent classes included hypertension (14%), musculoskeletal disorders (10%), and mental disorders (7%).

Thus, there is a need to understand the common patterns of multimorbidity defined as chronic diseases that cluster together most frequently [14]. There were studies which describe disease clusters that occur with the highest frequency or prevalence. However, it may be more meaningful to focus on the associations beyond chance or patterns of diseases, known as associative multimorbidity [15]. Associative multimorbidity is derived by different statistical methodologies, such as observed to expected ratios or odds ratios among the most commonly dyads or triads of chronic conditions, or cluster and factor analyses to identify systematic clusters among diseases. We need a better understanding of the clustering of multimorbidity patterns in the population. Thus, we aimed to explore the profiles of multimorbidity patterns in outpatients of different levels of public health care facilities. Our hypothesis was (a) the presence of distinct patterns with a small but existing proportion of individuals and (b) that these patterns would be associated with sociodemographic factors (gender, age) and selected health outcomes.

Materials and methods

DATA SOURCE AND SAMPLING DESIGN

The present study utilized data from the survey “burden of diseases among patients attending public health care settings of Odisha-2015”, undertaken across ten public health care facilities. The project was conducted under the stewardship of the Department of Health and Family Welfare, Government of Odisha, India. The survey utilized a stratified random sampling design to select the study participants [16]. Considering the non-response rate of 10%, a total of 3377 participants were included in the survey in the age-range of 14-95 years. However, as the study is based on the working age-group population, data on 2912 individuals in the age-group 15-64 years as derived from the original dataset for the purpose of the present study.

ETHICAL CONSIDERATION

All the survey tools and documentations received an ethical approval from the Public Health Foundation of India (PHFI) research ethics committee [16]. They were performed in accordance with the relevant guidelines and regulations. Additionally, all essential prior official permission was acquired to conduct the study at health facilities. An informed consent was obtained from all the study participants after disclosing the purpose and procedure of the study. Confidentiality and anonymity were maintained at all stages of data collection and dissemination [16].

MEASURES

The present study utilized information of 18 self-reported chronic diseases including acid peptic disease, arthritis, chronic back pain, diabetes, epilepsy, filariasis, hearing

disorder, heart disease, hypertension, kidney disease, lung diseases, mental disorder, osteoarthritis, skin diseases, stroke, tuberculosis, thyroid diseases and vision disorder to identify frequently occurring diseases groups among the working population (15-64 years) in Odisha, India.

The correlates of the identified latent disease classes were further computed, utilizing variables age-group (15-34 years/ 35-49 years/50-64 years), sex (male/female), ethnicity (aboriginal/non-aboriginal), schooling (no education/ primary/secondary and above), current marital status (in union/not in union), socio economic status (above poverty line/below poverty line), place of living (rural/urban), health insurance (no/yes), and health care facility visited (primary/secondary/tertiary) as predictors and identified latent disease classes as outcome of interest.

Furthermore, the present study utilized three perception-based health outcomes, namely poor self-rated health, poor quality of life and health score. Self-rated Health (SRH) was computed by recoding the responses received from the question, “Would you say that your health is?” The responses for the question had five categories, excellent, very good, good, fair and poor, which were recoded into binary variable poor SRH/not poor SRH.

Furthermore, quality of life was assessed utilizing 81 items which were classified into five domains related to quality of life. These domains included acute and chronic symptoms, self-care, mobility, physical activities and usual activities. All the items were recoded to provide a logical direction (unidirectional). Further, a Cronbach’ alpha statistics was utilized check the scale reliability ($\alpha = 0.87$), which suggested the scale to be reliable for further computation. A principal component analysis was utilized to compute a quality of life (QoL) score, which was further segmented into two parts, namely “poor QoL/non-poor QoL”. A detailed description of the items used in the generation of QoL scores is provided in the Additional Document 1.

The third health outcome was a health score, which was based on the question: “Think about a scale of 0-100, with zero being least desirable state of health that you could imagine and 100 being the perfect health. What number, from 0 to 100 would you give to the state of your health. On average over the last three days?”

DATA ANALYSIS

A descriptive analysis was used to study the background characteristics of the working age sample under consideration. Additionally, a weighted prevalence was computed for all the 18 chronic disease conditions included in the present study. To identify multimorbidity patterns among the working age-group population a latent class analysis (LCA) approach was carried out [14, 17, 18]. All the eighteen chronic diseases, namely acid peptic disease, arthritis, chronic back pain, diabetes, epilepsy, filariasis, hearing disorder, heart disease, hypertension, kidney disease, lung diseases, mental disorder, osteoarthritis, skin diseases, stroke, tuberculosis, thyroid diseases and vision disorder were included as observed indicators. Four latent classes were included in the study. Fit indices Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC) (lowest values were indicative of the best

fitting model) were used to identify the optimal number of latent classes to be included in the study [14, 17, 19]. After identification of the optimal number of latent disease classes, all the units (sampled individual/participants) were segregated into one of the identified latent class using the computed probability of membership [14, 17, 19]. Additionally, item-response probabilities were utilized to assign labels to the identified latent disease classes, i.e. the labels were based on the item(s) (disease(s)) with higher probabilities [14, 17, 19].

In the present analysis only two latent disease classes were identified, out of which the first group had low item-response probabilities of all the eighteen-disease included, and was therefore labelled as 'low comorbidity' group. This 'low comorbidity' group was considered as the base outcome for the unadjusted (bivariate) and adjusted (multivariable) binary logistic regression. Multivariable binary logistic regression was adjusted for age, sex, ethnicity, education level, marital status, socio-economic status, residence, health insurance, and type of facility and was used to identify the correlates of being in the second latent disease class as compared to 'low co-morbidity' group. Linkages of the identified latent disease classes were observed with three perception-based health outcomes, namely poor self-rated health, poor quality of life and health score. To study the association between latent disease classes and perception-bases health outcomes chi-squared tests of significance were performed.

Data wrangling, analysis and visualization were performed using R studio Version 1.3.1093, (R Studio, Inc. PBC) and MS Excel. The R package 'poLCA' (2014) was used to conduct LCA [18]. All the estimates computed in this study are derived by applying appropriate sampling weights derived utilizing the surveys sampling plan.

Results

DESCRIPTION OF THE STUDY POPULATION

The background characteristics of the study participants is presented in Table I.

The prevalence of chronic diseases is presented in Figure 1. Our analysis suggests that 2.4% of the individuals in the working age-group were affected with multimorbidity. The findings suggest that among the working age population, skin disease (5.99%), hypertension (5.92%), arthritis (4.91%), acid peptic disorder (3.87%), diabetes (3.49%), and chronic back pain (1.76%) were the six most commonly occurring disease conditions.

Table II illustrates the findings from the latent model fits. For the present analysis four latent classes were well identified. Smallest values of AIC and BIC were utilized to identify the optimal number of latent classes. Findings suggest that latent class 2 has the lowest AIC (7605.7) and BIC (7826.8) values and therefore, two latent classes were identified from the study sample.

As shown in Table III, these classes were assigned labels on the basis of the item-response probabilities, which were 'low co morbidity' and 'Hypertension-Diabetes-Arthritis', respectively. Each of the study participant

Tab. I. Descriptive characteristics for working population (15-64 years).

| Variables | Frequency (N = 2912) | Percentage |
|-------------------------------|----------------------|------------|
| Age group (in years) | | |
| 15-34 | 1371 | 51.72 |
| 35-49 | 940 | 31.61 |
| 50-64 | 601 | 16.67 |
| Sex | | |
| Male | 1517 | 51.66 |
| Female | 1395 | 48.34 |
| Ethnicity | | |
| Aboriginal | 1276 | 44.68 |
| Non-aboriginal | 1636 | 55.32 |
| Schooling | | |
| No | 1031 | 34.49 |
| Primary | 862 | 29.41 |
| Secondary and above | 1019 | 36.10 |
| Current marital status | | |
| In union | 2238 | 75.33 |
| Not in union | 674 | 24.67 |
| Socio-economic Status | | |
| Below poverty Line | 1374 | 47.03 |
| Above poverty Line | 1538 | 52.97 |
| Place of living | | |
| Rural | 812 | 28.39 |
| Urban | 2010 | 71.61 |
| Health Insurance | | |
| No | 1711 | 61.25 |
| Yes | 1095 | 38.75 |
| Facility | | |
| Primary | 430 | 15.28 |
| Secondary | 1902 | 65.53 |
| Tertiary | 580 | 19.19 |

was segregated into one of the two identified latent classes based on the highest item-response probability. Around sixty seven percent of the participants belonged to 'low comorbidity' class, whereas 32.89% belonged to 'Hypertension-Diabetes-Arthritis' group. The 'low comorbidity' group included those with low prevalence of all the assessed chronic diseases, whereas 'Hypertension-Diabetes-Arthritis' included individuals with high probabilities of diabetes, arthritis and hypertension, with latent class proportion of 50.60%, 50.20% and 46.10%, respectively.

Table IV provides the description of two latent classes identified in the present study. In the 'low co morbidity' group, 51.90% of the participants belonged in the age-group 15-34 years. Around 52% of the individuals in 'low co morbidity' group were males, 54.90% belonged to non-aboriginal ethnicity group, 36.04% had education level secondary and above, 74.68% were in a marital union, 52.82% reported to be above poverty line, 71.79% resided in urban areas, 61.13% had no health insurance, and 20.17% attended tertiary healthcare facility for curing their ailment. The 'Hypertension-Diabetes-Arthritis' group constituted 53.07% males, 66.99% of the non-aboriginal

Tab. II. Fit statistics for latent class analyses.

| Number of latent classes | Number of observations | Number of parameters estimates | AIC | BIC | G ² | X ² | DF | LL |
|--------------------------|------------------------|--------------------------------|--------|---------|----------------|----------------|------|---------|
| 2 | 2912 | 37 | 7605.7 | 7826.8 | 120.8 | 333.5 | 2875 | -3765.9 |
| 3 | 2912 | 56 | 7632.3 | 7966.9 | 109.4 | 265.4 | 2856 | -3760.2 |
| 4 | 2912 | 75 | 7645.3 | 8093.59 | 84.5 | 226.1 | 2837 | -3747.7 |
| 5 | 2912 | 94 | 7670.5 | 8232.32 | 71.7 | 369.4 | 2818 | -3741.3 |

L: Log Likelihood; BIC: Bayesian Information Criterion; AIC: Akaike Information Criterion.

Tab. III. Class Proportions and class-specific Probabilities from all Latent Class Model of Chronic Conditions.

| Class | 1 | 2 |
|-----------------------------|-----------------|---------------------------------|
| Assigned label | Low comorbidity | Hypertension-Diabetes-Arthritis |
| Class Proportion | 67.11 | 32.89 |
| Item-response probabilities | | |
| Arthritis | 0.039 | 0.502 |
| Diabetes | 0.005 | 0.506 |
| Hypertension | 0.001 | 0.461 |
| Lung Disease | 0.007 | 0.001 |
| Acid Peptic disease | 0.026 | 0.068 |
| Back Pain | 0.015 | 0.030 |
| Heart Disease | 0.004 | 0.003 |
| Stroke | 0.002 | 0.001 |
| Vision | 0.001 | 0.002 |
| Deafness | 0.001 | 0.001 |
| Kidney Disease | 0.003 | 0.001 |
| Epilepsy | 0.003 | 0.001 |
| Thyroid Disease | 0.008 | 0.001 |
| Tuberculosis | 0.008 | 0.001 |
| Filariasis | 0.002 | 0.001 |
| Mental Disorder | 0.001 | 0.001 |
| Skin Disease | 0.079 | 0.001 |
| Osteoarthritis | 0.002 | 0.001 |

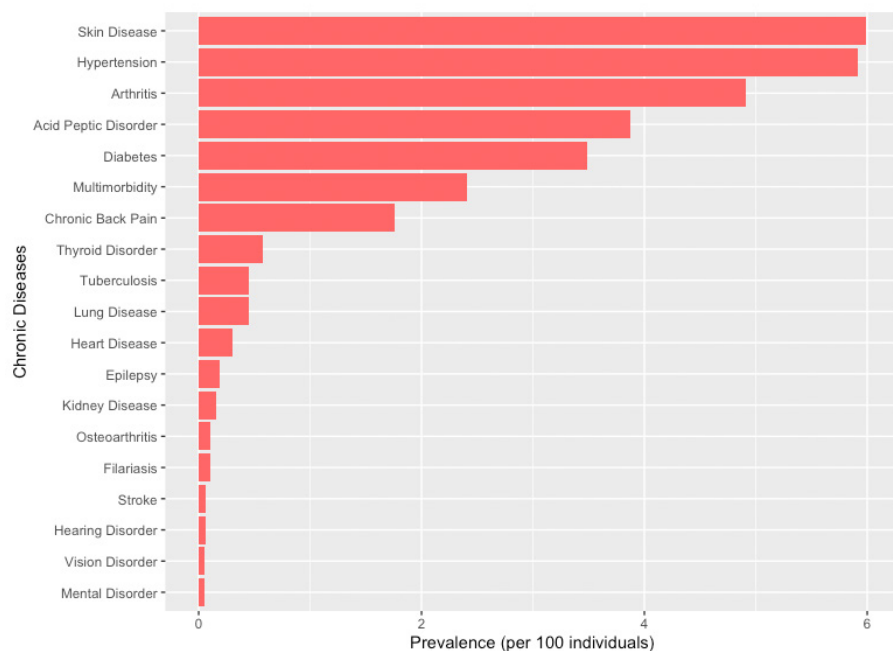
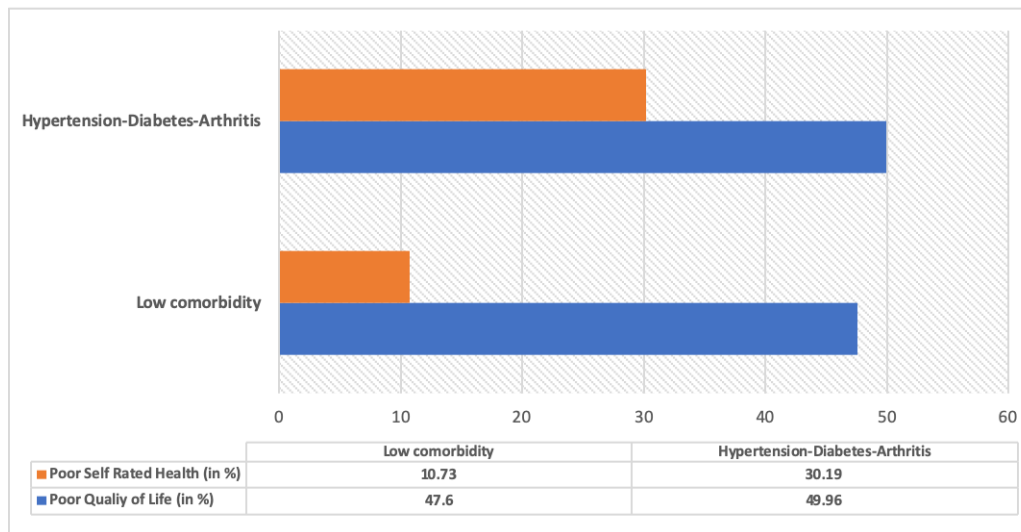
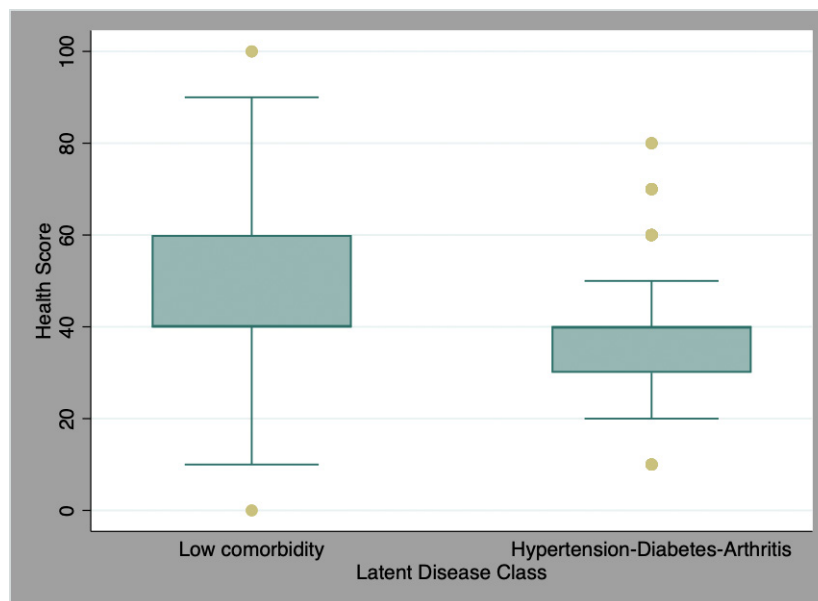
Fig. 1. Distribution of chronic diseases among the working age-group.

Fig. 2. Distribution of poor self-rated health and poor quality of life by identified disease clusters.**Fig. 3.** Boxplot depicting the distribution of health score between two latent disease classes (chi-squared p-value < 0.000) among older adults.

population, 38.83% not educated, 95.15% in marital union, 52.75% above the poverty line, 66.56% from urban areas, and 59.67% with no health insurance.

Binary logistic regression was adjusted for age, sex, ethnicity, education level, marital status, socio-economic status, residence, health insurance, and type of facility. The findings highlighted that age, ethnicity, and place of residence were found to be significantly associated with the being in one of the multimorbid groups. The findings suggest that with increasing age [(35-49 years: AOR = 9.69 (5.69,16.64); 50-64 years:10.80 (3.89, 15.77)] and belonging to a non-aboriginal ethnicity [AOR = 1.37 (1.02, 1.83)] increased the risk of being in the “Hypertension-Diabetes-Arthritis” group compared to ‘low-co morbidity’ group. Whereas, residing in urban

areas [AOR = 0.72 (0.53, 0.98)] reduced the risk of being in the “Hypertension-Diabetes-Arthritis” group by compared to ‘low co morbidity’ group.

The findings suggest a statistically significant association between latent disease classes with self-rated health ($p = 0.000$), quality of life ($p = 0.000$) and health score ($p = 0.000$). Figure 2 highlighted that 49.96% of the individual in the ‘Hypertension-Diabetes-Arthritis’ group reported poor quality of life, whereas 30.19% reported poor self-rated health (SRH) compared to only 10.73% reporting poor SRH in the “low comorbidity group”.

Additionally, the mean health score reported by the individuals in the ‘Hypertension-Diabetes-Arthritis’ group was 39.9 (scale 0-100) compared to 46.9 by their counterparts (Fig. 3).

Tab. IV. Bivariate and multivariable binary logistic regression results for covariates by latent disease class.

| Characteristics | Weighted percentage | | Latent Class 2 vs Latent Class 1 | |
|-------------------------------|-------------------------------|--|----------------------------------|------------------------|
| | Low comorbidity (N = 2603) | Hypertension- diabetes-arthritis (N = 309) | uOR (95% C.I.) | aOR (95% C.I.) |
| Age group (in years) | | | | |
| 15-34 (Ref.) | 51.90 | 6.47 | 1.00 | 1.00 |
| 35-49 | 31.12 | 42.07 | 10.84*** (6.72, 17.49) | 9.69*** (5.64, 16.64) |
| 50-64 | 16.98 | 51.46 | 14.29*** (5.07, 29.16) | 10.80*** (3.89, 15.77) |
| Sex | | | | |
| Male (Ref.) | 51.98 | 53.07 | 1.00 | 1.00 |
| Female | 48.02 | 46.93 | 0.95 (0.75, 1.21) | 1.21 (0.91, 1.60) |
| Ethnicity | | | | |
| Aboriginal (Ref.) | 45.10 | 33.01 | 1.00 | 1.00 |
| Non-aboriginal | 54.90 | 66.99 | 1.67*** (1.29, 2.13) | 1.37*** (1.02, 1.83) |
| Schooling | | | | |
| No education (Ref.) | 35.00 | 38.83 | 1.00 | 1.00 |
| Primary | 28.97 | 34.95 | 1.09 (0.82, 1.43) | 1.25 (0.91, 1.72) |
| Secondary and above | 36.04 | | 0.65** (0.48, 0.88) | 0.99 (0.70, 1.41) |
| Current marital status | | | | |
| In union (Ref.) | 74.68 | 95.15 | 1.00 | 1.00 |
| Not in union | 25.32 | 4.85 | 0.15*** (0.08, 0.25) | 0.97 (0.71, 1.32) |
| Socio-economic status | | | | |
| Below poverty line (Ref.) | 47.18 | 47.25 | 1.00 | 1.00 |
| Above poverty line | 52.82 | 52.75 | 0.99 (0.78, 1.26) | 1.03 (0.71, 1.31) |
| Place of living | | | | |
| Rural (Ref.) | 28.21 | 33.44 | 1.00 | 1.00 |
| Urban | 71.79 | 66.56 | 0.78* (0.61, 1.01) | 0.72*** (0.53, 0.98) |
| Health insurance | | | | |
| No (Ref.) | 61.13 | 59.67 | 1.00 | 1.00 |
| Yes | 38.87 | 40.33 | 1.06 (0.83, 1.35) | 1.03 (0.77, 1.38) |
| Facility | | | | |
| Primary (Ref.) | 14.56 | 16.50 | 1.00 | 1.00 |
| Secondary | 5.27 | 65.70 | 0.88 (0.64, 1.23) | 0.84 (0.58, 1.22) |
| Tertiary | 20.17 | 17.80 | 0.77 (0.52, 1.16) | 0.67 (0.43, 1.06) |

* p < 0.10, ** p < 0.05, *** p < 0.001. uOR: Unadjusted Odds Ratio; aOR: Adjusted Odds Ratio

Discussion

The study indicates the prevalence and patterns of multimorbidity among young working age group populations in primary care setting. The prevalence of multimorbidity was 2.4% in working age group and the most common conditions were skin diseases, hypertension, arthritis, acid peptic disorder, diabetes, and chronic back pain. Latent class analysis found two groups i.e., 'low comorbidity' and 'Hypertension-Diabetes-Arthritis'.

Similar to other studies from India increase in age is the most common risk factor for the higher morbidity group [18, 20, 21]. In contrast to most of studies from India where female gender is found to be predisposed for multimorbidity [11, 21, 22], in our study gender is not a risk factor for higher morbidity group. Hence, the relationship of multimorbidity with gender among the young adults does not seem similar to that in elderly and needs further assessment. We have found that chances of being in 'Hypertension-Diabetes-Arthritis' group is higher among rural population. Other studies from India have

also highlighted the growing burden of multimorbidity among rural India. Growing burden of multimorbidity even among rural young's is a concern for Indian health system. Although there are auxiliary nurse midwives (ANMs) and accredited social health activists (ASHAs) who are the main link between the community and health system i.e., Primary Health Care Centre (PHCs), there primary work is still oriented towards maternal and child care and they currently have very limited training in the field of non-communicable disease. In addition to this, there are paucity of qualified MBBS doctors (allopathic doctors) in rural India and PHCs are often managed by AYUSH (non-allopathic alternative system) physicians [23].

As different studies include different diseases for multimorbidity definition, comparing the pattern of multimorbidity from our study is unfeasible. Furthermore, there is lack of data on multimorbidity in productive age group. A recent community-based study from Kerala from productive age group found prevalence of multimorbidity to be 45%, reasons for high prevalence is that study are higher lower age limit cut off i.e., 30 years, whereas our

study includes participants aged 15 years and above. Also, that study includes participants with higher blood pressure and blood sugar reading measured at the time of study as hypertension and diabetes whereas our study included only doctor diagnosed hypertensive and diabetic participants [24].

A multi-country study conducted on national databases from high and low middle-income countries among participants aged 50 years and above have found hypertension, cataract, and arthritis as the most prevalent co-morbid conditions. Most common patterns found in this study were “cardio respiratory” (angina, asthma, and chronic obstructive pulmonary disease), “metabolic” (diabetes, obesity, and hypertension), and “mental articular” (arthritis and depression) [22]. Studies from across the world and India also found these as common multimorbidity clusters [22, 25-28]. UK bio-bank study on participants aged 40 years and above has also highlighted that diabetes, hypertension and asthma and usually the common clusters found [29]. Another study from nationally representative data of Danish Adults aged 16 years and above had identified seven classes: 1) Relatively healthy; 2) hypertension; 3) Musculoskeletal Disorders; 4) Headache-Mental Disorders; 5) Asthma-Allergy; 6) Complex Cardio metabolic Disorders; and 7) Complex Respiratory Disorders. However, patterns can't be compared they have also identified poor health-related quality of life in patients with multimorbidity clusters in comparison to relative healthy. Other studies also shows poor health related health among patient with multimorbidity [8, 21].

From previous studies and our study finding we can postulate that hypertension, diabetes, asthma and arthritis are few of the most common co morbid conditions in the multimorbid people and affects patient's quality of life and the multidisciplinary approach targeting these diseases could be helpful for the management for patients with multimorbidity. The national programme for prevention and control of cancer, cardiovascular disease, diabetes and stroke (NPCDCS) in India have recently include Chronic Obstructive Pulmonary Disease (COPD), Chronic Kidney Disease (CKD), Non Alcoholic Fatty Liver (NAFLD) and TB program [30]. Integration of all these programs was important because of their common risk factors such as obesity, alcohol use, diabetes and will lead to holistic management of these disease in future. Despite arthritis being the part of most common disease combination, both is young and old population it is still not part of our national programme. Also, there is dearth of rheumatology specialist in India which leads to late diagnosis and mismanagement of patient with arthritis. Therefore, there is need for integration of arthritis management in NPCDCS program and capacity building of primary care physician for its diagnosis and management. Multimorbidity thus requires a multifaceted approach which can be well integrated and approached with ease.

Most of studies on multimorbidity in India are from the older population, anticipating the growing prevalence of multimorbidity among working age group studying the prevalence, patterns, and its health impact in working age population are pivotal. Also, to the best of our knowledge

this is first study from India, to identify the pattern of diseases using latent class analysis among working class group as most of the studies usually report most common dyad and triads. Although the data of chronic conditions are self-reported we have cross verified the medical records to confirm the diagnosis. Another limitation is association observed doesn't infer causality because of cross-sectional study design.

Conclusions

‘Hypertension-Diabetes-Arthritis’ emerged as a recurrent disease group among the individuals in the working group. The findings hint towards sociodemographic inequality in the disease burden. Individuals in the disease group are more likely to be associated with poor perception-based health outcomes. Thus, interventions with equitable prevention approaches, ensuring improved physical and mental well-being, are vital to reducing the burden on the high-risk disease group. Study findings vary owing to the differential cut-off values used. There needs to be uniformity in deciding and defining where to start. Moreover, there is a shift in the causation of diseases, resulting in which preventive measures also need to be taken much prior. Similar studies based on a nationally-representative sample are warranted.

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Ethical approval

All the survey tools and documentations received an ethical approval from the Public Health Foundation of India (PHFI) research ethics committee. They were performed in accordance with the relevant guidelines and regulations. Additionally, all essential prior official permission was acquired to conduct the study at health facilities. An informed consent was obtained from all the study participants after disclosing the purpose and procedure of the study. Confidentiality and anonymity were maintained at all stages of data collection and dissemination.

Conflict of interest statement

The authors declare that they gave no competing interests.

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Authors' contribution

Conceptualization: SP. Methodology: SP, MP, MP, PP. Software: PP, PM, MP. Validation: PP, PM, MP. Formal analysis: PP, PM, MP. Data Curation: PP, PM, MP. Writing - Original Draft: SP, PP and PG. Writing - Review & Editing: SP, PP and PG. Visualization: PP, PM, MP. Supervision: SP. Project administration: SP.

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ORIGINAL ARTICLE

The role of statistical significance testing in public law and health risk assessment

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Key words

Public law • Statistical significance • Null hypothesis testing • Health risk assessment

Summary

Following a fundamental statement made in 2016 by the American Statistical Associations and broad and consistent changes in data analysis and interpretation methodology in public health and other sciences, statistical significance/null hypothesis testing is being increasingly criticized and abandoned in the reporting and interpretation of the results of biomedical research. This shift in favor of a more comprehensive and non-dichotomous approach in the assessment of causal relationships may have a major impact on human health risk assessment. It

is interesting to see, however, that authoritative opinions by the Supreme Court of the United States and European regulatory agencies have somehow anticipated this tide of criticism of statistical significance testing, thus providing additional support to its demise. Current methodological evidence further warrants abandoning this approach in both the biomedical and public law contexts, in favor of a more comprehensive and flexible method of assessing the effects of toxicological exposure on human and environmental health.

Introduction

Few aspects of scientific methodology as those related to statistical analysis and interpretation, and particularly to statistical significance testing, had and are currently having an effect on causal inference and more generally in the establishment of causal relations in science, including toxicology and biomedical sciences overall but not restricted to them, having major implications also in psychological and economic research [1]. Statistical tests are in fact becoming more complex and sophisticated, frequently relying on an advanced mathematical basis, and are largely employed in medicine and toxicology, among other sciences, to make inferences about causal relations and to inform the risk assessment of interventions such as drugs or of environmental chemicals. Among statistical tests, the most largely used is the so-called “statistical significance testing”, based on the evaluation of the compliance of the observed data in any study and experiment with the p-value function and the null hypothesis, i.e. the hypothesis of no association between the chemical or more generally the exposure of interest with the study endpoints [1-4]. In particular, statistical significance testing yields the identification of cut-points based on p-value function, e.g. $p < 0.05$ or $p < 0.001$, subsequently used as reference values for null hypothesis testing, with an ineludible spread of such deleterious and erroneous dichotomous approach relying only on fixed thresholds [5]. Unfortunately, this statistical significance testing has been the pillar and the tenet of risk assessment and biostatistics for decades,

despite the unheard complaints by several investigators and methodologists pointing out its ambiguous and confounded information [5, 6]. In somewhat recent times, however, authoritative bodies and scientific communities have raised their voice against the use of p-value and statistical significance testing, invoking the demise of such approach in establishing causation and performing risk assessment [1, 7, 8]. However, the legal world, through pronouncements of the Supreme Court of the United States and scientific contributions by public law scholars, has been advocating the same perspective, i.e., the dismissal of an approach exclusively reliant upon the existence of a dichotomous “statistical significance” in favor of a more flexible and comprehensive method based on a number of factors that include the overall statistical evidence but are not limited to it. We here summarized the history in the use of statistical significance testing and its implication for toxicological risk assessment and for public law, anticipating that the latter will increasingly deal with these methodological issues particularly when dealing with health risks.

Statistical significance & null hypothesis testing in public health

The statistical training of students and investigators in the biomedical field, including medicine and toxicology, and in other fields such as psychology and economics has been greatly influenced by famous British statistician Ronald Fisher, and more specifically by a small but extremely relevant piece of his intellectual contribution,

i.e. the idea of using a single statistical test and even more attractively a single figure to define if results were worth reliance or not in terms of causal inference [1]. Although the influential statistician was not the first to propose the use of p-values, he was the one who suggested a cut-point – 0.05 – “to set a low standard of significance at the 5 per cent point, and ignore entirely all results which fail to reach that level” [9]. In other words, Fisher proposed to start from the null hypothesis of being no effect of the investigated “exposure,” to compute a p-value function, and to look at the intersection of such function with the effect size observed in the experiment: should such intersection be below 0.05, the results could be considered as “significant” (later considered to mean “statistically significant”). Although Fisher did not encourage to disregard results having a p-value higher than 0.05 and later tempered his position [10], his approach became the boundary line of most scientific inferences based on data analysis in the biomedical and psychological sciences. Results were “significant,” i.e., “true” and allowing to reject the null hypothesis of no association, in case p-value was lower than 0.05, further allowing the additional use of the expression “highly significant” in case p-value was < 0.001 . By contrast, results exceeding this boundary line were generally dismissed, independently of the actual p-value, and the corresponding results were deemed to be due to chance and not reflecting a causal relation. Unfortunately, such an approach was not accompanied by considerations such as the study sample size (that, if low, inherently increases the p-value for any observed association), the risk of bias of the study, the dose-response relation of the observed phenomena, the biological and temporal plausibility of the associations and finally its consistency across studies, all elements of key relevance when assessing the relation of any cause and exposure to a putative effect as originally suggested by Hill’s criteria in 1965 [11], and still relevant when evaluating causal relations in biomedical sciences, especially in public health and toxicology [1, 12]. In many scientific studies and especially in risk assessments, such black and white approach led to the claim that only when p-values are below the 0.05 cut-point we can draw causal inferences and claim the existence of a causal relation between, for instance, a toxic chemical or a drug and any kind of health endpoints.

While many statisticians, methodologists, and even official agencies have long claimed the extreme subjectivity and the serious pitfalls of an approach based on statistical significance and null hypothesis testing, it eventually took almost one century to “officially” highlight these flaws and the most serious implications exerted, for instance, in toxicological risk assessment and in the establishment of causality in legal evaluations. While invitations to consider the fallacious nature in Fisher’s claims on statistical significance and p-value cut-points had already been made [1, 13-15], it was only in 2016 that an official statement by the American Statistical Associations officially recognized and highlighted the problem [7]. More recently, a seminal paper that was

published in Nature [8] and received the support of a large number of scientists from many disciplines all over the world has convincingly made clear that statistical significance testing and its use in drawing inferences is flawed and may seriously mislead the authors and the readers of scientific articles [2, 3, 16-19]. Along the same line, an increasing number of Editors of scientific journals in the field of epidemiology and public health, medicine, and psychology have accordingly decided to ban or to discourage the reporting of the results as related to “statistical significance testing” [1, 20-23], while putting emphasis on other methodological aspects such as the magnitude and statistical precision of the estimates. Overall, there seems to be an overwhelming majority of methodologists now supporting the demise of statistical significance testing, thus precluding further use of the p-value tool to establish in a black and white manner “causality” in scientific research.

Recent trends in American public law on the use of statistical significance testing

Contrary to the wide and frequently uncritical propagation of statistical significance testing among scientists in the biomedical field, it is interesting to observe that the legal world has generally been more cautious in its use in scholarly inquiries, as well as in public law practice. This is arguably merit of the long tradition of the legal community in approaching with caution single “absolute” sources of certainty of any type-statistical significance testing undoubtedly and erroneously claiming to be one-and instead weighing the entire body of evidence in favor and against a specific thesis in a more balanced and nuanced way.

A recent example of such a cautious and thoughtful approach, somehow even become a paradigm, can be seen in the 2010 case *Matrixx Initiatives, Inc. v. Siracusan* [24], a seminal decision by United States Supreme Court that has been widely commended and appreciated even beyond the legal circuit [25-29]. The case, involving the pharmaceutical company Matrixx Initiatives, centered on the question of “whether a plaintiff can state a claim for securities fraud based on a pharmaceutical company’s failure to disclose reports of adverse events associated with a product” if the reports did not contain statistically significant evidence that the adverse effects may be caused by the use of the product [24]. Delivered by Justice Sonia Sotomayor, the unanimous opinion (9-0) of the Court affirmed the Court of Appeals for the Ninth Circuit’s judgment, concluding that the “allegations, ‘taken collectively,’ give rise to a ‘cogent and compelling’ inference that Matrixx elected not to disclose the reports of adverse events not because meaningless but because it understood their likely effect on the market ‘A reasonable person’ would deem the inference that Matrixx acted with deliberate recklessness (or even intent) ‘at least as compelling as any opposing inference one could draw from the facts alleged.’” We conclude, in agreement with the Court

of Appeals, that respondents have adequately pleaded *scienter*. Whether respondents can ultimately prove their allegations and establish *scienter* is an altogether different question” [24]. The opinion contains several notable statements that directly address the core of the statistical issue at stake, and more generally the basic issues and limitations of statistical significance testing. For instance, the Supreme Court stated that the “lack of statistically significant data does not mean that medical experts have no reliable basis for inferring a causal link between a drug and adverse events” and that “medical experts rely on other evidence to establish an inference of causation.” In addition, the Supreme Court emphasized that “medical professionals and researchers do not limit the data they consider to the results of randomized clinical trials or to statistically significant evidence.” Moreover, “the FDA similarly does not limit the evidence it considers for purposes of assessing causation and taking regulatory action to statistically significant data. In assessing the safety risk posed by a product, the FDA considers factors such as ‘strength of the association,’ ‘temporal relationship of product use and the event,’ ‘consistency of findings across available data sources,’ ‘evidence of a dose-response for the effect,’ ‘biologic plausibility,’ ‘seriousness of the event relative to the disease being treated,’ ‘potential to mitigate the risk in the population,’ ‘feasibility of further study using observational or controlled clinical study designs,’ and ‘degree of benefit the product provides, including availability of other therapies’”. Moreover, the opinion mentions other statements that support the conclusion that statistical significance is not required (and in some cases not achievable) to consider the possibility of causal relations between exposure and an adverse health effect. Overall, the opinion represents an excellent example of correct handling of the concept of statistical significance, under the assumption that it cannot be used as a surrogate indicator of the absence of causal relations. This approach is highly relevant since it goes beyond the traditional approach based on p-value traditional cut-points of 0.05/0.001, dismissing a key role of null hypothesis testing according to Fisher’s rule in establishing (and refusing) proof of causation. Unsurprisingly, many scholars have expressed appreciation for this highly relevant opinion, thus indicating how public law theory can take on board a correct approach in dealing with a highly specific and “sophisticated” statistical concept such as statistical significance/null hypothesis testing [25-29]. This comes as no surprise, however, since the issues raised in this seminal sentence by the Supreme Court have long been known to the public law scholarship, as comprehensively illustrated in a relevant paper by David Kaye published as early as 1986 on the Washington Law Review [30]. Most recently, the U.S. Supreme Court has returned to the topic of statistical significance testing in the case *Brnovich v. Democratic National Committee* of March 2021 [31]. Rather than risk assessment and public health, the case dealt with election law and its impact on access to vote. The Democratic National Committee

had filed a suit against the State of Arizona’s election law since it allegedly “had an adverse and disparate effect on the State’s American Indian, Hispanic, and African-American citizens,” and had been enacted “with discriminatory intent.” To this article, the interesting aspect lies in the statistical significance argument employed by Elena Kagan in her dissenting opinion, where she affirms that Section 2 of the Voting Rights Act of 1965 “demands proof of a statistically significant racial disparity in electoral opportunities” to strike down election rules. Adhering to the Circuit Court’s argumentation that voided the District Court’s initial dismissal of the suit, Kagan concludes that in the case at hand “Arizona’s policy creates a statistically significant disparity between minority and white voters.” However, the Court’s majority opinion, written by Samuel Alito, rejected what is described as a “procrustean” interpretation of Section 2 of the Voting Rights Act. Citing the Federal Judicial Center’s Reference Manual on Scientific Evidence, Alito’s majority opinion recalls that “statistical significance may provide ‘evidence that something besides random error is at work,’ but does not necessarily determine causes.” Alito’s opinion finds faults with the “statistical manipulation” of emphasizing statistical differences out of a proper context: in that case, while it was factually true that minority voters stood double the chance of having their vote nullified as an out-of-precinct ballot than non-minority voters, the practical difference was in absolute terms so slight that the law could not be held discriminatory.

As a final note, it should be emphasized that not only American public law but also the warnings of European risk assessment institutions signaled and somehow anticipated the shifting tide against the use and misuse of statistical significance testing. For instance, in 2011 the European Food Safety Authority, the official body in charge of assessing the toxicity of food and food constituents, issued a relevant opinion to define how statistical significance testing should (and should not) be used in risk assessment [32]. The opinion represents a good example of the growing awareness, even in a period antecedent to the ASA 2016 statement and the subsequent key scientific contributions, that the dichotomous approach entailed methodological pitfalls and that even in risk assessment null hypothesis testing proved inadequate, despite that being a field generally requiring a final yes/no outcome. The opinion correctly highlighted the need to always report effect/risk estimates and their measures of statistical stability (such as confidences limits), and to give attention to the real biological relevance of the effects even in the presence of small p-values and so-called statistically significant findings [32]. Therefore, it is not surprising that subsequent EFSA assessments and opinions have generally given a limited (if any) reliance on statistical significance testing, putting weight on the strength and the precision of the effect estimates, on dose-response relations, consistency across studies and study designs, quality of the studies and biological plausibility of the associations found in human studies. The convergence

in legal and toxicological-epidemiologic approaches toward the rejection of statistical significance testing in risk assessment mirrors the evolution of scientific methodology and appears to be much more adequate to account for all the complexities, the uncertainties but also the potential insights characterizing toxicological risk assessment and its public law implications and litigations [33].

Conclusions

Implications of abandoning statistical significance testing in public law and to health risk assessment. For the aforementioned methodological reasons and issues, the approach taken by the U.S. Supreme Court in the case *Matrixx v. Syracusan* case appears to be scientifically sound and somehow even anticipated the methodological shift of several scientific communities, including the statistical one, indicating the growing awareness of the public health community about the pitfalls of simply relying on a conventional black and white approach instead of a balanced assessment of the entire available evidence. Given the large and serious consequences induced by the use of the erroneous approach in data synthesis and causal interpretation represented by statistical significance testing and conventional p-value cut-points, a complete demise of this simplistic approach appears fully justified in both public law and health risk assessment in favor a more challenging but methodologically correct method based on the comprehensive assessment of the strengths and limitations of all the available evidence, and thus abandoning an unwarranted simplification devoid of scientific basis.

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Ethical approval

Ethical approval was not required for this study.

Conflict of interest statement

The Authors declare no conflict of interest.

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Authors' contributions

TF and SRV conceived the idea, and equally contributed to the writing of the manuscript.

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REVIEW

Mapping COVID-19 related research from Vietnam: a scoping review

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Key words

COVID-19 • SARS-CoV-2 • Coronavirus • Pandemic • Vietnam • Scoping review

Summary

Introduction. *The situation of COVID-19 pandemic is becoming more complex. The research institutes should focus on the most important challenge related to this outbreak at the national level. We aim to realize this scoping review to map publications on COVID-19 in Vietnam in order to guide research priorities and policies in the country.*

Methods. *This study was conducted at the Thai Binh University of Medicine and Pharmacy, from May to August 2020, according to the guidance for conducting systematic scoping review.*

Results. *A total of 72 studies met the inclusion criteria. The most frequent publications were original articles (27.8%), followed by letter to editor/correspondence (26.4%). According to the research priorities for COVID-19 set by the WHO, 41.7% studies*

focused on control and prevention of COVID-19, but none of studies on personal protective equipment or protocol for healthcare workers' safety were conducted. 12.5% studies carried out a thorough investigation into epidemiology of the COVID-19 pandemic in Vietnam. Virology and genomics, natural history of the virus and its transmission in Vietnam were described by 18.1% papers. Only one study was conducted in terms of development for candidate therapeutics.

Conclusion. *We call for national investigation on treatment against SARS-CoV-2 and protocol for medical staff protection. The government and academic institutions should work in collaboration with international stakeholders, including the WHO, to combat together the COVID-19.*

Introduction

In December 2020, the first case of an emerging respiratory infectious disease (COVID-19) due to a novel coronavirus, named SARS-CoV-2 was reported in Wuhan, China [1]. This outbreak is highly contagious with the reproduction number R_0 of SARS-CoV-2 which is estimated up to 3.5 [2-4]. In addition, this can be transmitted directly between humans via droplet, close contact with infected persons and indirect contact with contaminated surfaces or objects [1]. The outbreak has quickly spread out of China and affected the whole world. The World Health Organization (WHO) declared that it was a Public Health Emergency of International Concern on January 30, 2020, and then a pandemic on March 11, 2020 [1]. At the time of writing, the COVID-19 pandemic has affected 213 countries worldwide with 767,346 deaths and 21,564,286 confirmed cases [5].

The situation of pandemic is becoming more complex, and it is increasingly difficult to control diseases in order to reduce both morbidity and mortality rate. The outbreak has overwhelmed most countries in the world, even in high-income countries with modern, advanced medical system. Vietnam is a neighboring country of China with an approximately 1500 km of common border; therefore, the country faces a high risk of a severe COVID-19 pandemic. In addition, Vietnam is middle-income country and has a population density of nearly 100 million people, so this raises more challenges in fighting the outbreak.

The COVID-19 pandemic broke out in Vietnam on January 23, 2020 with the two first cases [6]. As of August 15, 2020, The Ministry of Health (MOH) reported 950 confirmed cases (447 recovered) and 23 deaths [7]. The COVID-19 has caused a complex emergency. The lockdown has seriously affected the domestic economy and the morale as well as quality of life of its citizens. The academic institutions must be primarily responsible for investigating this pandemic from a holistic perspective, including the distribution of asymmetric severity, morbidity, mortality and spread among different geographical areas. Especially in the context of low- and middle-income countries with limited human and economic resources, it is needed to avoid duplication of research topics. However, the research institutes should focus on the most important challenge related to COVID-19 pandemic at the national level. We aim to realize this scoping review to map publications on COVID-19 in Vietnam in order to guide research priorities and policies in the country.

Methods

We realized our scoping review according to the guidance for conducting systematic scoping review proposed by Peters et al. [8]. Development and reporting were followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) extension for scoping reviews [9].

We mapped the literature by 5 key steps: i). we identified the research question, then ii). we identified the literature relevant to COVID-19 in Vietnam and iii). We selected only those studies; iv) the data from the articles, including population type, participation of foreign experts, multinational study, hospital affiliation, studied topics and research priorities for COVID-19 set by the WHO were thereafter collected and summarized; v). Finally, we reported the results. The study was conducted at the Thai Binh University of Medicine and Pharmacy, from May to August 2020.

This scoping review was guided by the following questions: “What type of research on COVID-19 was carried out by Vietnamese institutions? What aspects of this pandemic and its impact were investigated in Vietnam?”

The following databases were investigated in all relevant studies published on: PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), Web of Science (<http://webofknowledge.com>) and Google Scholar (<http://scholar.google.com/>). The most recent search was conducted on July 31, 2020. The topic search terms used for searching the databases were the following:

#1: “COVID-19” OR “COVID19” OR “SARS-CoV-2” OR “nCoV”

#2: “Vietnam” OR “Viet Nam”

#3: #1 AND #2

No language, type of article or date of publication restrictions were applied. Search criteria were developed to capture articles relevant to research regarding COVID-19 pandemic from Vietnamese institutions. The studies which were not conducted in Vietnam and/or not related to COVID-19 were excluded.

Duplicate citations were initially removed in Zotero. All studies related to COVID-19 which were realized in the Vietnamese institutions, and authored by a Vietnamese researcher or a non-Vietnamese researcher were eligible for inclusion. Published and accepted articles in press that were already published online, or preprints were also included.

Two researchers (TLD and VTH) independently performed the screening of the articles. Any discordant result was resolved by agreement. In case of dispute, a third reviewer (MMT or TDN) was consulted for the decision. Reference lists of selected articles were screened to identify studies that might have been missing from the research. After the abstracts had been screened, the full texts of the articles were assessed for eligibility by the same two researchers and selected or rejected for inclusion in the systematic review.

Included publications were abstracted and summarized in Microsoft Excel 2016 using the following items: title, authors, name of the Vietnamese institutions involved in the study, time of publication (month and year), type of study (Original article, review, short communication, letter to editor/correspondence, perspective, commentary, editorial, preprint), studied topics, national or collaborative international, name of the countries in case of multinational studies and funding.

Results

STUDY RESEARCH

The initial search provided 256 papers. Of which 161 duplicate were deleted. After being screened by authors, 23 records were excluded because they did not meet the eligibility following criteria: research not conducted in Vietnam (19) and research not related to COVID-19 but mentioned COVID-19 in their abstract or in the text (4). Finally, 72 studies met the inclusion criteria [6, 10-80]. Figure 1 shows the research strategy according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

CHARACTERISTICS OF INCLUDED STUDIES

Table I shows the characteristics of the included papers. The most frequent publications were original articles (20/72, 27.8%), followed by letter to editor/correspondence (19/72, 26.4%), preprints (12/72, 16.7%) and short communication (6/72, 8.3%). Two studies were published early February 2020 on the first cases of COVID-19 in Vietnam. Six, 18, 20, 22 and 4 papers were published from March to August 2020, respectively. The majority of the studies (43/72, 59.7%) were conducted in collaboration with scientists from other countries but only 4 (5.6%) were multinational research. A total of 13/72 (18.1%) studies were affiliated by the authors of hospitals.

The funding was declared in 39 studies (54.2%) with 19 research (26.4%) were funded. Regarding the funding of selected studies, 11 studies were funded by non-government organizations and 8 received a governmental funding.

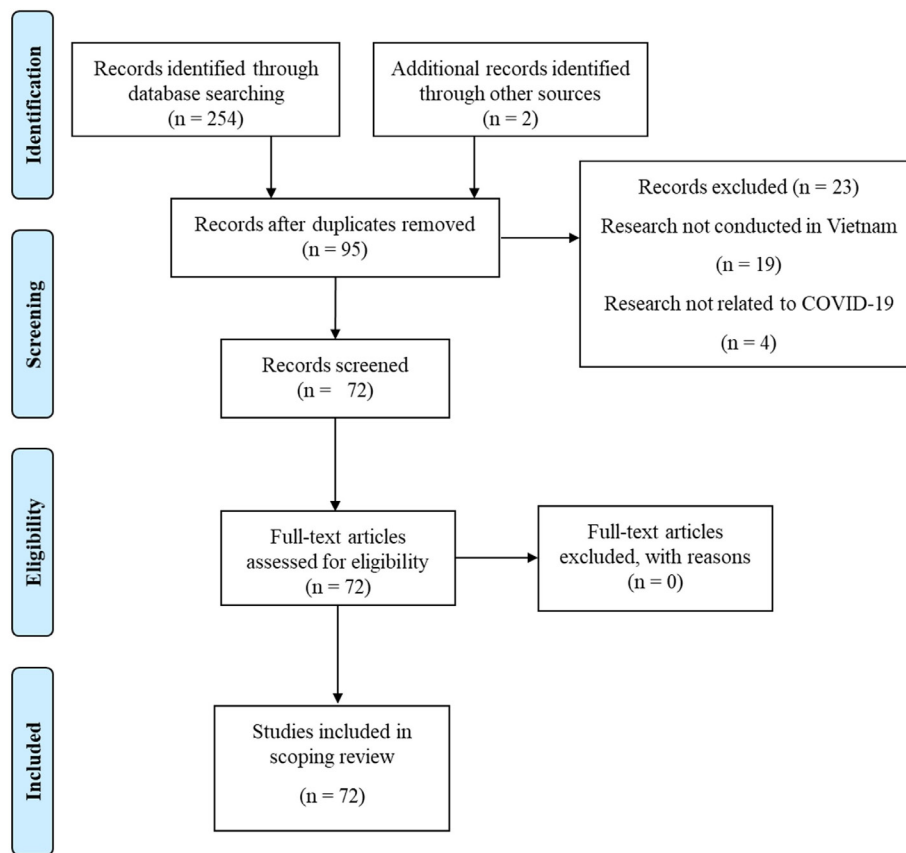
RESEARCH PRIORITIES

According to the research priorities for COVID-19 set by the WHO [81], a total of 30/72 (41.7%) studies focused on control and prevention of COVID-19 but no study on personal protective equipment or protocol for healthcare worker safe was conducted. Nine (12.5%) studies carried out a thorough investigation into epidemiology of the COVID-19 pandemic in Vietnam. Thirteen (18.1%) studied the virology and genomics, natural history of the virus and its transmission in Vietnam. The clinicopathological features of COVID-19 were described by 8 papers (11.1%). Two studies (one original article and one review) concentrated on the treatment of SARS-CoV-2 (Tab. II).

Discussion

Until now, Vietnam has reported three waves of COVID-19 outbreaks. After each wave, the pandemic is increasingly completed, and the new cases are on the increase [7]. Particularly, in the third outbreak which started on July 26, 2020, the rate of spread of this disease is higher than before. A total of 476 autochthonous cases within 3 weeks were recorded (50.1% of all cumulative

Fig. 1. Study flow diagram



cases in the country from nearly 7 months), including medical staff. Furthermore, 23 deaths were recorded in this time [7]. Especially, the source of infection in the community has not been determined. Studies on epidemiology, transmission, preventive measures, and treatment strategies are essential to reduce morbidity and mortality of COVID-19. Especially in poor countries, with limited financial capacity, it is necessary to identify priority studies according to each period of pandemic in the national level.

Our review is useful in the actual context of COVID-19 in Vietnam for fund allocation from the government to support health care and related research. We identified 72 articles, including 12 preprints conducting on the COVID-19 pandemic in the country. Unfortunately, the current published research on COVID-19 in Vietnam seems to be discordant from the epidemic research priorities set by the WHO. This is possible that some of projects are still ongoing and have not been captured in this review, but the current publications do not provide a strong preparation for the country to neither adequately tackle the pandemic nor to accumulate experience for prevention of other outbreaks in the future. The research gap related to COVID-19 identified by the WHO are: i) natural history of SARS-CoV-2, its transmission and diagnosis; ii) animal and environmental research on the origin of the virus; iii) epidemiological studies; iv) clinical characterization

and management of COVID-19; v) infection prevention and control, including health care workers protection; vi) research and development for candidate vaccines and treatment; vii) ethical considerations for research; and viii) integration of social sciences into the outbreak response [81]. These points should be utilized for focusing the topic and planning future research steps in Vietnam.

Most of the included studies in this scoping review were letter to editor and focused on control and prevention aspect. It is important because multiple effective measures have been applied to fight the COVID-19 pandemic in Vietnam such as: early lockdown, a strong political commitment and prompt actions with a multi-sectoral response plan, blanket media coverage of COVID-19 prevention, intensive surveillance, case management and large-scale health quarantine not only for patients, but also for persons in close contact with cases [10-24]. But these articles were narrative and described on experiences and reported views and experimental studies remain limited. Moreover, since the SARS-CoV-2 virus is highly contagious [2-4], safety for all healthcare workers must be ensured to protect themselves and to prevent nosocomial transmission. In fact, several medical staff in Vietnamese health facilities such as Bach Mai and Da Nang hospitals were infected by SARS-CoV-2 [7]. Isolation of infected health workers and colleagues

Tab. I. General characteristics of 72 included papers.

| Characteristics | Number of papers | Percentage |
|-------------------------------------|------------------|------------|
| Publication type | | |
| Original article | 20 | 27.8 |
| Letter to editor/ correspondence | 19 | 26.4 |
| Short communication | 6 | 8.3 |
| Review | 5 | 6.9 |
| Perspective | 3 | 4.2 |
| Case report | 1 | 1.4 |
| Commentary | 1 | 1.4 |
| Editorial | 1 | 1.4 |
| Viewpoints | 2 | 2.8 |
| Preprints | 12 | 16.7 |
| Other | 2 | 2.8 |
| Participation of foreign experts | 43 | 59.7 |
| Multinational study | 4 | 5.6 |
| Hospital affiliation | 13 | 18.1 |
| Studied topics | | |
| Clinicopathologic | 8 | 11.1 |
| Control and prevention | 30 | 41.7 |
| Economic impact | 7 | 9.7 |
| Epidemiology | 9 | 12.5 |
| Health impact | 3 | 4.2 |
| Medical management | 5 | 6.9 |
| Social impact | 3 | 4.2 |
| Treatment | 2 | 2.8 |
| Virology and genome | 11 | 15.3 |

who have contact with them aggravates the overload of medical human resources. Therefore, research on personal protective equipment, protocol for its safety and the implementation of designated hospital units for COVID-19 patients are essential [82]. But in Vietnam, research on this field is scarce.

Thirteen included studies in this review investigated the COVID-19 epidemiology in Vietnam, but epidemiological studies focused on viral transmission or health resources utilization remained lacking. We also find that there is a lack of experimental studies and large multicenter, clinical trials inspecting treatment modalities of COVID-19. Only one original article focused on new treatment options. This can be explained

by the poor participation of hospitals, especially central and provincial hospitals, in research.

The funding was declared in 39 studies. Of which, only 8 were Vietnamese government funders, while the remaining funding was raised by non-government organizations. Furthermore, despite the participation of foreign experts in 43 research, only 4 multinational studies were conducted. The government and academic institutions should work in collaboration with international stakeholders, including the WHO, to combat together the COVID-19.

This review has some limitations. We have screened the published papers only on PubMed, Web of Science and Google scholar. Ongoing research projects have not been captured. Finally, we have so far focused on only COVID-19-related studies in Vietnam. But this work shows the gap in research on COVID-19 of the country. It is the first step toward contributing to the development of a national research agenda. It helps government make decisions about prioritizing and allocating resources. We call for national investigation that takes emerging epidemics along with other public health priorities into consideration. In addition, we recommend establishing national capacity and encourage the investment in national companies for laboratory research materials. Furthermore, we strongly encourage hospitals and health facilities to get involved in therapeutic research strategies of SARS-CoV-2. Moreover, leading national universities must conduct projects to come up with solutions in the public health crisis, and provide guidance for the government based on the most scientific evidence. A COVID-19 national research framework with specific research projects should be thoroughly discussed to address critical gaps identified through this scoping review. This can be achieved through a partnership between the government, the Ministry of Health, and researchers in collaboration with WHO and international partners.

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Tab. II. Research priorities for COVID-19 in Vietnam.

| Research priorities for COVID-19 set by the WHO | Number of included studies | Percentage |
|---|----------------------------|------------|
| Natural history of the virus, its transmission and diagnosis | 13 | 18.1 |
| Animal and environmental research on the origin of the virus, including management measures at the human-animal interface | 0 | 0 |
| Epidemiological studies | 9 | 12.5 |
| Clinical characterization and management of disease caused by the virus | 8 | 11.1 |
| Infection prevention and control, including best ways to protect health care workers | 30 | 41.7 |
| Research and development for candidate therapeutics and vaccines | 1 | 1.4 |
| Ethical considerations for research | 0 | 0 |
| Integration of social sciences into the outbreak response | 15 | 20.8 |

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Authors' contributions

Thi Loi Dao: Conceptualization, methodology, validation, formal analysis, investigation, resources, data curation, writing – original draft. Minh Manh To: Validation, formal analysis, investigation, resources, data curation, writing – review and editing. The Diep Nguyen: Validation, formal analysis, investigation, resources, data curation, writing – review and editing. Van Thuan Hoang: Conceptualization, methodology, validation, formal analysis, investigation, resources, data curation, writing – review and editing, visualization, supervision, coordination.

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REVIEW

A comprehensive assessment of preconception health needs and interventions regarding women of childbearing age: a systematic review

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Key words

Preconception health • Childbearing • Needs • Pregnancy

Summary

Background. *This systematic review summarizes the preconception health needs of women in childbearing age, necessary to be addressed to have an eventual safe and healthy pregnancy.*

Methods. *Web of Science, PubMed and Scopus were searched. We excluded studies involving women with reproductive system pathologies and referring to interconceptive or pregnancy period and non-empirical or only abstract studies. Two researchers independently performed the blind screening based on titles/abstracts and full-text and the quality assessment.*

Results. *Four major domains resulted from the thematic analysis:*

knowledge, behaviors and attitudes, health status and access to healthcare services. The most examined topics were knowledge and awareness on preconception health, folic acid assumption, tobacco and alcohol consumption, physical activity and healthy diet.

Conclusions. *This review could assist healthcare professionals (physicians, nurses, midwives) in guiding tailored counselling to women to provide the adequate level of preconception care and act as a reference to policymakers.*

Introduction

Preconception health refers to a woman's condition before she becomes pregnant. Preconception period can be defined from a biological, individual and public health point of view. From a biological perspective, it includes a critical period spanning the weeks around conception when gametes mature, fertilization occurs and the developing embryo forms. In relation to individual action, the preconception period starts whenever a woman or a couple decide they want to have a baby. From a public health perspective, the preconception period can relate to a sensitive phase in the life course, such as adolescence, when health behaviors are established, before the first pregnancy [1]. Improving preconception health and healthcare can ultimately improve pregnancy outcomes [2]. Preconception health is a broad concept including management of chronic and genetic diseases, correct nutrition, adequate consumption of folic acid, exercise, control of body weight and healthy lifestyles [3]. The first step in providing preconception care requires an understanding of women's access to health services and their knowledge of preconception risk factors. Nevertheless, sometimes, women's knowledge of preconception health is poor, especially in those who have never had or are not planning a pregnancy [4, 5]. In a study conducted among Swedish teenagers, participants recognized the relevance of preconception

health and the importance of leading a healthy lifestyle. However, not everyone had the same level of knowledge and they had difficulty understanding some aspects of preconception health. Participants expressed the need to have more information on the topic despite having heterogeneous beliefs on the methods of providing education [6].

Women may be aware of some risk factors, such as tobacco use, alcohol, drug use and domestic abuse. Nonetheless, few women discuss preconception health with their doctor [7].

Habits of women in fertile age are of utmost importance, especially among women who are not planning a pregnancy. Such women are often very young, and the lack of preconception health knowledge can lead to negative consequences on the fetus / child's development and health. It is reported that women with unintended pregnancies do not have insurance coverage, continue to smoke and to be exposed to physical violence [8]. Among these women, the recognition of pregnancy is delayed by 5 or more weeks after conception [9], which does not give them the opportunity to adopt adequate behaviors.

An important aspect during the preconception period is folic acid intake. Women who use folic acid are generally those who plan the pregnancy and request a preconception health visit from a doctor / gynecologist [10]. In fact, women are far from meeting the preconception

recommendations of folic acid intake, especially in countries without fortification requirement [11].

A fundamental role in preconception health is played by the dietary and lifestyle habits of the woman. It is highlighted how an unhealthy lifestyle, being overweight or obese favors the development of gestational diabetes mellitus [12].

However, preconception health covers a much wider spectrum, including physical, mental, emotional, and social health and not just the abovementioned aspects. This is important to understand, since in the absence of knowledge and education, women tend to perpetuate unhealthy behaviors. Given that the preconception period presents a critical window of opportunity to improve pregnancy outcomes, starting from adolescence, it is of utmost importance for public health services to know and address all women's preconception health needs. Hence, the aim of this review is to summarize the literature on preconception health needs in women of childbearing age. The focus is on behavior and factors affecting behavior, such as knowledge, attitude and access to care, that represent priority issues for a safe and healthy pregnancy outcome.

Methods

This systematic review is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [13].

The protocol of this systematic review was registered to PROSPERO, registration number CRD42020143421.

SEARCH STRATEGY

The electronic databases of Web of Science, PubMed and Scopus were searched to look for pertinent articles. A search string was built for PubMed consisting of Medical Subject Headings (MeSH) terms and free text words. The Boolean operators were used to combine keywords such as “Women”; “Female”; “Preconception”; “Preconceived”; “Health”; “Healthcare”; “Medical”; “Medication”; “Dietary”; “Nutrition”; “Mental”; “Behavioral”; “Social”; “Physical”; “Environmental”; “Need”; “Service”; “Demand”; “Requirement”; “Necessity”; “Determinant”; “Counseling”; “Utilization”; “Assessment”; “Tool”; “Determination”; “Research”. Afterwards, this search string was adapted for the other electronic databases. The last search for all databases was performed on January 3rd, 2021 and was restricted to articles published in English, without any further restrictions.

STUDY SELECTION AND INCLUSION/EXCLUSION CRITERIA

We included studies conducted in countries in Europe, USA, Canada, Australia and New Zealand. These areas were chosen because of their relatively homogeneous cultures and a similar vision of women and pregnancy. The criteria for inclusion focused on women's prevention behaviors and factors influencing those behaviors, such as knowledge, attitudes and access to care. We excluded

studies involving women with pathologies directly associated to the reproductive system, as well as studies referring to pregnancy and interconceptive period. Genetic screening prior to conceiving to reduce the possibility of genetic disorders goes beyond the scope of this paper. When studies included both pregnant and non-pregnant women, we presented information only for the latter. Furthermore, we excluded non-empirical studies, conference abstracts, book reviews and abstracts not accompanied by a full text. All studies retrieved from the search strategy were imported to Rayyan and duplicates were removed. Four researchers (AO, AMV, DZ, VV) independently performed the first screening based on titles and abstracts. In a second step, studies with full texts available were carefully reviewed by four researchers (AO, AM, DZ, VV) and disagreements were resolved by consensus. The reference lists of the included studies were hand searched to look for additional articles.

DATA EXTRACTION AND SYNTHESIS

Data extraction was performed by two researchers (AO and DZ). A dedicated data extraction form was used retrieving the following information for each eligible study: (1) Study identification: first author, title, publication year; (2) Study characteristics: country, design, objective, tool used to collect information; (3) Population characteristics: sample, women's age, education level, ethnicity, setting; (4) The domain being assessed, i.e. knowledge, attitudes and behaviors, health status and access to healthcare services; (5) The specific healthcare need assessed.

Thematic analysis of each preconception health need was conducted, grouping them into four major domains: knowledge, behaviours and attitudes, health status and access to healthcare services, reporting the main findings associated to them.

QUALITY ASSESSMENT

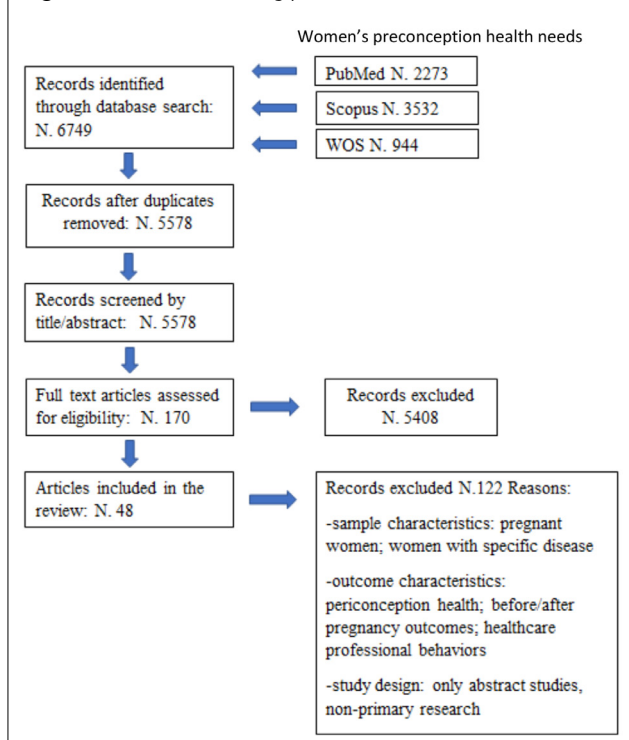
Two researchers assessed the quality of all included studies. Based on the study design, the Critical Appraisal Skills Programme for qualitative studies (CASP Qualitative Checklist, 2018), ROBINS-I for non-randomized trials [14], Jadad tool for randomized controlled trials (RCT) [15] and Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group (NIH, 2014) were used. The Newcastle-Ottawa Scale was used for cohort and case-control studies [16] and an adapted version of this scale for cross sectional studies [17].

Results

CHARACTERISTICS OF THE INCLUDED STUDIES

Our search strategy produced a total of 6749 articles. After the screening process 48 studies were included in the review (Fig. 1, Supplementary Tab. I.)

Among the selected studies, 22/48 were cross-sectional, 4/48 were randomized clinical trials, 7/48 were cohort studies, 3/48 were qualitative, 5/48 were pre-post studies, 2/48 were non-randomized clinical trial, 1/48

Fig. 1. Flow chart: screening process of the included studies.

case-control studies and 4/48 were non randomized interventional study. Most of the studies were conducted in the USA (33/48), 2/48 in Poland, 2 in Italy, 2/48 in Sweden, 3/48 in Australia, 3/48 in Netherland 1/48 in Spain, 1/48 in Norway and 1/48 in Canada. Study sample of selected articles is represented by women of childbearing age between 16 and 44 years old, students and workers, of various ethnicities and social backgrounds and with different levels of education. The smallest sample enrolled 14 participants [18], and the largest 58,365 participants [19].

Results of the quality assessment reported that 23% of the studies satisfied more than 75% of the items on the rating scales and 64% of the studies satisfied between 50 and 75% of the items on the rating scales. The rest satisfied less than 50% of the items in the quality assessment scale (Supplementary Tab. II).

KNOWLEDGE REGARDING PRECONCEPTION HEALTH

Forty three percent of the articles reported women's knowledge and 10.4% awareness on preconception health. Most studies targeted knowledge on folic acid, dietary habits and lifestyle behaviors. High awareness and knowledge on the importance of a healthy lifestyle were reported, including healthy food, normal Body Mass Index (BMI), exercise, sleeping habits, avoiding alcohol, smoking and drugs, and mental and emotional health [7, 20-26]. There was less awareness on risks deriving from the consumption of raw foods (54%), exposure to animals such as cats (64.4%), impact of genetic history and use of condoms [7]. Meanwhile a lower level of knowledge regarding folic acid and the birth defect it

helps prevent (61.9%) was reported in some studies [7, 27, 28].

Important part of the knowledge regarding preconception health concerned knowing to seek medical care for chronic conditions, and review of medication in the preconception period [23, 29, 30]. However, Italian women of childbearing age affected by autoimmune diseases reported several unmet needs in their knowledge about reproductive issues [31].

The majority of women in the study by Lammers et al. believed that preconception healthcare has a positive impact in their health, but still less than half (44.2%) were somewhat or very interested in receiving preconception healthcare [32].

Knowledge regarding taking some medical exams (such as HIV test), infectious diseases, sexually transmitted infections and immunization were also reported to play a crucial role in preconception health [7, 22, 23, 25].

For a better preconception health, of utmost importance is the information on preconception counselling, how to apply for it, when to ask for one and the health providers that may give the information [30, 33, 34].

While it was acknowledged that the best time to receive information about preconception health is before conception [7, 23], some women reported that seeking preconception care was not relevant to them if they were not planning a pregnancy [18].

BEHAVIORS AND ATTITUDES REGARDING PRECONCEPTION HEALTH

More than 70% of studies discussed behaviors and attitudes in women of childbearing age, most of which focusing on physical activity (37%), tobacco avoidance (33%), folic acid assumption and diet (33%).

Following the recommended levels of physical activity is associated to healthy diet and weight [12, 35]. As for diabetes mellitus, while some studies have found a statistically significant association (OR 0.79, 95% CI 0.65-0.96) with physical activity [36], others have failed to do so [12]. The percentage of women that met the recommended amount of weekly physical activity went from 26% [36] to 72% [34].

Comparing women with low vs high probability for unintended pregnancy, the latter were 35% less likely to exercise [3]. Neighborhood composition and implementation of targeted interventions also influenced the level of physical activity [24] [37]. The importance of physical activity was also acknowledged by other studies [24, 25, 38-40].

Among the modifiable behaviors during the preconception period, the intake of substances and alcohol is of utmost importance. Despite the negative effects, women report alcohol consumption in the three months preceding pregnancy [10, 41], smoking during the first few months of pregnancy and in the last three months of pregnancy [41] and in the preconception period [10, 38, 42], as well as drug use [38]. The latter was reported by up to 8% of women in the month before pregnancy [43] and 25.1% during preconception [44]. Higher rates of these at-risk behaviors are seen in women in general, out

of the preconception period [9, 22] and are associated with lack of screening services and general health counseling [24], migration status [45], racial and ethnic disparities [46]. In addition, the value system and the perception of happiness symbols may influence women's health behaviors at different stages of their reproductive life [39]. Other studies have assessed behaviors of women during preconception period, reporting also the effect of educational interventions or the role of general practitioners and midwives on changing negative behaviors into positive ones [3, 23, 47].

The intention to have a pregnancy impact on preconception health. In fact, Nowicki et al report that 57.7% of women with an unplanned pregnancy, realized several weeks after conception that they were pregnant. Among these women 28.8% were smoking and 21.7% did not have any health insurance. In addition, those who reported unexpected pregnancies were victims of abuse and physical violence (10 and 7.36%, respectively) [39]. Folic acid consumption plays a crucial role in the preconception health. Despite the relevance of the topic, folic acid intake is low among women in childbearing age [10, 11, 28, 29, 38, 47]. The low levels of folic acid are due to the inappropriate eating habits, which automatically cause an inadequate supply of folic acid and lack of supplement intake [27].

Women who do not plan a pregnancy are less likely to take folic acid [38]. The use of folic acid in the preconception period is often associated with older age, a high level of education [10] and migration status [48]. The importance of folic acid consumption for preconception health was also highlighted in other studies [3, 24, 32].

As for a healthy lifestyle and diet, it is necessary to remember that the attention to the latter should not be underestimated even if a woman is not planning a pregnancy [12, 23, 24, 35, 39, 61]. The studies' results support general dietary recommendations for women of reproductive age to consume a diet rich in vegetables, whole grains, nuts, fish, low in red meats and snacks. 'Meats, snacks and sweets' diet pattern has been associated with significantly higher Gestational Diabetes Mellitus risk, while the 'Mediterranean-style' pattern with lower GDM risk [12]. Reporting any exercise or fruit/vegetable consumption was associated with decreased odds of overweight or obesity [35].

However, women of childbearing age often do not reach the recommended minimum levels of consumption of cereals, vegetables, and proteins [27, 38]. High prevalence of inadequate dietary micronutrient intake was observed for calcium (47.9%), folate (80.8%), magnesium (52.5%), potassium (63.8%) and vitamin E (78.6%) [49]. Worse dietary intakes were associated with younger age, lower education level, lower annual household income, not planning a pregnancy, obesity/overweight and smoking [42].

Among behaviors that are important for a good preconception health there were also birth control use [22-24, 32, 50-52], avoidance of exposure to toxic chemicals [24] and appropriate sleep [39].

WOMEN'S HEALTH STATUS

Studies assessing the health status of women of childbearing age reported information on BMI (23%), mental health (10.4%), chronic and infectious diseases (14.6%) immunization (6.3%) and control of prescription drugs (6.3%).

Weight and a normal BMI play an important role in preconception health and have been associated with eating habits and physical activity [3, 10, 22, 24, 32, 38, 39, 42]. A diet composed of meats, snacks and sweets has been associated with significantly higher Gestational Diabetes Mellitus risk in parous and obese women, and in women with lower educational qualifications [12, 36, 49]. Evaluating ethnic disparities in body weight, a study in USA [46] found a higher BMI among black women (38.1%).

Mental health has an imperative role in the wellbeing of women in the preconception period [24, 39]. Women who experience any preconception stressful life events are more likely to give birth to very low birth weight infants [41]. The studies by Dunlop et al. and Denny et al. emphasize the importance of ethnicity and race on preconception mental health [23, 46].

Among the conditions to be controlled in the preconception period, there are anemia, STIs (sexually transmitted infections) pressure, diabetes [32]. However, only a small proportion of women have discussed about these conditions with their doctor [23, 32]. These women take one or more medications for their chronic conditions, often without any contraception management [52] and sometimes have low level of knowledge regarding the topic [31]. Immunization is another important variable for the health status of women in preconception period [22, 32]. Oral health in preconception care is certainly not to be underestimated. Better oral health outcomes have been reported by young women who have never had a pregnancy [53].

ACCESSIBILITY TO HEALTH SERVICES IN PRECONCEPTION PERIOD

Women report the need to speak with their reference doctors about preconception health [8]. However, many doctors report that their patients are more likely to deal with the topic of contraceptive techniques, leaving out aspects more related to preconception health itself [30, 54]. Preconception healthcare conversation has been associated with race, health care provider type, number of visits to a health care provider, pregnancy planning [32] and educational interventions [34]. Generally, patients would prefer to receive information on preconception health from their general practitioner, but only a few of them remember having ever discussed it during a visit [7]. Women who do not plan pregnancies have a higher probability of not receiving routine physical exams, screening services and health advice [10, 9, 24].

These services include receiving a PAP test and HIV testing [3, 22, 24]. Studies in USA highlight that having health insurance during the pre-pregnancy period is associated with greater health [19, 40, 55, 56] and with variables such as ethnicity, socio-economic

conditions [56].

INTERVENTIONS TO ADDRESS PRECONCEPTION HEALTH NEEDS

An intervention to address preconception health needs was reported in 37.5% of studies, and in most cases (44.4%), it was an educational one. Educational intervention increased knowledge about the benefits of folic acid [28, 29] and awareness of factors affecting preconception health, such as tobacco, alcohol, excessive weight [8, 26]. Educational intervention improved the use of prenatal vitamins (folic acid) [24, 29, 30], preconception counselling [57], addressing chronic conditions and discussing medications with a provider [23, 30], screening for sexually transmitted infections [23] use of contraception [30], diet, physical activity [24]. However, increased knowledge on folic acid and its role or contraception, was not always associated with changes in behaviors [28, 57].

Educational interventions on young population increased knowledge regarding overall preconception health and obesity, but not concerning alcohol, smoking, diabetes, or use of condoms [21] and did not demonstrate a statistically significant change in the self-reported preconception health behavior index [58].

Expanded Medicaid eligibility was associated with increased healthcare coverage and utilization, better self-rated health, and decreases in avoidance of care [19].

Use of a Web-based virtual animated health counsellor or a Risk Assessment (RA) digital tool, had an impact on participants' behaviors (18-34) [59] and increased the identification of risk factors [25]. Sending written invitations to women increased the participation of women in preconception counselling [33] and the number of women applying for a preconception consultation [34]. Individual visits by a general practitioner or a midwife increased folic acid intake, decreased the frequency of binge drinking, but had no impact on smoking [47] and increased family planning service offered to women of childbearing age [51].

Finally, a training targeting healthcare professionals increased the rates of clinicians counseling women about contraception and recommending a long-acting reversible contraceptive [54].

Discussion

Preconception health includes a wide spectrum of health dimensions and cannot be comprehended without a holistic and multidisciplinary approach. The aim of this review was to comprehensively summarize the health needs of women of childbearing age, necessary to be addressed in order to have an eventual healthy pregnancy, for the woman and her child (summarized in Tab. I).

Based on the similarities among studies, health needs were divided into four categories, including knowledge and awareness on preconception health, behaviors and attitudes regarding preconception health, women's health status and access to healthcare services. Among

the most examined topics by the studies included in the review there were knowledge and awareness on preconception health, folic acid assumption, tobacco and alcohol consumption, physical activity, healthy diet and body weight.

Some studies reported a satisfactory level of knowledge and awareness concerning preconception health. Women recognized the importance of taking care of their health in anticipation of a possible pregnancy [7, 20-22, 33, 58, 59]. Knowledge was higher regarding topics like adopting a healthy lifestyle, including healthy diet, exercise, sleeping habits, and avoiding alcohol and smoking. Less was known regarding the consumption of folic acid, consumption of raw foods and impact of genetics (84.1%) [7, 25, 31, 61]. Studies concluded that educational interventions are effective in increasing knowledge on preconception health, so future interventions, especially on topics in which women have less knowledge should be implemented [18, 21-24, 26, 28-30, 57, 58]. The level of knowledge in the population is linked to the relationship with health professionals who are the main providers of health-related information. However, even though studies report a high level of knowledge and awareness and an impact of educational interventions on that, the knowledge alone or the recommendations provided by a healthcare professional are not always sufficient to change behaviors [28, 58]. Nonetheless, the positive impact of educational interventions on women's attitudes and behaviors, especially those related to nutrition and physical activity was seen in the study by Hillemeier et al. [24]. Beyond the primary role of the health professionals, public health is involved in promoting preconception care. Various strategies can be applied to this purpose, for example, schools and public health campaigns were identified by women themselves as methods for achieving greater awareness, or, similarly to the screening prevention campaigns, the use of invitation letters from the municipalities and general practitioners [18, 34]. Future longitudinal studies should focus on assessing the type of interventions that could have an impact not only on knowledge and awareness, but also on women's behaviors concerning preconception health. These interventions should be tailored to women's characteristics considering social, psychological and environmental factors that shape preconception health. A crucial role in this regard is played by health promotion which should start from early in life with a particular reinforcement in adolescence.

Amid the included articles, the most studied behaviors among women of childbearing age were physical activity, tobacco avoidance and folic acid assumption. Studies acknowledged the importance of physical activity on preconception health but reported that not always women met the recommended amount of physical exercise [35, 37]. Women who have a higher probability for unintended pregnancy exercise less and neighborhood composition may play a role on preconception physical activity status. The use of alcohol and tobacco in the preconception period was not uncommon, even though their negative consequences are well known. Women who

Tab. I. Recommendations for healthcare professionals on preconception health.

| | |
|---|---|
| Knowledge | <ul style="list-style-type: none"> • Provide adequate information on risk factors during preconception period that could have a negative impact on the pregnancy and the unborn child • Best time for the women to receive information on preconception health • Who would most benefit from is preconception counselling • Information on multivitamin use including folic acid and NTD (neural tube defects) • Information on a healthy lifestyle including smoking, alcohol use, diet and physical activity • Information on family planning and contraception methods • Information on chronic diseases and medication use • Provide educational interventions to increase knowledge and awareness |
| Behaviors | <ul style="list-style-type: none"> • Promote adequate levels of physical activity • Promote a healthy diet • Promote adequate amounts of folic acid • Advice avoiding alcohol, tobacco and drugs use • Promote an appropriate number of hours of sleep, based on age and daily activities • Avoiding exposure to toxic chemicals • Provide guidance and prevention on environmental hazards • Advice adequate use of contraceptive techniques or fertility regulation methods • Promote thinking about the value of pregnancy: the perception of happiness symbols may influence women's health behavior at different stages of their reproductive life • Define the probability of having a pregnancy: women who have unplanned pregnancies realize their condition late and are more likely to have unhealthy behaviors, such as smoke, alcohol and drugs in the preconception period as well as after conception |
| Women's health status | <ul style="list-style-type: none"> • Control the weight and BMI • Control for chronic, genetic and infectious diseases • Check for sexually transmitted diseases • Control of prescription drugs • Assessment of mental health issues • Check the immunization status |
| Accessibility to health services | <ul style="list-style-type: none"> • Provide preconception health counselling to all women in childbearing age • Provide routine physical exams, screening services (ex. i.e. PAP test) and health advices • Provide a sexually transmitted disease counselling • Check the health coverage condition (where applicable) • Provide interventions to increase women's participation in preconception counselling |

binge drink in the preconception period are, also, more likely to smoke and be exposed to violence during this period, as well as to consume alcohol, binge drink, and smoke during pregnancy. Along with these risk factors, the consumption of marijuana is another underestimated issue that is strictly connected with the previous ones [43], but with deeper social differences: compared with tobacco users, pre-pregnancy marijuana users were more likely to have low education, low income and mental health disorders [44]. In addition, the increasing use of medical cannabis, particularly in USA, should be considered as an issue of preconception health, even if there is a gap in knowledge in the examined literature. Racial and ethnic disparities in behaviors concerning preconception health were seen in several studies [40, 46]. Women who have unintended pregnancies are more likely to engage in risky health behaviors. According to Srinivasulu et al, interventions should act in this regard also by offering family planning services [51]. Meanwhile, positive behaviors in preconception period are associated with receiving screening services and general health counselling.

As it is widely reported, the consumption of folic acid during preconception period is of utmost importance to prevent neural tubal defects [60]. However, the percentage of women who were taking folic acid in the included studies ranged from 5% [29] to 48.9% [38].

Folic acid intake is affected by pregnancy planning and is often associated with older maternal age and a high level of education. Younger women have often worse eating habits, which automatically cause an inadequate supply of folic acid [42]. Also, immigration status was negatively correlated with folic acid consumption, that, however, increased as the time of residence was lengthened, showing the importance of socio-cultural environment in changing this behavior [48]. Fortunately, simple educational intervention in preconception care can contribute to initiation of folic acid supplementation, because it is a well-accepted habit, compared to the cessation of smoking that is hard to obtain [47]. Positive health behaviors for a good preconception health include, also, birth control use [22-24, 32, 40], avoidance of exposure to toxic chemicals or teratogenic medication without proper concomitant contraception [24, 52] and appropriate sleep [39]. The existence of several risky behaviors among women of childbearing age calls for a better health promotion and public health interventions. For a pregnancy to be healthy and at low risk for both the woman and her child there is the need for the woman to be in an optimal health status before conceiving. In this context, a normal BMI, a good mental health, chronic and infectious diseases control, immunization and control of prescription drugs were the most important aspects that emerged from the studies included in the review.

Women who went through stressful events during the preconception period were more likely to have low birth weight infants [41]. This highlights that a good mental health is imperative for a healthy pregnancy. Racial and ethnic disparities were, also, important for mental health. A comprehensive assessment of a woman's health status should also include checking for anemia, STI, blood pressure, diabetes and oral health.

In order to have the right knowledge, attitude, behavior and health status women need to have access to healthcare services. Women report the necessity to speak to their reference doctors about preconception health [8, 31]. Still, many doctors state that women are more interested in discussing about contraception techniques than about preconception health in general [54]. Since most women would prefer receiving information from their doctor, the latter should not fail to discuss preconception health during consults and involve their patients in programs that provide information on this topic. Doctors should encourage women to receive the basic examinations related to preconception health like a PAP test, HIV testing and Sexually transmitted Disease Counseling. Health insurance was also deemed to be important for women's access to healthcare services. Most of the studies analyzed were actually conducted in the USA, where insurance coverage is needed to access treatment, thereby causing more ethnical and social disparities, as the preconception care is the first to be sacrificed in difficult socio-economic situations [56].

As discussed, preconception health is a wide concept, including several aspects that need a multidisciplinary approach. Integrating preconception health promotion into the continuum of women's healthcare asks for multi-dimensional and multistrategic programs involving a range of health professional expertise.

It is important that women of childbearing age have the adequate level of knowledge, adopt the right behaviors and attitudes, and have access to healthcare services in order to start a pregnancy, even when unintended, in good health. As the critical period for fetal development may extend to the preconception period, a proper management of women's health should start well before conception. Policy makers and healthcare professionals should not fail to address all women's preconception health in a holistic and multidisciplinary way, which may ultimately improve the long-term health of women and their children.

IMPLICATIONS AND FUTURE RESEARCH

Preconception health care has the potential for substantial public health benefit. For this, it is important to have a holistic view of healthcare needs of women of childbearing age. This review could assist healthcare professionals (physicians, nurses, midwives) in guiding tailored counselling to provide the adequate level of preconception care to women. It could also act as a reference to policy makers in developing guidelines or policies.

This article represents the first step of a multistage project. It will be followed by the creation and validation of a questionnaire, based on the results of this review, to comprehensively assess the preconception health needs

of women of childbearing age and evaluate at what level they are met in the Italian context.

Ethical approvals

This systematic review has been registered in Prospero protocol; the approval of Ethical Committee was not necessary.

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Conflict of interest statement

Authors declare no conflict of interest in the study design, data acquisition, analysis and interpretation, and writing of the manuscript.

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Authors' contributions

All Authors contributed in equal measure.

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Supplemental Tab. I.

| Article | Study design | Used scale | Overall quality (% satisfied items) |
|---------------------------------|-------------------------------------|--|-------------------------------------|
| Andreoli et al., 2019 [31] | Cross-sectional study | NOS adapted by Herzog et al. | 70% |
| Azofeifa, 2014 [53] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Batra et al., 2018 [57] | RCT | Jadad-RCT | 80% |
| Bello et al., 2013 [8] | Qualitative study | CASP-Qualitative studies | 90% |
| Bello, 2018 [35] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Bickmore et al., 2019 [59] | RCT | Jadad-RCT | 60% |
| Bromwich et al., 2020 [44] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Carmichael et al., 2019 [42] | Cohort study | NOS-CC, Cohort | 46.10% |
| Cuervo, 2014 [38] | Cross-sectional study | NOS adapted by Herzog et al. | 70% |
| Daw et al., 2020 [56] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| DeJoy et al., 2014 [58] | Pre-post study | BAQA-Pre-post studies | 42% |
| Denny, 2012 [46] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Dunlop et al., 2013 [23] | Non randomised interventional study | ROBINS-INRC studies | 50% |
| Flores et al., 2017 [29] | Pre-post study | BAQA-Pre-post studies | 83% |
| Frey, 2004 [7] | Cross-sectional study | NOS adapted by Herzog et al. | 40% |
| Głabska, 2016 [62] | Cross-sectional study | NOS adapted by Herzog et al. | 50% |
| Harellick, 2009 [22] | Cross-sectional study | NOS adapted by Herzog et al. | 50% |
| Hawks, 2011 [55] | Cross-sectional study | NOS adapted by Herzog et al. | 70% |
| Hillemeier, 2008 [24] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Hillemeier et al., 2008 [5] | RCT | Jadad-RCT | 60% |
| Hilton, 2001 [27] | Cross-sectional study | NOS adapted by Herzog et al. | 20% |
| Kvach et al., 2018 [30] | Pre-post study | BAQA-Pre-post studies | 67% |
| Lammers, 2010 [32] | Cross-sectional study | NOS adapted by Herzog et al. | 70% |
| Margerison et al., 2020 [63] | Cohort study | NOS-CC, Cohort | 46.10% |
| Moniek Looman et al., 2019 [49] | Cohort study | NOS-CC, Cohort | 38.40% |
| Montanaro et al., 2019 [25] | Cross-sectional study | NOS adapted by Herzog et al. | 70% |
| Murugesu et al., 2019 [33] | Qualitative study | CASP-Qualitative studies | 88% |
| Naimi et al., 2002 [9] | Case-control study | NOS-CC, Cohort | 46.10% |
| Nilsen et al., 2019 [48] | Cross-sectional study | NOS adapted by Herzog et al. | 80% |
| Nilsen, 2016 [10] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Nowicki, 2018 [39] | Cross-sectional study | NOS adapted by Herzog et al. | 70% |
| Panchal et al., 2019 [52] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Quillin et al., 2000 [28] | Pre-post study | BAQA-Pre-post studies | 50% |
| Ragnaret al., 2018 [20] | Qualitative study | CASP-Qualitative studies | 90% |
| Richards et al., 2012 [21] | Non randomised interventional study | ROBINS-I-NRC studies | 32% |
| Richards et al., 2012 [21] | RCT | Jadad-RCT | 20% |
| Schoenaker et al., 2015 [12] | Cohort study | NOS-CC, Cohort | 61.30% |
| Short et al., 2020 [43] | Cross-sectional study | NOS adapted by Herzog et al. | 80% |
| Sijpkens et al., 2019 [34] | Interventional study | Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group. | 58% |
| Sijpkens et al., 2021 [47] | Cohort study | NOS-CC, Cohort | 38.40% |
| Skogsdal et al., 2019 [26] | RCT | Jadad-RCT | 60% |
| Srinivasulu et al., 2019 [51] | Interventional study | Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group. | 66.60% |
| Stulberg et al., 2019 [54] | Pre-post study | BAQA-Pre-post studies | 75% |
| Vamos, 2015 [37] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Walker et al., 2021 [18] | Qualitative study | CASP-Qualitative studies | 77% |
| Whitaker et al., 2018 [36] | Cohort study | NOS-CC, Cohort | 61.30% |
| Witt et al., 2016 [41] | Cohort study | NOS-CC, Cohort | 69.20% |
| Xaverius, 2009 [3] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |
| Xaverius, 2012 [40] | Cross-sectional study | NOS adapted by Herzog et al. | 60% |

Supplemental Tab. II.

| First Author, Year | Country | Design | Sample size | Women's age (years) | Setting/source | Duration | Intervention | | TOOLS (test/scores/questionnaire) | Type of need assessed | Main results |
|------------------------------|---------|-----------------------------|--|---------------------|---|-------------------------|---|--|--|--------------------------------------|---|
| Andreoli et al., 2019 [31] | Italy | Cross-sectional | 398 (249 Connective Tissues Diseases, 149 Chronic Arthritis) | 39.8 ± 9.21 | Hospital centres | NA | NA | | Self-reported questionnaire, comprising 65 multiple-choice and 12 open-answer questions | Knowledge | Nearly one third of patients declared not to have received any counselling about either pregnancy desire nor contraception. The average Disease Knowledge Index (DKI) Score for the patients who received counselling was higher than that of patients who did not receive it: 0.61 versus 0.52 for CTD (p = 0.09) and 0.55 vs 0.44 for CA (P = 0.01). Italian women of childbearing age affected by RD reported several unmet needs in their knowledge about reproductive issues. |
| Azofeifa et al., 2014 [53] | USA | Cross-sectional | 3,971 nonpregnant | 15-44 | National Health and Nutrition Examination Survey (NHANES) | 1999-2004 | NA | | Questionnaire | Behaviours/Health status/Oral health | The percentage of women who reported having very good or good oral health was significantly higher among younger nonpregnant women (75.3 vs 67.0%, p = 0.003). Non pregnant and non-Hispanic white woman (74%) with a high level of education (79%) and high socio-economic level (81%) reported having very good or good mouth and teeth condition and having a dental visit in the previous year. A higher percentage of nonpregnant women with family income greater than 200% of the FPL reported having a dental visit in the previous year compared with nonpregnant women with lower incomes (74.1 vs 52.9% for those with < 100% FPL and 74.1 vs 51.4%, for those with 100-199% FPL; P < .001 for both). |
| Batra et al., 2018[57] | USA | Cluster RCT | 292 | 18-45 | Urban academic medical center | September 2015-May 2016 | Educational intervention | | Questionnaire. MyFamilyPlan module online | Behaviours, access to healthcare | Participants completing the MyFamilyPlan health education module prior to a well-woman visit were significantly more likely (OR = 1.97; CI 1.22-3.19) to report that study participation led them to discuss reproductive health with their physicians . Exposure to MyFamilyPlan did not have an impact on folic acid use, contraceptive method initiation/change self-efficacy score. |
| Bello et al., 2018 [35] | USA | Cross-sectional | 5704 | 18-45 | National Eating Trends (NET) [®] Survey | 2003-2011 | NA | | Daily diary (recordings food and beverage) Self-reported height and weight, chronic illnesses, and exercise habits | Behaviours, health status | 25.5% of women were overweight and 30.7% were obese. Women of reproductive age exercised a mean of 3 days per week and consumed fruits/vegetables 9.7 times, sugar-sweetened beverages 10.7 times, and concentrated sweets 8.5 times during a 2-week period. Across BMI categories, exercise (79.2%) and eating fruits/vegetables (96,1%) were significantly associated with healthy weight Reporting any exercise or fruit/vegetable consumption was associated with decreased odds of overweight or obesity (aOR 0.73, 95% CI 0.64-0.83 and aOR 0.74, 95% CI 0.58-0.95, respectively). |
| Bello et al., 2013 [8] | USA | Qualitative | 22 | 18-44 | Community primary care health center for low-income African-American population | July-October 2012 | Reproductive health self-assessment tool (RH-SAT) | | Semi-structured interviews | Knowledge, behaviours | RH-SAT provides new information women had not previously considered about preconception health and reproductive goals. Most patients said they would feel comfortable bringing up contraception, preconception health, and their reproductive goals with their primary provider. RH-SAT could increase patient awareness and participation in discussion of these topics. Patients find reproductive goals assessment to be important and relevant to their care, but have limited knowledge. |
| Bickmore et al., 2020 [59] | USA | Randomized controlled trial | 262 | 18-34 | Web-based | 12 months | Use of Gabby Preconception Care Conversational (PCC) intervention, a Web-based virtual animated health counsellor, to screen women on 108 preconception care risks and address them | | The “Gabby” PCC agent; Six single-item scale questions to assess participants’ satisfaction with the virtual counselor | Behaviours; knowledge | At the end of the year, almost all (96.4%) indicated they had either acted on recommendations made by the agent or planned to. Most (75.0%) said they would recommend the system to someone they knew. There were no significant differences between the two age groups on intervention use or satisfaction. No significant differences across usage patterns for participants based on education, employment, computer literacy or health literacy. |
| Bromwich et al., 2020 [44] | USA | Cross-sectional | 1683 | Mean 26.92 | Reproductive health and maternity services centers | 2014-2017 | Telephone survey | | Questionnaire on: 1) demographics (age, income, education, ethnicity); 2) marijuana use (before pregnancy, frequency, method, and mode of use; 3) tobacco use; 4) alchol use | Behaviours | 25.1% of respondents reported using marijuana during preconception. Marijuana users were younger, poorer, and less educated than non-users (p < 0.001) and more likely to report alcohol use and mental illness (ps < 0.001). Prepregnancy marijuana users, vs tobacco users, were more likely (< 0.001) to: have low education (73 vs 66%), have low income (76 vs 66%), have mental health disorders (11,1 vs 7,1%). |
| Carmichael et al., 2019 [42] | USA | Cohort | 11 109 | All | National Birth Defects Prevention Study | 1997-2011 | NA | | Diet Quality Index | Behovaviours/ Healthy lifestyle/Diet | 5.1% of women were Underweight, 51.4% had a normal weight, 21.9% were overweight and 17.5% obese. Folic acid 3 months before pregnancy, No: 7042 (63.4%), Yes 3934 (35.4%). Smoked cigarettes 1 month before pregnancy, No 9106 (82.0%), Yes 1965 (17.7%). Participants who were aged < 0, were nulliparous, had < high school diploma or < \$ 20 000 annual household income, were non-Hispanic black, were underweight or obese, did not intend to become pregnant, did not take folic acid-containing vitamin supplements, or smoked had worse dietary intakes than their reference groups. |

Supplemental Tab. II.

| First Author, Year | Country | Design | Sample size | Women's age (years) | Setting/source | Duration | Intervention | | TOOLS (test/scores/questionnaire) | Type of need assessed | Main results |
|--------------------------|---------|-------------------------------------|-------------|---------------------|--|--------------------------|--|--|--|--------------------------|--|
| Cuervo et al., 2014 [38] | Spain | Cross-sectional | 4471 | 20-45 | 2794 pharmacies, in urban and rural areas | November 2009-March 2010 | Nutritional educational intervention | | Face-to-face interview | Behaviours/Health status | Only 48.9% of women were consuming folic acid (supplements or enriched food) and 14.1% multivitamins. Self-perception of health: good 66%; Self-perception of actual nutrition: very balanced 44%; tobacco: never 56,3% smoker 20,1%; alchool yes 49%; illicit drugs 1,5% actual use; Diet supplementation: Enriched milk with calcium/vitamins 21.1% Folic acid/vitamin B12 48.9% Iodine/Iodine salt 26.1% Iron 16.0% Multivitamin and minerals 14.1%; Women in preconception period did not reach the recommendation for consumption in the following food groups: proteins, cereals, salad vegetables. |
| Daw et al., 2020 [56] | USA | Cross-sectional | 10792 | 19-35 | Pregnancy Risk Surveillance and Monitoring System (PRAMS) | 2015-2017 | NA | | Standardized mail and telephone survey, including demographic characteristics, insurance status, health care utilization, and health outcomes | Access to healthcare | Rate of preconception uninsurance: 9.4% (95% CI 9.0-9.8) among white non-Hispanic women. Among black non-Hispanic (12.8%, 95% CI 12.0-13.7), Hispanic English-speaking (22.3%, 95% CI 20.6-24.1), Hispanic Spanish-speaking (55.1%,95% CI 53.0-57.1), and indigenous women (23.7%, 95% CI 21.3-26.2). In adjusted models, lower income Hispanic women and indigenous women had a significantly higher predicted probability of uninsurance in the preconception and postpartum period compared with white non-Hispanic women. |
| DeJoy, 2014 [58] | USA | Pre-post study | 20 | 20-25 | Public liberal arts college | 4 weeks | Educational intervention | | 6-item index measuring preconception health knowledge 3-item index on knowledge of midwifery care; a 3-item index on knowledge of the complications of cesarean birth and preterm birth; an 8-item index measuring self-reported preconception health behaviors (multivitamin supplementation, alcohol use, exercise frequency, fruit and vegetable consumption, immunizations, contraception use, screening for HIV screening for other STIs) | Knowledge, Behaviours | After the intervention 75% of students replied that preconception health was important to them “a lot,” and the remaining students stating it was “somewhat (35%). On the post-test,75% of participants expressed a preference for midwifery care in future pregnancies. Half of participants responded that they had heard the term preconception health prior to the program, whereas 35% stated they had not and 15%were unsure. Program participants gained increased knowledge about all the covered topics but did not demonstrate a statistically significant change in the self-reported preconception health behaviour index (0.4 of 8 possible points; 95% CI, -0.4 to 1.3). |
| Denny et al., 2012 [46] | USA | Cohort study | 54,612 | 18-44 | Behavioral Risk Factor Surveillance System (BRFSS) | 1991-1992 /2000-2001 | NA | | BRFSS questionnaires | Behaviours/Health status | Five risk factors examined: drinking, cigarette smoking, obesity, diabetes, and frequent mental distress. Multiple risk factors 18.7%, one risk factor 33.3%, no risk factors 48.0%. The most prevalent co-occurring risk factors was at-risk drinking and smoking (5.7%). Obesity (23.4%) was the most common and diabetes the least (5.8%). The most common combinations of risk factors were smoking, obesity , and frequent mental distress (24.3%, 95% CI 21.2-27.7).American Indian and Alaska Native women were almost 50% more likely to have multiple risk factors than white women. Women with less than a high school education were three times more likely to have multiple risk factors than women with at least a college education. |
| Dunlop et al., 2013 [23] | USA | Non randomised interventional study | 600 | 18-40 | Five publicly funded primary care clinics of low-income, nonpregnant African-American and Hispanic women | 12 months | Targeted brief counselling (counselling + brochures). After 3-6 months women were contacted by telephone | | 12 item knowledge questionnaire. Reproductive and Preconception Health Risk Assessment Questionnaire | Knowledge | For women in the intervention cohort, there was a significant increase in knowledge related to the importance of screening for sexually transmitted infections (+12%) in the preconception period; they experienced a significant increase in knowledge related to the preconception period as the best time to seek an appointment to discuss reproductive health with a provider (+24%), to control chronic conditions (+19%),and to discuss medications with a provider (+20%). Among women with chronic medical conditions, those in the intervention cohort significantly increased their knowledge that the condition could lead to problems in pregnancy (p43%) relative to the lesser improvement in knowledge observed for those in the comparison cohort (p4%) (p = 0.05). |



Supplemental Tab. II.

| First Author, Year | Country | Design | Sample size | Women's age (years) | Setting/source | Duration | Intervention | | TOOLS (test/scores/questionnaire) | Type of need assessed | Main results |
|-----------------------------|---------|------------------|-------------|---------------------|---|---------------------------|---|--|--|---------------------------------------|---|
| Flores et al.,2017 [29] | USA | Pre-post study | 1.446 | 18-45 | Churches, community centers, targeted health fairs, and other locations that offer community services | 4 months follow-up | Educational intervention + a 90-day supply of multivitamins | | Pre and post intervention questionnaire | Knowledge/Awareness/Folic acid | Folic acid supplement consumption and knowledge about the benefits of folic acid increased dramatically by the end of the study, after the educational intervention (p < 0.0001). The number of participants who reported taking vitamins every day increased (pre-test: n= 329, 23%, post-test: n = 888, 62%)(p < 0.0001). |
| Frey, Files, 2006 [7] | USA | Cross-sectional | 499 | 18-45 | Primary care services | August 2004 and July 2005 | NA | | Four-page questionnaire | Knowledge/awareness | 98.6% realized the importance of optimizing their health prior to a pregnancy, and realized the best time to receive information about preconception health is before conception. 95.3% preferred to receive information about preconception health from their primary care physician. Only 39% of women could recall their physician ever discussing this topic. Awareness of certain risk factors that are potentially affecting a pregnancy, such as tobacco (98%), alcohol (95,8%), drug use (98,8%), and domestic abuse (97,7%). Other risks: consumption of fish (54%), exposure to cat litter (64,4%), folic acid use (79,6%), medication use (97,4%), impact of genetic history (84,1%), infectious disease (89,3%). |
| Glabska et al., 2017 [62] | Poland | Cross-sectional | 95 | 20-30 | NA | August-December 2016 | NA | | Folate-Intake Calculation-Food Frequency Questionnaire (Fol-IC-FFQ). 3-Day Dietary Record | Behaviours | Adequate intake of folic acid with diet varies 15-27%. The Fol-IC-FFQ may be a valid tool for the assessment of folate intake in young women. |
| Harelick et al., 2011 [22] | USA | Crossc-sectional | 340 | 18-44 | Two community health centers | 4 weeks | NA | | Healthy Babies Are Worth the Wait: 2007, Baseline Survey Pregnancy Risk Assessment Monitoring System Phase 5 | Knowledge/Behaviours | 70% of women reported that taking folic acid was beneficial, and 92% knew that smoking had a harmful effect. Healthcare provider's recommendations were correlated with an HIV test (chi2 = 24.2; p < .001) and using birth control (chi2 = 7.6; p < .05). Multivitamin use, drinking alcohol , and smoking were not influenced by the provider's recommendation. Correlation between presence of risk factors and respondent's knowledge existed for immunizations (chi2 = 9.6; p < .05), but not for multivitamin use, drinking alcohol, or smoking. |
| Hawks et al., 2018 [55] | USA | Cross-sectional | 3929 | 18-40 | New York City Pregnancy Risk Assessment Monitoring System | 2009-2011 | NA | | Preconception Health Score (PHS), including healthcare worker visit, cleaning teeth, taking prenatal (folic acid containing) vitamins 3 or more times per week, access to family planning and/or birth control, drinking, smoking, BMI, physical exercise, planning for and /or trying to get pregnant, preconception visit in the last year | Access to healthcare/Health Insurance | Having health insurance during the pre-pregnancy period is associated with greater health among white women, but not among black or Hispanic women in New York City. |
| Hillemeier et al., 2008 [5] | USA | RCT | 362 | 18–35 | Low-income local rural communities | 14 weeks | Educational intervention | | Questionnaire, anthropometric measures, and biomarkers | Knowledge, Behaviours | Women in the intervention group had higher: <ul style="list-style-type: none">• <i>self-efficacy</i> for eating healthy food (OR = 1,75; p = 0,008) and to perceive higher preconception control of birth outcomes (OR = 1,916; p = 0.031);• <i>intent</i> to eat healthy foods and be more physically active (OR = 2,185; p < 0.001);• <i>frequency</i> of reading food labels (OR = 2,264; p = 0.001), physical activity consistent with recommended levels (OR = 1,867; p = 0.019), and daily use of a multivitamin with folic acid (OR = 6,595; p < 0.001). |

Supplemental Tab. II.

| First Author, Year | Country | Design | Sample size | Women's age (years) | Setting/source | Duration | Intervention | | TOOLS (test/scores/questionnaire) | Type of need assessed | Main results |
|---------------------------------|-----------|-----------------|-------------|---------------------|--|--------------------------|--|--|---|---|---|
| Hillemeier et al., 2008 [24] | USA | Cross-sectional | 1325 | 18-45 | Rural region in Central Pennsylvania | 2002 | NA | | Population-based telephone survey. Five indicators of health services use: 1. receipt of a regular physical exam, 2. obstetrician-gynecologist [ob/gyn] visit, 3. receipt of a set of recommended screening services, 4. receipt of health counseling services on general health topics, 5. receipt of pregnancy-related counseling | Access to healthcare | 50% at risk of pregnancy report receiving counselling about pregnancy planning in the past year. 33% of women did not receive routine physical examinations and screening services, and over half received little or no health counselling. Having had an ob/gyn visit in the past 2 years was negatively associated with two measures of need: cardiovascular risk and lower self-rated health status. Positive health behaviour was positively associated with reported receipt of recommended screening services. |
| Hilton, 2002 [27] | USA | Cross-sectional | 42 | 18-24 | Small private college | NA | NA | | Questionnaire assessing diet, folic acid intake and knowledge, socio economic and demographic variables | Knowledge/ Behaviours | Young women ages 18–24 often have poor dietary habits and inadequate folic acid intake. Only 33.3% reported taking daily multivitamins. |
| Kvach et al., 2018 [30] | USA | Pre-post study | 1.677 | 12-45 | A teaching health center in Denver, Colorado | April 2015 February 2016 | Educational intervention | | Routine Pregnancy Intention (PI) Screening | Knowledge/ Behaviours/ Access to healthcare | Addressing of unmet preconception health needs (prenatal vitamins, preconception counselling, addressing chronic conditions, use of contraception) increased from 47%-48% in April to 66%- 67% in July after the educational intervention. |
| Lammers et al., 2017 [32] | USA | Cross-sectional | 868 | 18-45 | Network of offices providing community health services | 9 months | NA | | Questionnaire ex novo | Knowledge/ Access to healthcare | The prevalence of healthcare providers' preconception healthcare (PCHC) conversations was 53.9%. Significant predictors of PCHC conversation were race (Native American 76% greater than White), health care provider type (non-physician 63% greater than physician), visits to a health care provider (3+ times 32% greater than 1–2 times), and pregnancy planning (considering in next 1-5 years 51% greater than no plans). Significant predictors of PCHC interventions received in the past 12 months were race (Native American 22% greater than White), PCHC conversation with a health care provider (yes 52% lower than no), reporting PCHC as beneficial (yes 32% greater than don't know), and visits to a health care provider in the past year (3+ times 90% greater than 1-2 times). |
| Margerison et al., 2020 [63] | USA | Cohort | 58,365 | 18-44 | Behavioral Risk Factor Surveillance System (BRFSS) | 2018-2019 | Compare the change from pre- to post-Medicaid expansion in prevalence of self-reported outcomes in low-income women | | Self-reported questionnaire | Access to healthcare | Expanded Medicaid eligibility was associated with increased healthcare coverage and utilization, better self-rated health, and decreases in avoidance of care because of cost, heavy drinking, and binge drinking. Medicaid eligibility did not impact diagnoses of chronic conditions, smoking cessation, or BMI. |
| Moniek Looman et al., 2019 [49] | Australia | Cohort | 277 | Mean 27 | Australian Longitudinal Study on Women's Health | 12 years (2003-2015) | | | Dietary Questionnaire for Epidemiological Studies; self-report questionnaire | Behaviours | High prevalence of inadequate dietary micronutrient intake was observed for calcium (47.9%), folate (80.8%), magnesium (52.5%), potassium (63.8%) and vitamin E (78.6%). Inadequate intakes of individual micronutrients were not associated with risk of developing GDM. Women in the highest quartile of the Micronutrient Adequacy Ratio had a 39% lower risk of developing GDM compared to women in the lowest quartile (RR = 0.61, 95% CI 0.43-0.86, p = 0.01). |
| Montanaro et al., 2019 [25] | Canada | Cross-sectional | 300 | 15-49 | Seven primary care sites | 2016 | 1) Implementation of a Risk Assessment (RA) digital tool. 2) Discussing results with Healthcare Providers in scheduled meetings. 3) Customized handout generated and printed in the primary care sites. 4) One-week and two-month online follow-up surveys | | Risk assesment tool (RA): Body mass index; Genetic/family history; Immunizations; Infectious diseases; Medical history; Medication exposures; Mental health history; Nutrition; Oral health; Physical activity | Knowledge/ behaviours | The RA screened for 34 PCH risk factors. The number of risks identified per participant ranged from 4 to 24, averaging 15. The majority reported a positive experience using the RA and would recommend the intervention. Most prevalent risk factors identified: consumption of unsafe foods and caffeine (98%), stress in the past year (92%), consumption of alcohol in the past year (89%), and immunizations not up-to-date (87%). |

Supplemental Tab. II.

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| Murugesu et al., 2019 [33] | The Netherlands | Qualitative | 139 | 18-42 | General practices, mother and child healthcare centers and youth healthcare centers in low SES neighborhoods | NA | In a problem analysis (stage 1) structured interviews were used to assess comprehension of the initial invitations sent to women for preconception care, perception of perinatal risks, attitude and intention to participate in preconception counseling. Feedback was used to adapt the invitation | | Interviews, telephone interviews, pre-test, post-test, Short Assessment of Health Literacy in Dutch (SAHL-D) | Knowledge | Women in stage 3 (who read the adapted flyer) had a more positive attitude towards participation in preconception counselling and a better understanding of how to apply for a consultation than women in stage 1 (who read the initial invitations). No differences were found in intention to participate in preconception counseling and risk perception. Systematic adaptation of written invitations can improve the recruitment of low health-literate women for preconception counselling. |
| Naimi et al., 2003 [9] | USA | Case-control study | 72907 | Mean age: 26 | Population-based mail and telephone survey. Pregnancy Risk Assessment Monitoring System | 1996/1999 | NA | | Population-based mail and telephone survey. | Behaviours, Access to healthcare | In preconception period, women with unintended pregnancies were more likely to lack health insurance (51,7%), smoke (29,8%), and be exposed to physical violence and have delayed pregnancy recognition (57.7%) Women with unintended pregnancies were significantly more likely to report binge drinking in the preconception period compared with women with intended pregnancies (16.3% vs 11.9%). |
| Nilsen et al., 2016 [10] | Italy | Cross-sectional | 2.189 | 15-50 | Data from seven maternity clinics located in six Italian regions | January-June, 2012 | NA | | Questionnaire | Behaviours/ Access to healthcare | 23.5 % of the participants used folic acid . Of these, 93 % had taken folic acid supplements on a daily basis.. Women who both had intended their pregnancy and had requested a preconception health visit to a doctor/gynecologist were more likely to initiate folic acid supplementation before their pregnancy (48.6 vs 4.8 %). Preconception folic acid use was also associated with higher maternal age (28% in 35-39 years old women), higher education (31% of university graduated women), marriage /cohabitation (24%).Women who did not plan their pregnancy had a prevalence of 21,4% of preconception folic acid use. |
| Nilsen et al., 2019 [48] | Norway | Cross-sectional | 1,055,886 (202,234 and 7,965 were 1 st and 2 nd generation immigrant women, respectively) | Mean 27-30 | Medical Birth Registry of Norway (MBRN) and Statistics Norway (SSB) | 1999-2016 | NA | | Medical Birth Registry of Norway | Behaviours | Folic acid supplement use: non immigrant women 29.2%; 1 st generation 25.5%; second generation (21.2%). Folic acid supplement use increased with increasing length of residence in immigrant women from most countries, but the overall prevalence was lower compared with Norwegian-born women even after 20 years of residence (AOR = 0.63; 95% CI:0.60-0.67). |
| Nowicki et al., 2018 [39] | Poland | Cross-sectional | 182 | NR | Two-way paper and pencil interview (PAPI) and computer-assisted web interviewing (CAWI) | September 2013-May 2014 | NA | | Paper and pencil interview (PAPI) and computer-assisted web interviewing (CAWI). Health Behaviour Inventory (HBI): 1. dietary habits; 2. prophylactics; 3. medical examination and information; 4. health practices (sleep, exercise, monitoring of body weight or past times; 5. positive mental attitude (avoidance of excessively strong emotions, stress, depressive situation). Personal Value List: value attributed to health, symbols of happiness | Behaviours, Health status Social support | HBI = 82.44 (SD = 11.80) (max = 140). Healthy eating habits 3.53 (0.75) (max = 5). Prophylactic Behaviors 3.43 (0.67) (max = 5). Positive Mental Attitude 3.38 (0.69) (max = 5). Health Practices 3.40 (0.57) (max = 5). Reasons for not having children: No employment, low income, little social support. |

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| Panchal et al., 2019 [52] | USA | Cross-sectional retrospective | 3956 | 13-45 | Ambulatory care family medicine residency program practices | January, 2015-December, 2015 | NA | | Clinical charts (reviewed for medication use and forms of birth control) | Health behaviour/ Medication use/ Contraceptive use | In a family medicine setting, 25% of women of childbearing age were prescribed at least one high-risk medication with over half not having evidence of contraception management. Women less than 25 years had decreased odds of receiving contraception when prescribed a teratogenic medication (AOR = 0.47; 95% CI, 0.34-0.66). |
| Quillin et al., 2000 [28] | USA | Pre-post study | 71 | 17-50 years | College, participate in psychology groups | NA | Educational intervention on neural tube problems and prevention through folic acid | | Health Belief Model (HBM) and the Fetal Health Locus of Control Scale (FHLCS) | Knowledge/ Awareness/ Behaviours | Following the intervention, a significant increase in knowledge of both folic acid (p = 0.0001) and of NTDs was found (p = 0.0002), and there was a significant increase in scores for the perceived benefits factor (p = 0.0001), for the perceived barriers factor (p = 0.0001), and for the perceived threat factor (p = 0.0001).Awareness of folic acid was not associated with multivitamin consumption. |
| Ragnar et al., 2018 [20] | Sweden | Qualitative | 47 | 16–18 | Upper secondary school | 2015-2016 | NA | | Focus group interviews | Knowledge | Participants recognised the importance of preconception health and were highly aware of the importance of a healthy lifestyle. They had difficulties relating to fertility and preconception health on a personal and behavioural level. Participants wanted more information but had heterogeneous beliefs about when, where and how this information should be given. Gender roles influence beliefs about fertility and preconception health. |
| Richards et al., 2012 [21] | USA | Non randomised interventional study | 77 | 11-14 | Residential summer program for American Indians high school students | 6 weeks | Educational interventions on youth population | | Questionnaire. Lesson. | Knowledge, Behaviours | The intervention group scored higher than the non-intervention group in overall preconception health knowledge (96% vs 90%, p = 0.03) and obesity knowledge (44% vs 33%, p = 0.01). There were no significant differences in T2 scores between the intervention and non-intervention groups on knowledge of alcohol (87% vs 81%, p = 0.33, smoking (76% vs 67%, p = 0.35), diabetes(72% vs 63%, p = 0.34, or use of condoms (78% vs 74%, p = 0.12). |
| Schoenaker et al., 2015 [12] | Australia | Cohort study. | 3,853 | Mean 28 (1.4) | Australian Longitudinal Study on Women's Health (ALSWH) | 2003/2012 | NA | | Survey | Behaviours/ Diet/ Health status | No associations were found for the 'Fruit and low-fat dairy' and 'Cooked vegetables' patterns and GDM. The 'Meats, snacks and sweets' pattern was associated with higher GDM risk after adjustment for socioeconomic, reproductive and lifestyle factors (RR = 1.38 [CI 1.02, 1.86]). In stratified analysis, the 'Meats, snacks and sweets' pattern was associated with significantly higher GDM risk in parous and obese women, and in women with lower educational qualifications. The 'Mediterranean-style' pattern was associated with lower GDM risk in the fully adjusted model (0.85 [0.76, 0.98]). |
| Short et al., 2020 [43] | USA | Cross-sectional retrospective | NR | NR | Pregnancy Risk Assessment Monitoring System (PRAMS) data from 6 states | 2016 | NA | | Questionnaire | Behaviours/ marijuana use | 8% of respondents reported that they had used marijuana in the month before pregnancy. Marital status, education level, parity, and living in a state with medical or recreational marijuana legalization or decriminalization remained independently associated with marijuana use. Those who reported marijuana use were 3–5 times more likely to also report symptoms of depression and tobacco and alcohol use before or during pregnancy than respondents who did not report marijuana use. |
| Sijpkens et al., 2019 [34] | The Netherlands | Interventional study | 587 | 18-41 | Primary care practices within Health Pregnancy 4 All program. Ten Dutch municipalities in deprived neighbourhoods. Target population: 165,615 women | February 2013-December 2014 | Four approaches: (1) letters from municipal health services; (2) letters from general practitioners; (3) information leaflets by preventive child healthcare services and (4) encouragement by peer health educators | | Questionnaires | Knowledge/ Access to healthcare | The majority of applications (n = 424; 72%) were prompted by the invitation letters (132,129) from the municipalities and general practitioners. The effect of the municipal letter seemed to fade out after 3 months. The outreach strategy led to women with different socioeconomic backgrounds and different motivations applying for a PCC consultation. |
| Sijpkens et al., 2021 [47] | Netherlands | Prospective cohort | 259 | 18-41 | 14 deprived municipalities selected based on their relatively high perinatal morbidity and mortality rates | 3 months | 2 individual visits by a general practitioner or a midwife. 1. Risk assessment and advice according to the national guideline. 2. Identified risk factors and formulated plan were evaluated | | Self-reported and biomarker data on behavioral changes were obtained at baseline and 3 months later. Web-based questionnaire (including the domains lifestyle, medical, reproductive, and family history) | Behaviours/ Lifestyle | Considering the risk factors no folic acid supplementation, smoking, and alcohol consumption, 15.8% had no risk factor, 55.6% had 1 risk factors, 25.7% had 2 risk factors, and 2.9% had 3 risk factors. Baseline self-reported prevalence of no folic acid use was 36%, smoking 12%, weekly alcohol use 22%, and binge drinking 17%. 42.1% of women who reported not taking folic acid at baseline had started taking folic acid at the follow-up measurement (p < 0.001). The percentages of smoking showed no change between baseline and follow-up. Prevalence of reported binge drinking decreased significantly (p = 0.007). |



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| Skogsdal et al., 2019 [26] | Sweden | Randomized controlled trial | 1,946 women Q1 and 1,198 Q2 | 20-40 | 28 outpatient clinics | February 2015-March 2016 | 1. Routine contraceptive counseling. 2. General information about preconception health. 3. Folic acid supplementation. 4. Information about fertility and age | | Two questionnaires: at baseline (Q1) and at follow-up (Q2) | Knowledge/Awareness | Knowledge about fertility was low. After the intervention a larger proportion of women in the intervention group thought that it was more important to make lifestyle changes before a pregnancy. The intervention had great influence on if and when they will become pregnant. They also increased their awareness of factors affecting preconception health, such as to stop using tobacco, to refrain from alcohol, to be of normal weight, and to start with folic acid before a pregnancy. 76% stated that the Reproductive Life Plan Counselling should be part of the routine during visits to midwives or other healthcare providers. |
| Srinivasulu et al., 2020 [51] | USA | Interventional study | 27,817 | 13–44 | Institute for Family Health | March 2017-September 2018 | Electronic medical record-based clinical decision support designed to increase family planning services for women of reproductive age | | Clinical decision support tool | Behaviours/Family planning and contraception | Unadjusted documentation of family planning services increased by 2.7 percentage points (55.7% pre-intervention to 58.4% intervention). In the adjusted analysis, documentation increased by 3.4 percentage points (95% CI: 2.24, 4.63). Modification of effect by race, insurance, and site were substantial, but not by age group nor ethnicity. Additionally, patient-level subset analysis showed that those exposed to the intervention had 1.26 times the odds of having family planning services documented after implementation compared to controls (95% CI: 1.17-1.36). |
| Stulberg et al., 2019 [54] | USA | Pre-post (pilot) study | 63 | 18-49 | Urban community health center | NR | Implementation in the Electronic Medical Record of One Key Question® (would you like to become pregnant in the next year) 2. Provided a brief training to primary care clinicians on reproductive life plan assessment, preconception counseling, and contraception | | Electronic Medical Records/Questionnaire | Access to healthcare/Counselling | Higher rates of clinician counseling women about contraception (52% vs 76%, p = 0.040) and recommending a long-acting reversible contraceptive (LARC) method (10% vs 32%, p = 0.035). There were no significant changes in preconception counseling. |
| Vamos et al., 2015 [37] | USA | Cross-sectional | 7,596 | 18-28 | 80 high schools | 1994-2008 | NA | | Questionnaire + interview | Behaviours | Older females were less likely to be physically active (OR 0.94, 95% CI 0.91-0.97). Population density was positively associated with more than 5 instances of Moderate-Vigorous Physical Activity (MVPA) among women (OR 1.34, 95% CI 1.02-1.77). Median household income was also positively associated with MVPA in those women (OR 1.33 95% CI 1.06-1.66). A significant inverse trend was found between high MVPA and proportion of the community without a high school diploma. |
| Walker et al., 2021 [18] | Australia | Qualitative | 14 | 24-41 | Community setting | September-December 2019. | NA | | Interviews comprised open-ended questions to elicit their views and expectations of preconception care | Knowledgw/behaviours | <ul style="list-style-type: none">Identified nutrition, physical activity and looking after their mental health as being the most important lifestyle factors for preconception health.Most women reported that seeking preconception care was not relevant to them if they were not planning a pregnancy.Only a few women could describe their experiences seeking preconception care.Best place to provide preconception advice: health professional with some sort of qualification.Women reported wanting more information about preconception health earlier in their reproductive years. Schools and public health campaigns were identified as methods of achieving greater awareness. |
| Whitaker et al., 2018 [36] | USA | Cohort study | 1333 | 20-35 | Four field centers | 1987-2010 | NA | | Questionnaire Coronary Artery Risk Development in Young Adults (CARDIA) | Behaviours | Women who developed GDM were more likely to have a family history of diabetes (21,3% p: 0,017), higher prepregnancy BMI (22,9% p:0,011) and waist circumference (70% p: 0,010), and lower levels of fitness compared with those without GDM. Women with GDM also had worse cardiometabolic profiles, including elevated fasting glucose (70% p: 0,010), insulin (80% p: 0.005), and HOMA-IR levels and lower HDL levels (11,1% p: 0,033). |
| Witt et al., 2016 [41] | USA | Cohort study | 9,350 | 20-40 | Early Childhood Longitudinal Study-Birth Cohort | 2001 | NA | | Birth certificate; self-report questionnaire about tobacco, alcohol, stressful events, prenatal health and stress | Behaviours/Health status | 34.8% and 3.3% of women reported alcohol use during the three months prior to pregnancy and in the final three months of their pregnancies, respectively. 12.3% and 11.0% of women reported tobacco use during the three months prior to pregnancy and in the final three months of pregnancy, respectively. Compared to women who never smoked, women who smoked prior to conception (AOR: 1.31; 95% CI: 1.04-1.66) or during their last trimester (AOR: 1.98; 95% CI: 1.56-2.52) were more likely to give birth to LBW infants. Women who experienced any stressful life events were more likely to deliver a VLBW infant (OR = 1.73; 95% CI: 1.48-.01). |

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| Xaverius et al., 2012 [40] | USA | Cross-sectional | 8,095 | 12-44 | National Health and Nutrition Examination Survey | 1996-2006 | NA | | Questionnaire, physical examination NHANES | Behaviours/ Access to healthcare | Non-pregnant (NP-US) women were 45% less likely to have a normal BMI , 1.9 times more likely to drink any alcohol , 2.0 times more likely to binge drink, 1.9 times more likely to smoke , and 3.7 times more likely to have used illicit drugs , 1.7 times more likely to engage in moderate physical activity and over 1.7 times more likely to use birth control than FB-US women. Non-pregnant foreign born women (NP-FB) were less likely to have health insurance (40.3 vs 17.2%); reported lower food security (78.4 vs 86.4%); were less likely to own their home (48.2 vs 62.4%); and were more likely to be impoverished (29.7 vs 17.4%). |
| Xaverius et al., 2009 [3] | USA | Cross-sectional | Women at high-risk (16,113) or low-risk (39,426) for pregnancy | 18-44 | Behavioral Risk Factor Surveillance System (BRFSS) | 2002-2004 | NA | | Telephone survey | Behaviours/ Health status/ Access to healthcare | Women at high-risk for pregnancy were 1.23 times more likely to be obese (CI, 1.12-1.34) and 1.2 times more likely to smoke (CI, 1.11-1.31). They were 27% less likely to exercise (CI, 0.67-0.79), 62% less likely to receive a Pap test (CI, 0.31-0.46), 19% less likely to have HIV testing (CI, 0.75-0.87), and 44% less likely to have received sexually transmitted diseases counselling (CI, 0.50-0.63) compared to low-risk women. High-risk women were 27% less likely to use any alcohol (CI, 0.67-0.79) and 11% less likely to binge drink (CI, 0.80-0.99) compared with women at low-risk for an unintended pregnancy. 29% of women at risk for an unintended pregnancy are not using any contraceptive method . |

