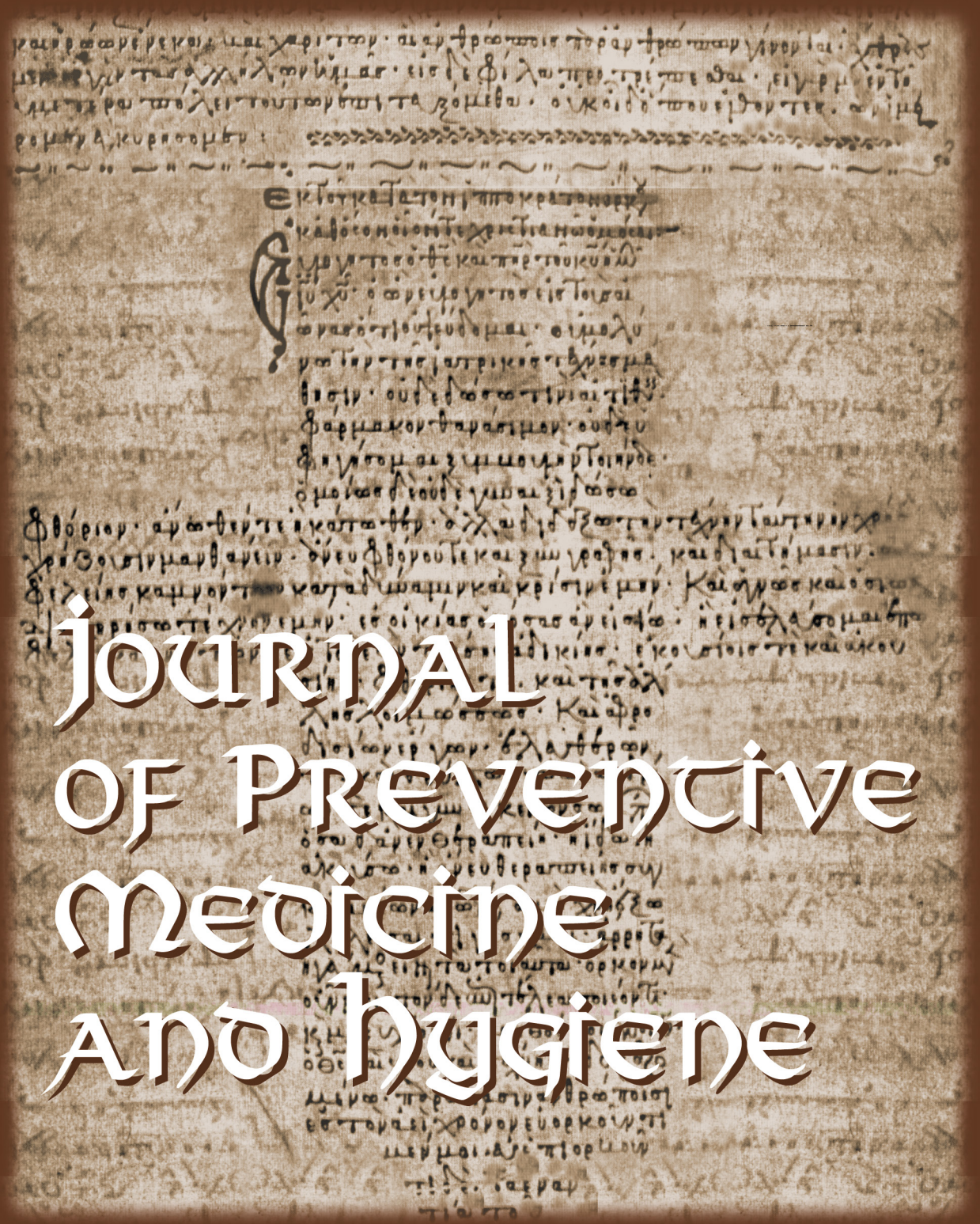
ISSN 2421-4248

vol. 63/4 n.

December 2022

Cited in Index Medicus / Medline
NLM ID 921440 (Pub-Med)



The original document of Hippocrates' oath

Journal of Preventive Medicine and Hygiene

The Journal has been accreditated, on occasion of the 17th December 2004 Meeting of the Executive and Scientific SItI Councils, by the Italian Society of Hygiene, Preventive Medicine and Public Health

PACINI EDITORE MEDICINA

JOURNAL OF PREVENTIVE MEDICINE AND HYGIENE

Managing Editor: Patrizia Alma Pacini

Publisher; Pacini Editore Srl, Via Gherardesca 1, 56121 Pisa, Italy
Tel. +39 050 313011 - Fax +39 050 3130300
info@pacinieditore.it - www.pacinimedicina.it

Published online February 2023

Authorization Tribunal of Genoa, Italy n. 507 - 10/6/1960
Journal registered at "Registro pubblico degli Operatori della Comunicazione" (Pacini Editore srl registration n. 6269 - 29/8/2001).

Volume 63 - Issue 4 December 2022
www.jpmh.org

Contents

COVID-19

Healthcare system preparedness for the next pandemic beyond COVID-19 situation

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Keywords

COVID-19 • Healthcare • Monkeypox • Pandemic

Dear Editor,

Monkeypox (MPX), first discovered in 1970 and becoming endemic in Africa, is a zoonotic viral disease that has recently caused outbreaks in different regions worldwide since May 2022. Following this situation, MPX has been designated as a Public Health Emergency of International Concern (PHEIC) since 23rd July 2022 [1]. The recent epidemic resulted in more than 77,000 MPX confirmed cases across over 100 countries globally until 30th October 2022 [2].

In the meanwhile, the world is still struggling with the COVID-19 pandemic, which has caused a significant impact on healthcare services [3]. In a systematic review by Moynihan et al., the authors noted a 37% reduction in overall utilisation of medical care services throughout the COVID-19 pandemic period compared to the pre-pandemic years, as measured by visit (42%), admission (28%), diagnostic testing (31%), and treatment (30%) parameters [4]. This phenomenon could significantly hinder the ability of healthcare systems to overcome new global health problems.

With the dispersion of MPX, public health preparedness must be extended to nonendemic areas. Human resources, testing capacities, and personal protective equipment (PPEs) are needed for quick interventions and emergency responses. All of these requirements must be fulfilled, although it has been severely depleted during the three-year course of the COVID-19 pandemic [1]. Thus, it is vital to determine the readiness of these resources for future pandemics.

Undoubtedly, the COVID-19 pandemic has negatively affected healthcare workers in terms of mental and physical health. Moreover, this pandemic has affected the healthcare systems' financial capacities, which became unable to provide the needed beds, treatments, vaccines, and intensive care units. It is clear that healthcare systems have not yet fully recovered from the COVID-19 pandemic [5]. With the growing threat of infectious diseases, healthcare systems might not be well prepared to face the next pandemic, whether related to the current emergence of MPX or any other infectious agents.

Protecting healthcare providers should be prioritised to combat the alarming threat of future pandemics. Based on the early scenario of the COVID-19 pandemic, the healthcare system is not well prepared and thus medical personnel support is insufficient. Several countries, including Italy, Spain, United Kingdom, and United States, encountered delays in implementing containment measures and did not anticipate the impact of the pandemic due to inadequate response of stakeholders, according to data from the initial phases of the COVID-19 pandemic [6]. Three main areas of medical personnel support can be identified: harm prevention (primarily through adequate access to PPE, training, and hospital hygiene practice), access to mental health services, and promotion of positivity (using peer support intervention or feedback sessions) [7].

Global leaders and health organizations should share the same vision to improve future pandemic preparedness. As soon as an emerging pathogenic agent is discovered, governments should endorse a comprehensive research approach focusing on in public health and biomedicine [8]. The goal is clear: by gathering better evidence in the early stages of an epidemic, its overall impact could be minimized and its development into a pandemic could be averted. Treatment options, such as antiviral agents, supportive treatments, symptom-specific interventions, and immunization approaches, should be investigated. In the case of MPX, vaccination initiatives may be an essential consideration due to the cross-protection with the currently available smallpox vaccine, such as JYNNEOS™ and its ability to limit the spread of the disease while preventing the occurrence of severe disease forms [1]. Considering the relatively slow transmissibility and long incubation period of the monkeypox virus (MPXV), ring vaccination is considered a better option to protect against it than mass vaccination [9]. In addition, investigations on safety of the available therapeutic and immunization approaches should be prioritized.

Due to the pandemic potential of MPX, it is recommended for healthcare professionals to participate in educational activities on the clinical manifestation of MPX cases, universal precaution, and suitable contact tracing. Although the current MPX outbreak has a low mortality rate (< 0.01%) globally, we must still be aware of higher mortality rates in several regions,

such as Eastern Mediterranean (1.38%), Africa (1.5%), and Southeast Asia (3.33%) [2]. To prevent the loss of human resources, as experienced in the early COVID-19 pandemic, the satisfaction of healthcare workers must be monitored and invested into, especially regarding workload and incentives [10].

The global surge of MPX should serve as a red flag for stakeholders to begin meaningful efforts to combat this outbreak through cooperative collaboration. Public awareness should be raised, and governments should enhance their support for research activities, primarily to determine the virus characteristics while investigating the safety and effectiveness of potential therapeutic and preventive strategies [11]. However, the most important intervention is to avert misleading information, which intensifies vaccine hesitancy, reduces vaccination rates, and suppresses public health programs, resulting in substantial loss of life and resources during the current COVID-19 pandemic [12].

Acknowledgements

Funding sources: this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The author declares no conflict of interest.

Authors' contributions

Manuscript ideation: TPU, AKMSK, and MOS; Reference acquisition: TPU, AKMSK, and YAM; Manuscript drafting: TPU, AKMSK, and YAM; Manuscript revision: TPU and MOS. All authors have read and approved the final version of the manuscript.

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Received on November 8, 2022. Accepted on January 19, 2023.

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How to cite this article: Umar TP, Kadir AKMS, Mohammed YA, Setti MO. Healthcare system preparedness for the next pandemic beyond COVID-19 situation. J Prev Med Hyg 2022;63:E493-E494. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2786

HEALTH PROMOTION

Access to water, sanitation and hygiene in schools: A prerequisite to achieving SDGs in India

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Keywords

Sustainable development goals • Water Sanitation and Hygiene (WASH) • Schoolchildren's • India

Dear Editor,

In 2015, the United Nations General Assembly (UNGA) adopted 17 Sustainable Development Goals (SDGs), comprising 169 targets, aimed at achieving worldwide sustainable development. The eight targets specified in SDG 6 focus on clean water and sanitation, the aim being to ensure the availability and sustainable management of water and sanitation for all by 2030. This involves ending open defecation and providing access to sanitation and hygiene, improving water quality, ensuring the supply of fresh water, implementing integrated water resource management and restoring water-related ecosystems [1, 2].

Since 2019, the world has been fighting the COVID-19 pandemic, and water, sanitation and hygiene (WASH) stand at the forefront of disease prevention efforts worldwide. However, the WASH situation in low- and middle-income countries (LMICs) remains an obstacle to the prevention of COVID-19 infection [3]. WASH play a critical role in improving schoolchildren's education, health and overall well-being. Indeed, the lack of WASH in schools facilitates the spread of preventable diseases and increases school absences, particularly among females. Inadequate funding and budgeting have been identified as a major impediment to integrating successful and sustainable WASH programs into school settings.

An integral and essential part of the social structure, children are known to be receptive to new ideas, and the school serves as a conduit for these [4]. Children spend much of their time at school, which is the best place to learn and practice good water, sanitation and hygiene habits. Furthermore, children can influence their family members and society, thereby changing the community's attitudes towards WASH. Children are therefore critical in shaping the WASH behaviors of future generations [4]. In this respect, school is a cornerstone of the future of an informed and healthy society. Thus, the provision of clean water, sanitation and hygiene in schools can be seen as a necessary prerequisite to achieving SDG 6.

According to the United Nations, billions of people still lack access to safe drinking water, adequate sanitation and adequate hygiene. As per the United Nations' 2021 report, 129 nations worldwide will be unable to manage water resources sustainably by 2030 unless the current rate of improvement is doubled [5]. According to the 2018 global baseline report, providing universal access to necessary WASH services in schools by 2030 will be a significant challenge. Indeed, in 2016, only 69% of schools globally had access to safe drinking water. Moreover, although schools play a critical role in children's fundamental education, in 2013-14 approximately 22% of schools in India lacked girls' bathrooms, while today water quality still remains a major concern in rural India [6]. In addition, open defecation is a significant global health issue, and in rural India, about 360 million people lack access to latrines [7].

Several national and international initiatives have addressed the above-mentioned concerns. The United Nations Water global analysis and assessment of sanitation and drinking water (GLAAS) initiative is a worldwide effort by the WHO to improve the monitoring, management and reporting of national WASH policies in diverse geographic locations throughout the world [8]. UNICEF estimates that less than half of India's population has access to safe drinking water [9]. According to the 2018 global baseline study, most schools in India now have sanitary facilities, whereas in earlier years half of them did not [6].

India, which is the world's second-most populous country, faces major public health concerns. To tackle these issues, it has implemented measures such as the Swachh Bharat Mission (SBM) and the Total Sanitation Campaign (TSC) project for school sanitation. Moreover, under India's new leadership, a new government ministry was established. Called "Jal Shakti", this ministry has primary responsibility for water, sanitation and hygiene, and works to achieve SDGs [10]. After the construction of school latrines in India, the number of girls' enrollments has increased in comparison with those of boys [11]. Furthermore, as India is a culturally diversified country, the caste system can also impact sanitation.

Thus, in India, there are still key challenges regarding WASH, such as poor water supply, scant sanitary conditions and deficient knowledge of the use of toilets; these are significant barriers to achieving the country's sanitation objectives [12].

Every child deserves an education and the knowledge necessary to thrive in life, and sanitation, hygiene and access to safe water are fundamental components of a child's development. Moreover, it has been demonstrated that children are significantly more receptive than adults to novel ideas and can readily acquire positive habits during their formative years [13]. If these children are provided with facilities and are educated in the importance of hygiene, they will become powerful agents of change, handing down their knowledge to the next generation. It is therefore critical to incorporate WASH into the school curriculum and infrastructure and to equip teachers to promote essential hygiene behaviors. As India has unmet public health needs, the government needs to improve school education programs by implementing separate toilet facilities for boys and girls and raising awareness through short movies, education on sanitation-related behavioral change, etc. In this way, we can achieve universal sanitation for all and achieve the SDGs.

Acknowledgements

Funding sources: this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The author declares no conflict of interest.

Authors' contributions

The first author wrote the manuscript with the help of three other authors. All the authors have equal contributions to developing ideas to write the manuscript. The corresponding author supervised and reviewed the manuscript.

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Received on May 3, 2022. Accepted on January 13, 2023.

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How to cite this article: Jena S, Satpathy N, Sahoo KC, Epari V. Access to water, sanitation and hygiene in schools: A prerequisite to achieving SDGs in India. J Prev Med Hyg 2022;63:E495-E496. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2539

COVID-19

Parents' knowledge, attitude, and practices towards COVID-19 in children: A Lebanese cross-sectional study

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Keywords

Knowledge • Attitude • Practices • COVID-19 • Children

Summary

Introduction. *The Coronavirus disease 2019 (COVID-19) pandemic, a serious public health crisis, can affect all ages, even children. This study aimed to investigate the knowledge, attitude, and practices of parents living in Lebanon towards the COVID-19 in children.*
Methods. *A cross-sectional online survey was conducted between June and July 2021, targeting parents living in Lebanon. The questionnaire was divided into 4 parts: socio-demographic, knowledge, attitude, and practices. A score was calculated to evaluate parents' knowledge towards COVID-19 in children. Descriptive and bivariate analyses were conducted. Then, determinants of COVID-19 knowledge were assessed using multivariable linear regression. P < 0.05 was considered statistically significant.*
Results. *A total of 429 parents were included. The mean knowledge score was 11.28 ± 2.19 out of 15. Knowledge was significantly lower among older (p = 0.022), and single parents (p = 0.035), who don't know if COVID-19 is a serious disease (p < 0.001) and if it will be successfully controlled (p = 0.007), and higher among female parents (p = 0.006). The majority of parents had a positive attitude and good practices towards COVID-19 in children, but 76.7% of them were worried about their child getting coronavirus. About 66.9% of parents expressed their willingness to vaccinate their kids when a vaccine would be available for them, and 66.2% answered that they are sending or willing to send their children to the school or the nursery.*
Conclusions. *Parents' knowledge about COVID-19 in children was good, but remains lower among older and single parents. Health authorities should conduct awareness campaigns to target specific groups of parents who lacked critical knowledge about COVID-19 in children.*

Introduction

Coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a serious public health crisis threatening humanity since the middle of December 2019. This new form of coronavirus has emerged in Wuhan, China, and has quickly spread globally [1]. The World Health Organization (WHO) declared a public health emergency of worldwide significance by the end of January 2020, and urged all governments to work together to avoid its fast spread. COVID-19 was later named a "global pandemic" by the WHO [2].
The first confirmed case infected with SARS-CoV-2 was diagnosed in Lebanon on February 21, 2020 [3]. Up to February 7, 2022, there have been 978,125 confirmed cases of COVID-19 with 9,730 deaths. The COVID-19 incidence rate in the age group 0-9 was over 400 cases per 100,000 children, and over 800 cases per 100,000 children in the age group 10-19. The fatality rate was 0.06% in the age group 0-9, and 0.03% in the age group 10-19 [4].
Although a lower incidence of COVID-19 cases in children than adults has been demonstrated [5], investigating the burden in this special population is essential as a part of contact tracing.
As of February 7, 2022, over 12 million children have been tested positive for COVID-19 since the beginning of the pandemic in the United States, and this number represented 18.9% of all cases (16,000 cases per 100,000 children). Children accounted for 1.6 to 4.7% of total cumulative hospitalizations in the states, and 0.00-0.24% of all COVID-19 deaths [6]. Children aged 0-4 years had the highest percentage of hospitalizations and ICU admissions among children, adolescents, and young adults [7]. In this age group, immaturity of the respiratory tract and immune system is considered to have a role in severe viral respiratory disease [8].
The average incubation period for COVID-19 is 5.2 days [9]. COVID-19 infection in children appears to be primarily transmitted through the family cluster [10]. Because younger children cannot wear masks and have not taken particular preventive and control measures, the number of child infection cases has increased dramatically since then [11]. Unlike adults, most infected children are asymptomatic or have only minimal clinical symptoms [10]. The flu-like syndrome, fluctuating fever, pneumonia, upper respiratory signs (cough, sore

throat, stuffy nose, sneezing, and rhinorrhea), diarrhea, and abdominal pain are the main COVID-19 symptoms in children [11].

To add, children, particularly those from racial and ethnic minorities, as well as those with underlying medical conditions and disabilities, can become seriously ill. They could develop multisystem inflammatory syndrome in children (MIS-C), a life-threatening hyperinflammatory state 4-6 weeks after infection with primary COVID-19, with symptoms ranging from severe abdominal pain to organ damage [12]. Up to January 31, 2022, 6,851 cases of MIS-C and 59 MIS-C deaths were reported in the United States [13].

The majority of children who developed MIS-C were school-aged, and previously healthy. In these patients, the original COVID-19 infection is often mild or asymptomatic. They usually get a persistent fever, gastrointestinal symptoms (pain, vomiting, diarrhea), evidence of mucocutaneous inflammation (rash, conjunctivitis, oromucosal alterations), lymphopenia, and high circulating inflammation levels. A small proportion of MIS-C patients develops a severe disease, such as hypotension/shock, and evidence of cardiac involvement, including myocarditis, myocardial dysfunction, and alterations in coronary arteries. Immune modulation has been applied in conjunction with optimum supportive care to treat MIS-C, and in most cases, the inflammation has resolved quickly. Fatal cases are rare (2%) [14, 15].

COVID-19 in children poses a significant challenge due to the asymptomatic presentations and role in community transmission. The confirmed diagnosis is important, and cannot be without microbiologic testing. COVID-19 is primarily diagnosed through direct detection of SARS-CoV-2 RNA in the upper respiratory tract using nucleic acid amplification tests (NAATs), most commonly reverse-transcription polymerase chain reaction (RT-PCR) [16]. Also, tests that detect SARS-CoV-2 antigen can be performed quickly with rapid results, but are less sensitive than NAATs [17]. Serologic tests that detect antibodies to SARS-CoV-2 in the blood have insufficient utility for diagnosis in the first days to weeks of infection, but help identify patients who have previously had a SARS-CoV-2 infection, as well as, patients with current infection, who have had symptoms for 3 to 4 weeks [18].

Regarding the vaccine, the US Food and Drug Administration (FDA) on May 10, 2021, expanded the emergency use authorization for the Pfizer-BioNTech COVID-19 vaccine for the prevention of COVID-19 caused by SARS-CoV-2 to include adolescents aged 12 to 15 [19]. On 29 October 2021, the FDA authorized its emergency use to include children aged 5 to 11 [20]. As of February 4, 2022, 16.4 million children aged 12 to 17 in the United States have received at least one dose of the COVID-19 vaccine, with 13.9 million of these children fully vaccinated, representing 65 and 55% of 12-17 year old children, respectively. In addition, 8.6 million children aged 5 to 11 in the United States have received at least one dose of the COVID-19 vaccine, with 6.2 million of these children fully vaccinated, as of February 4, 2022, representing 30% and 22% of children at this age, respectively [21].

In Lebanon, approximately 30.40% of residents completed their vaccinations on February 8, 2022 [22]. There is no data regarding the number of vaccines administered for the age group 12-18 in Lebanon since the vaccine is still unavailable for the younger group.

While keeping the focus on continuing safety measures for the younger group, knowledge regarding the clinical characteristics and disease burden in children, positive attitudes and good practices among their parents are critical at this stage of the pandemic.

Parents must educate their children, and help them practice preventive measures and hygiene behaviors. Assessing the knowledge, attitude, and practices (KAP) related to COVID-19 in children among parents would be helpful to identify knowledge gaps, provide control of transmission and proper allocation of healthcare resources in this age group, and develop preventive strategies and programs for health promotion in children.

Few studies about KAP towards COVID-19 in children among parents and caregivers were conducted [23, 24]. In addition, to the best of our knowledge, there was no published study among the Lebanese parents towards COVID-19 in children. Thus, we aimed to investigate the KAP among parents towards COVID-19 in children.

Methods

Study design and population

A cross-sectional anonymous survey was designed, targeting parents living in Lebanon to evaluate their KAP towards the COVID-19 pandemic in children between 17 June and 22 July 2021. Parents (having at least one child aged less than 18 years), that were over 18 years old and living in Lebanon were eligible to participate in the survey. This study was conducted through a link shared on social networking platforms using the Snowball sampling technique.

Survey instrument

The structured questionnaire was developed based on the literature [23, 25, 26] and was designed in English and then translated to Arabic, the native language in Lebanon.

The online survey was divided into four parts that included 54 mandatory questions. The first one required the sociodemographic information of the participant (sex, age, nationality, marital status, number of children of all ages, level of education, occupation, family income, and place of current residence), his medical history, his experience with the COVID-19 pandemic, and his vaccination status. The second one, having 15 knowledge questions (K1 to K15) about COVID-19 symptoms, treatment, mode of transmission, MIS-C, and measures for prevention in children, required true/false/I don't know the answers. Each right answer was given

one point, and each wrong or I don't know the answer was given a zero. The total knowledge score ranged from 0 to 15, with a higher score denoting a better knowledge about COVID-19 in children. The Cronbach's alpha coefficient of the knowledge questionnaire was 0.613 in our sample, indicating acceptable internal consistency.

The third part included 6 questions reflecting the attitude of the respondents towards the disease and the vaccine, and the last part consisted of 6 questions about the practice of the parents towards COVID-19 in children, like social distancing, wearing a mask, washing hands, avoiding the touch of eyes, nose, and mouth, and willing to send children to the school or the nursery. Parents were asked to respond "yes" or "no" to the practice items. For the first five practice questions, a score of one was given to answers that reflected good practice, and a score of zero was given for answers that reflected bad practice. The total score ranged from zero to five, with high scores indicating better practices.

A preliminary phase was conducted to check the reliability and the validity of the questionnaire. Two experts in the pediatric medical field were asked to review the questions to make sure that it reflects the KAP of the Lebanese parents towards COVID-19 in children. The next step was pretesting of the questionnaire on 10 participants who were excluded later from the study sample. Accordingly, modifications have been applied to meet the aim required. The data generated from the initial pilot study was excluded from the final analysis.

Data collection

On the first page of the online survey, respondents were informed about the background and objectives of the study. Participants were informed that they were free to withdraw at any time, and that all information and opinions provided would be anonymous and confidential. Online informed consent was obtained before proceeding with the questionnaire.

An online open-access google form survey was created and participants from all areas of Lebanon were invited via social media platforms (Facebook° and Instagram°) through the accounts of the members of the research team with all our contacts and friends. In addition, members of the research team shared the survey link through our contacts lists in the chatting group "WhatsApp°".

Sample size

The sample size was determined using the Epi Info™ software, version 7.2. As there were no similar studies related to COVID-19 in children, the calculations were based on the assumption that the probability of having good knowledge, positive attitude, and effective practices towards preventive measures against COVID-19 among parents was 50.0%, at a 95% confidence interval (CI), a margin of error of 5%, with a design effect of 1.0, the calculated sample size was 384 participants.

Statistical analysis

The results were analyzed using Statistical Package for the Social Science (SPSS) software version 22 (IBM, New York-USA). No missing data were obtained. Categorical data were expressed as frequencies (percentages) while continuous data as means ± standard deviation (SD). The dependent variable is a continuous variable: knowledge score. Normality was checked for variables with $n < 30$ in one or more of the categories. Student's t and ANOVA tests were used to compare the mean knowledge score between different demographic groups for variables with adequate normal distribution. Mann - Whitney U or Kruskal - Wallis tests were used for non-normally distributed continuous variables. Multivariable linear regression analysis was performed to identify factors associated with the knowledge score. Only variables with $p < 0.2$ in the bivariate analysis were included in the multivariate linear regression, using the Enter method. All results were considered "statistically significant" when the p-value was < 0.05 with a CI of 95%.

Results

Out of 454 participants, 447 completed the survey, generating a response rate of 98.46%. Eighteen of them were excluded because they reported that they don't have children. So, a total of 429 parents were included in the study.

Descriptive analysis

Table I details the socio-demographic characteristics of the studied participants. The majority of parents were females (n = 344, 80.2%), aged 30-39 years (n = 186, 43.4%), married (n = 412, 96%), Lebanese (n = 422, 98.4%), had a bachelor's degree (n = 173, 40.3%), and had a family income between 675,000 and 1,999,000 LBP (n = 132, 30.8%). In addition, 12.4% (n = 53) of parents were healthcare workers.

Additionally, 66.7% (n = 286) of the parents had 1-2 children, 52% (n = 223) had at least one child aged 4 or less, 55.9 % (n = 240) had at least one child aged between 5 and 11 years, and 37.3 % (n = 160) of them had at least one child aged between 12 and 18 years.

About 54.3% (n = 233) of the respondents were living in Mount-Lebanon.

Moreover, 22.8% (n = 98) of the parents were smokers, 16.3% (n = 70) of the parents and, 8.9% (n = 38) of the children had a history of one or more chronic diseases (Tab. II).

Concerning their experience with the COVID-19 pandemic, 55.5% (n = 238) of the parents reported that they were once in quarantine because of symptoms or because they were in close contact with someone tested positive for COVID-19 or because they returned from a country that had a large number of cases, 32.2% (n = 138) have tested positive with coronavirus using PCR or other tests, 24.7% (n = 106) of parents reported that at least one of their children experienced COVID-19 symptoms and 11.9% (n = 51) of them had at least one of their children tested positive with coronavirus using PCR or other tests.

Tab. I. Socio-demographic characteristics of parents.

Variable	Frequency (n = 429)	Percentage (%)
Sex		
Female	344	80.2
Male	85	19.8
Age		
18-29	72	16.8
30-39	186	43.4
40-49	118	27.5
≥ 50	53	12.4
Nationality		
Lebanese	422	98.4
Other nationalities	7	1.6
Marital status		
Married	412	96
Not married	17	4
Number of children		
1-2	286	66.7
3-4	129	30.1
≥ 5	14	3.3
At least one child aged 4 years or less	223	52
At least one child aged between 5 and 11 years	240	55.9
At least one child aged between 12 and 18 years	160	37.3
Level of education		
High school's degree and below	118	27.5
Bachelor's degree	173	40.3
Master's degree and above	138	32.2
Occupation		
Unemployed	147	34.3
Student	10	2.3
Healthcare worker	53	12.4
Other occupations	219	51
Family income		
No current income	58	13.5
< 675,000 LBP	22	5.1
675,000-1,999,000 LBP	132	30.8
2,000,000-3,999,000 LBP	123	28.7
≥ 4,000,000 LBP	94	21.9
Place of current residence		
Beirut governorate	35	8.2
Mount-Lebanon governorate	233	54.3
South-Lebanon governorate	41	9.6
Bekaa + Baalbeck - Hermel governorates	40	9.3
Nabatieh governorate	34	7.9
North + Akkar governorates	46	10.7

Regarding the vaccine, 33.8% (n = 145) of the parents have already received one of the available vaccines for COVID-19, 42% (n = 180) of those who had not been vaccinated were willing to receive it, 36.1% (n = 155) had a partner who received the vaccine and 42.2% (n = 181) of them had a partner who had not been vaccinated and was willing to receive it.

For their information on COVID-19, parents primarily relied on social media (n = 128, 29.8%) (Tab. III).

The total knowledge score ranged from 0 to 15, with a mean of 11.28 ± 2.19. Table IV below details the knowledge score, the attitude, and the practices of parents towards COVID-19 in children.

Participants gave the most correct answers when asked about the ways of the spread of the COVID-19 virus (K7-95.3%), the need for isolation (K13-94.9%), and some practices related to prevention and control of the infection (K10-95.1%, K11-95.6%, K12-93.9%) (Supplementary Tab. I).

The questions with the lowest rates of correct answers were those related to eating habits related to COVID-19 transmission (K5-24.2%) and the MIS-C (K15-29.1%) (Supplementary Tab. I).

Concerning the attitude of the parents towards COVID-19 in children, 85.3% (n = 366) agreed that COVID-19 is a serious disease, 76.7% (n = 329) of

Tab. II. Medical history of parents and children.

Variable	Frequency (n = 429)	Percentage (%)
Smoking status of parents		
No	331	77.2
Yes	98	22.8
Chronic diseases in parents		
No	359	83.7
Yes	70	16.3
Type of chronic diseases in parents		
No chronic diseases	338	78.8
Cardiac problems	13	3
Respiratory problems	3	0.7
Neurological problems	1	0.2
Diabetes	4	0.9
Allergies	23	5.4
Other diseases	22	5.1
More than 1 chronic disease	25	5.9
Chronic diseases in children		
No	391	91.1
Yes	38	8.9
Type of chronic diseases in children		
No chronic diseases	379	88.3
Cardiac problems	2	0.5
Respiratory problems	2	0.5
Neurological problems	0	0
Diabetes	2	0.5
Allergies	29	6.8
Other diseases	10	2.3
More than 1 chronic disease	5	1.1

Tab. III. Parents' experience with the COVID-19 pandemic and their vaccination status.

Variable	Frequency (n = 429)	Percentage (%)
Were you ever in quarantine because of symptoms or because you were in close contact with someone tested positive for COVID-19 or because you returned from a country that had a large number of cases?		
No	191	44.5
Yes	238	55.5
Have you tested positive with coronavirus using PCR or other tests?		
No	291	67.8
Yes	138	32.2
Did any of your children experience any COVID-19 symptoms?		
No	323	75.3
Yes	106	24.7
Have any of your children tested positive with coronavirus using PCR or other tests?		
No	378	88.1
Yes	51	11.9
Did you receive one of the available vaccines for COVID-19?		
No	284	66.2
Yes	145	33.8
Are you willing to receive one of the available vaccines for COVID-19?		
No	116	27
Yes	180	42
I already received my vaccine	133	31
Did your partner receive one of the available vaccines for COVID-19?		
No	263	61.3
Yes	155	36.1
I don't have a partner	11	2.6

▶

▶

Tab. III. Parents' experience with the COVID-19 pandemic and their vaccination status.

Variable	Frequency (n=429)	Percentage (%)
Is your partner willing to receive one of the available vaccines for COVID-19?		
No	103	24
Yes	181	42.2
I don't have a partner	11	2.6
My partner has already received his vaccine	134	31.2
Most used source of information regarding COVID-19		
Social media	128	29.8
Google and search engines	48	11.2
Family, friends, neighbors	10	2.3
News channels	61	14.2
Ministry of health website	89	20.7
Scientific articles and research	93	21.7

Tab. IV. Knowledge, attitude and practices of parents towards COVID-19 in children.

Variable	Frequency (n = 429)	Percentage (%)
Knowledge score of the parents towards COVID-19 in children 11.28 ± 2.19 (mean ± standard deviation)		
Attitude of the parents towards COVID-19 in children		
Do you agree that COVID-19 is a serious disease?		
Agree	366	85.3
Disagree	47	11.0
I don't know	16	3.7
Are you worried about your child getting coronavirus?		
Yes	329	76.7
No	100	23.3
Do you agree that COVID-19 will finally be successfully controlled?		
Agree	299	69.7
Disagree	38	8.9
I don't know	92	21.4
Do you think that the pandemic will be controlled in Lebanon in the near future?		
Yes	257	59.9
No	172	40.1
Do you think authorities should close educational centers (kindergartens, schools, and universities) to limit the spread of the disease?		
Yes	220	51.3
No	209	48.7
Are you willing to vaccinate your kids when a vaccine will be available for them?		
Yes	287	66.9
No	142	33.1
Practices of the parents towards COVID-19 in children		
In recent days, have you taken your children to any crowded place (> 10 people indoor, > 25 people outdoor)?		
Yes	140	32.6
No	289	67.4
Have you asked your kids to wear a mask outside the house or when in presence with other people?		
Yes	338	78.8
No	91	21.2
Do you teach your children to wash their hands with soap and water for 20 seconds frequently?		
Yes	409	95.3
No	20	4.7
Do you teach your children to maintain an appropriate distance between them and other people?		
Yes	391	91.1
No	38	8.9
Do you teach your children to avoid touching their eyes, nose and mouth?		
Yes	397	92.5
No	32	7.5
Are you sending or willing to send your children to the school or to the nursery?		
Yes	284	66.2
No	145	33.8

Tab. V. Factors associated with COVID-19 knowledge score.

	Knowledge score			
Variable	Standardized β	Unstandardized β	95% CI	P-value
Sex - Female	0.137	0.751	0.213, 1.289	**0.006** *
Age ≥ 50 years	-0.157	-1.045	-1.941, -0.149	**0.022** *
Marital status - Single	-0.100	-1.123	-2.168, -0.078	**0.035** *
Don't know if COVID-19 is a serious disease	-0.188	-2.168	-3.228, -1.108	**0.000** *
Don't know if COVID-19 will finally be successfully controlled	-0.126	-0.672	-1.163, -0.181	**0.007** *

CI: confidence interval; β: regression coefficient; *: $p < 0.05$ is considered significant.

them were worried about their child getting coronavirus, 69.7% (n = 299) agreed that COVID-19 will finally be successfully controlled and 59.9% (n = 257) thought that the pandemic will be controlled in Lebanon in the near future. For governmental measures, 51.3% (n = 220) of parents reported that authorities should close educational centers (kindergartens, schools, and universities) to limit the spread of the disease. Finally, 66.9% (n = 287) of parents expressed their willingness to vaccinate their kids when a vaccine would be available for them.

The mean practices score was 4.25 ± 1.03 out of 5. Many parents indicated that they avoided crowded places (67.4%) and taught their children to wear a mask (78.8%), wash their hands (95.3%), maintain an appropriate distance between them and other people (91.1%), and avoid touching their eyes, nose, and mouth (92.5%). Furthermore, 66.2% of parents answered that they are sending or willing to send their children to the school or the nursery.

Characteristics of participants according to COVID-19 knowledge

Regarding socio-demographic characteristics, parents' knowledge score significantly differed by sex (p = 0.001) and occupation (p = 0.002). The knowledge score was higher among female parents and those who were students. Participants' age, marital status, nationality, number of children of all ages, level of education, family income, and place of current residence were not related to the knowledge level of COVID-19 (Supplementary Tab. II).

Regarding parents' and children's medical history, smoking status of parents, chronic diseases in parents and children, and the type of chronic diseases in parents and children, were not related to the knowledge level of COVID-19 (Supplementary Tab. III).

Parents' knowledge score significantly increased by the experience of COVID-19 symptoms in children (p = 0.027) (Supplementary Tab. IV).

There was no significant association between the knowledge score and being in quarantine because of symptoms or because of close contact with someone tested positive or because of returning from a country that had a large number of cases (p = 0.097), positive diagnostic with COVID-19 using PCR or other tests in parents (p = 0.078), and in children (p = 0.317), and the most used source of information regarding COVID-19 (p = 0.061). Received the vaccine (p = 0.319), willing to receive the vaccine (p = 0.127), had a partner who received the vaccine (p = 0.515), or who is willing to receive it (p = 0.332) were not significantly associated with the knowledge score (Supplementary Tab. IV).

Concerning parents' attitudes towards COVID-19 in children, parents' knowledge scores significantly increased if the parent agreed that COVID-19 is a serious disease (p = 0.014) and if he was worried about his child getting coronavirus (p = 0.022) (Supplementary Tab. V).

Concerning parents' practices towards COVID-19 in children, parents' knowledge scores significantly increased if the parent had not taken his children to a crowded place in recent days (p = 0.043), and if the parent taught his children to avoid touching their eyes, nose, and mouth (p = 0.002) (Supplementary Tab. V).

In the multivariable linear regression model estimating factors associated with the COVID-19 knowledge score (Tab. V), we found that age ≥ 50 years (β = -1.045; p = 0.022; 95% CI: -1.941, -0.149), being single (β = -1.123; p = 0.035; 95% CI: -2.168, -0.078), don't know if COVID-19 is a serious disease (β = -2.168; $p < 0.001$; 95% CI: -3.228, -1.108) and don't know if COVID-19 will finally be successfully controlled (β = -0.672; p = 0.007; 95% CI: -1.163, -0.181) were inversely associated with COVID-19 knowledge score. Female sex (β = 0.751; p = 0.006; 95% CI: 0.213, 1.289) was positively associated with COVID-19 knowledge score.

Discussion

To the best of our knowledge, this is the first study in Lebanon that assesses the KAP towards COVID-19 in children among parents. In general, participants in our survey had good general knowledge about the disease, its ways of transmission, and measures for prevention in children. The mean knowledge score was 11.28 ± 2.19 over 15.

The results revealed that the mean knowledge score was significantly lower among older (≥ 50 years) and single parents, who don't know if COVID-19 is a serious disease and if it will be finally successfully controlled. The mean knowledge score was higher among female parents.

The majority of parents had a positive attitude and good practices towards COVID-19 in children. In details, 69.7% agreed that COVID-19 will finally be successfully controlled and 59.9% thought that the pandemic will be controlled in Lebanon shortly, but 76.7% of them were worried about their child getting coronavirus. About 66.9% of parents expressed their willingness to vaccinate their kids when a vaccine would be available

for them. Concerning their practices, many parents indicated that they avoided crowded places (67.4%) and taught their children to wear a mask (78.8%), wash their hands (95.3%), maintain an appropriate distance between them and other people (91.1%), and avoid touching their eyes, nose, and mouth (92.5%). Furthermore, 66.2% of parents answered that they are sending or willing to send their children to the school or the nursery. It can be considered that parents have more protective attitudes and adhere to more protective behaviors because, in addition to self-protection, they are responsible for their families.

The overall correct rate for the knowledge test was 75.2%, which can be attributed to the fact that nearly 73% of the parents had a university degree, and this was comparable to studies done elsewhere. For example, in the Arab countries, correct knowledge was found to be at 81.64% in Saudi Arabia [27], 74.5% in Egypt [28], 70.3% in Jordan, and 63.25% in Kuwait [29]. In addition, correct knowledge was found to be at 90% in China [25], 80.5% in Malaysia [30], and 70.16% in South Korea [31]. The difference in correct knowledge rate can be attributed to the absence of a question about the MIS-C in other countries' KAP questionnaires. Most parents (70.9%) were unaware of this rare and uncommon condition in children infected with COVID-19.

In our study, women showed more COVID-19 awareness than men, which is different from what was reported in a previous study in Saudi Arabia [32], but consistent with studies conducted in Palestine [33], Iran [34], China [25], South Korea [31], and the United States [35]. Similarly, for other diseases like cancer, women showed better knowledge about the different characteristics of the health condition than men [36].

Our data showed that older parents (≥ 50 years) had less knowledge about transmission and the symptoms of COVID-19 in children. This observation can be explained by the fact that the older population has limited use of various social media channels, which are the primary source of information about COVID-19 in our study. The results are consistent with previous studies done in Egypt [28], Palestine [33], China [37], and incompatible with others done in Lebanon [38], and Saudi Arabia [27].

In our participants, the mean knowledge score was significantly lower among single parents. These results were based on a small sample size (17 single parents), but were similar to the results of a study done in three Middle Eastern countries (Jordan, Saudi Arabia, and Kuwait) in which divorced individuals had a lower knowledge score [29]. Also, in a study realized in Iran, being single was associated with a lower knowledge score [34].

Furthermore, a lower COVID-19 knowledge score was found to be significantly associated with a lack of knowledge about whether COVID-19 is a serious disease, and whether it can be controlled. These are some basic facts about the disease, known in its early stages. This shows the importance of working on parents' knowledge towards COVID-19 in children by health strategies which in turn, would improve their attitude and practices regarding COVID-19.

Concerning parents' attitude towards COVID-19 in children, the majority of them had a positive attitude towards the disease and the vaccine. And this was comparable to studies done in Palestine [33], Egypt [28], Saudi Arabia [27], and Iran [34].

About 67% of parents expressed their willingness to vaccinate their kids when a vaccine would be available for them. Similarly, in a study done in Lebanon about the willingness to pay for a coronavirus vaccine, 68.2% of adults were ready to do the vaccine if available [39]. This acceptability rate of the COVID-19 vaccine in children is comparable to a study done in Korea where 64.2% of parents intended to have their children vaccinated against COVID-19 [40]. Also, as found in a study done in Turkey about the willingness to accept the COVID-19 vaccine by healthcare professionals, having children was associated with an increased acceptance of the vaccine [41].

In comparison, a cross-sectional study done in Italy, found that 36.1% of families would not vaccinate their children [42]. The results of this study were consistent with ours, where 33,1% of parents reported that they would not vaccinate their children.

The desire to return to a normal life, the trust in sciences, and the fear of new outbreaks were the main reasons behind parents' willing to vaccinate their children. But, the reasons for children's vaccine resistance were centered on side effects, safety, and lack of vaccine effectiveness [43].

Also, parents adopted safe and good practices to protect themselves and their children against COVID-19. The same findings were reported by most of the studies done in countries around the world, where the governments imposed strict measures to control the spread of the virus [44–47]attitudes and practices (KAP.

About 66% of parents answered that they are sending or willing to send their children to the school or the nursery. This is consistent with a study assessing school hesitancy among parents, 84% of them were planning to send their children to school in fall 2021 [48].

There are several limitations to this study that should be considered. The main limitation was the use of a convenience sample (Snowball technique). Also, the surveying process, which excluded those who can't read and have access to the internet, generates a sample that may not represent all parents in Lebanon and may overestimate their knowledge level. Furthermore, this study did not use a validated instrument to measure the KAP of parents towards COVID-19 in children because, since that time, there was no reliable and validated instrument. In addition, because of the COVID-19 awareness done at this time, parents may have given socially desirable responses that are inconsistent with their actual practices towards COVID-19 in their children. Moreover, recall bias can be a result of self-reported data. Finally, a misclassification bias is likely to have occurred, such as when reporting the family income by the parent.

Despite these limitations, this study is believed to be the first in Lebanon to assess parents' KAP towards COVID-19 in children. Additionally, this study was conducted during a critical period of COVID-19 in Lebanon, when the vaccine was still unavailable for children under the age of 12. Also, the distribution of participants according to governorates was similar to the actual distribution of the population in Lebanon, where all the governorates were targeted with an overrepresentation of the Mount Lebanon governorate. The percentages of respondents' distribution were 10.7% in North Lebanon and Akkar governorates, 9.3% in Bekaa and Baalbeck-Hermel governorates, 7.9% in Nabatieh governorate, 9.6% in South Lebanon governorate, 54.3% in Mount Lebanon governorate, and 8.2% in Beirut governorate, in comparison with 22.07, 14.57, 7.9, 11.69, 34.50, and 9.27% respectively as mentioned in the statistical bulletin of the Ministry of Public Health 2019 [49].

Conclusions

To conclude, parents living in Lebanon participating in our study had good general knowledge, positive attitude, and effective practices towards COVID-19 in children. However, knowledge was lower among older and single parents, as well as those who lacked some basic facts about the disease's seriousness and control. More awareness should target those groups of parents, especially that the COVID-19 vaccine is still unavailable for use in children under 12 years in Lebanon, and that schools and nurseries reopened after a year and a half due to the pandemic. Nearly two-thirds of parents in our study reported their willingness to send their children to schools and nurseries, and to vaccinate them when a vaccine would be available. Schools and nurseries should take steps to slow the spread of COVID-19 among children and their families by maintaining good hygiene and ventilation in the classrooms, reducing the frequency of physical contact between students, and helping in their vaccination program.

Ethics approval

Participants' anonymity and autonomy were respected in the study. Ethical approval has been obtained from the Clinical and Epidemiological department. The participants had the option to participate and delay the submission of the completed form.

Consent to participate

Participants were informed that they were free to withdraw at any time, and that all information and opinions provided would be anonymous and confidential. Online informed consent was obtained before proceeding with the questionnaire.

Acknowledgements

Funding sources: this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

RS performed study, collected data, analyzed data and drafted the manuscript.
ZA, ME, NL reviewed the questionnaire, edited the manuscript and approved the final
version of the manuscript to be submitted.
RA designed study, analyzed data, reviewed and approved the final version of the manuscript to be submitted.

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Received on February 15, 2022. Accepted on December 27, 2022.

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How to cite this article: Saryeddine R, Ajrouch Z, El Ahmar M, Lahoud N, Ajrouche R. Parents' knowledge, attitude, and practices towards COVID-19 in children: A Lebanese cross-sectional study. J Prev Med Hyg 2022;63:E497-E512. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2521

Supplementary Tab. I. The correct answer rates of the COVID-19 knowledge questionnaire.

Variable	Frequency (n = 429)	%
K1. The main clinical symptoms of COVID-19 in children are fever, fatigue, dry cough, and myalgia		
Correct answer	298	69.5
Incorrect answer	131	30.5
K2. Unlike the common cold, stuffy nose, runny nose, and sneezing are less common in children infected with the COVID-19 virus		
Correct answer	231	53.8
Incorrect answer	198	46.2
K3. There currently is no effective cure for COVID-19, but early symptomatic and supportive treatment can help most children recover from the infection		
Correct answer	340	79.3
Incorrect answer	89	20.7
K4. Not all children with COVID-19 will develop to severe cases. Only those who have some medical conditions (asthma, diabetes, heart disease, obesity...) might be at increased risk of severe illness compared to other children		
Correct answer	342	79.7
Incorrect answer	87	20.3
K5. Eating or contacting wild animals (e.g., bats) would result in the infection by the COVID-19 virus in children		
Correct answer	104	24.2
Incorrect answer	325	75.8
K6. Persons with COVID-19 cannot infect the virus to others when a fever is not present		
Correct answer	350	81.6
Incorrect answer	79	18.4
K7. The COVID-19 virus spreads via respiratory droplets of infected individuals		
Correct answer	409	95.3
Incorrect answer	20	4.7
K8. Children aged 2 years and under should wear general medical masks to prevent the infection by the COVID-19 virus		
Correct answer	300	69.9
Incorrect answer	129	30.1
K9. Children aged 3-11 years should wear general medical masks to prevent the infection by the COVID-19 virus		
Correct answer	335	78.1
Incorrect answer	94	21.9
K10. Children aged 12 years and over should wear general medical masks to prevent the infection by the COVID-19 virus		
Correct answer	408	95.1
Incorrect answer	21	4.9
K11. It is not necessary for children and young adults to take measures to prevent the infection by the COVID-19 virus		
Correct answer	410	95.6
Incorrect answer	19	4.4
K12. To prevent the infection by COVID-19 in children, individuals should avoid going and taking their children to crowded places (> 10 people indoor, > 25 people outdoor) and avoid taking public transportations		
Correct answer	403	93.9
Incorrect answer	26	6.1
K13. Isolation and treatment of people (or children) who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus		
Correct answer	407	94.9
Incorrect answer	22	5.1
K14. Children who have contact with someone infected with the COVID-19 virus should be immediately isolated in a proper place. In general, the observation period is 14 days		
Correct answer	377	87.9
Incorrect answer	52	12.1
K15. Multisystem inflammatory syndrome (MIS-C) is a rare but serious medical condition associated with COVID-19 in children		
Correct answer	125	29.1
Incorrect answer	304	70.9

Supplementary Tab. II. Socio-demographic characteristics of parents according to COVID-19 knowledge score.

	Knowledge score		
	N = 429	Mean ± SD	P-value
Socio-demographic characteristics			
Sex			
Male	85	10.59 ± 2.75	**0.001** †*
Female	344	11.45 ± 2.00	
Age			
18-29	72	11.54 ± 2.34	0.166 ‡
30-39	186	11.06 ± 2.35	
40-49	118	11.55 ± 1.85	
≥ 50	53	11.07 ± 2.07	
Marital status			
Married	412	11.32 ± 2.12	0.168 §
Not married	17	10.18 ± 3.47	
Nationality			
Lebanese	422	11.28 ± 2.20	0.461 §
Other nationalities	7	11.14 ± 1.68	
Number of children			
1-2 children	286	11.23 ± 2.30	0.923 ¶
3-4 children	129	11.39 ± 1.87	
≥ 5 children	14	11.36 ± 2.7	
Number of children aged 4 or less			
0	206	11.34 ± 1.95	0.556 †
At least one child	223	11.22 ± 2.39	
Number of children aged between 5 and 11 years			
0	189	11.46 ± 2.17	0.130 †
At least one child	240	11.14 ± 2.21	
Number of children aged between 12 and 18 years			
0	269	11.15 ± 2.25	0.119 †
At least one child	160	11.49 ± 2.08	
Level of education			
High school's degree and below	118	11.08 ± 2.21	0.254 ‡
Bachelor's degree	173	11.48 ± 1.95	
Master's degree and above	138	11.19 ± 2.45	
Occupation			
Unemployed	147	11.25 ± 2.25	**0.002** ¶*
Student	10	12.1 ± 1.29	
Healthcare worker	53	12.04 ± 2.03	
Other occupations	219	11.08 ± 2.19	
Family income			
No current income	58	10.79 ± 2.35	0.294 ‡
< 675,000 LBP	22	11.82 ± 2.75	
675,000-1,999,000 LBP	132	11.36 ± 2.21	
2,000,000-3,999,000 LBP	123	11.41 ± 1.91	
> 4,000,000 LBP	94	11.18 ± 2.26	
Place of current residence			
Beirut governorate	35	10.91 ± 2.76	0.730 ‡
Mount-Lebanon governorate	233	11.35 ± 2.09	
South-Lebanon governorate	41	11.44 ± 2.05	
Bekaa + Baalbeck - Hermel governorates	40	11.10 ± 1.84	
Nabatieh governorate	34	10.94 ± 3.03	
North-Lebanon + Akkar governorates	46	11.46 ± 1.94	

SD: standard deviation; *: $p < 0.05$ is considered significant; †: T-Test; ‡: ANOVA; §: Mann-Whitney Test; ¶: Kruskal-Wallis Test.

Supplementary Tab. III. Medical history of parents and children according to COVID-19 knowledge score.

	Knowledge score		
	N = 429	Mean ± SD	P-value
Medical history of parents and children			
Smoking status of parents			
No	331	11.35 ± 2.07	0.240 †
Yes	98	11.05 ± 2.57	
Chronic diseases in parents			
No	359	11.28 ± 2.26	0.972 †
Yes	70	11.27 ± 1.85	
Type of chronic diseases in parents			
No chronic diseases	338	11.26 ± 2.27	0.762 ¶
Cardiac problems	13	11.54 ± 1.94	
Respiratory problems	3	12.33 ± 1.53	
Neurological problems	1	12 ± 0.00	
Diabetes	4	10.25 ± 1.26	
Allergies	23	11.09 ± 2.17	
Other diseases	22	11.73 ± 1.45	
More than 1 chronic disease	25	11.24 ± 2.03	
Chronic diseases in children			
No	391	11.28 ± 2.24	0.916 †
Yes	38	11.31 ± 1.71	
Type of chronic diseases in children			
No chronic diseases	379	11.27 ± 2.24	0.056 ¶
Cardiac problems	2	13 ± 0.00	
Respiratory problems	2	10 ± 0.00	
Diabetes	2	7.5 ± 3.53	
Allergies	29	11.55 ± 1.59	
Other diseases	10	10.9 ± 1.45	
More than 1 chronic disease	5	12.6 ± 1.14	

SD: standard deviation; *: $p < 0.05$ is considered significant; †: T-Test; ‡: ANOVA; §: Mann-Whitney Test; ¶: Kruskal-Wallis Test.

Supplementary Tab. IV. Parents' experience with the COVID-19 pandemic, their vaccination status according to COVID-19 knowledge score.

	Knowledge score		
	N = 429	Mean ± SD	P-value
Parents' experience with the COVID-19 pandemic and their vaccination status			
Were you ever in quarantine because of symptoms or because you were in close contact with someone tested positive for COVID-19 or because you returned from a country that had a large number of cases?			
No	191	11.08 ± 2.29	0.097 †
Yes	238	11.44 ± 2.10	
Have you tested positive with coronavirus using PCR or other tests?			
No	291	11.15 ± 2.3	0.078 †
Yes	138	11.55 ± 1.92	
Did any of your children experience any COVID-19 symptoms?			
No	323	11.14 ± 2.26	**0.027** †*
Yes	106	11.69 ± 1.93	
Have any of your children tested positive with coronavirus using PCR or other tests?			
No	378	11.24 ± 2.22	0.317 †
Yes	51	11.57 ± 1.94	
Did you receive one of the available vaccines for COVID-19?			
No	284	11.20 ± 2.30	0.319 †
Yes	145	11.43 ± 1.97	
Are you willing to receive one of the available vaccines for COVID-19?			
No	116	10.95 ± 2.51	0.127 ‡
Yes	180	11.33 ± 2.25	
I already received my vaccine	133	11.50 ± 1.75	

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Supplementary Tab. IV. Parents' experience with the COVID-19 pandemic, their vaccination status according to COVID-19 knowledge score.

	Knowledge score		
	N = 429	Mean ± SD	P-value
Did your partner receive one of the available vaccines for COVID-19?			
No	263	11.25 ± 2.09	0.515 ‡
Yes	155	11.38 ± 2.22	
I don't have a partner	11	10.64 ± 3.80	
Is your partner willing to receive one of the available vaccines for COVID-19?			
No	103	10.93 ± 2.45	0.332 ¶
Yes	181	11.43 ± 1.97	
I don't have a partner	11	10.64 ± 3.80	
My partner has already received his vaccine	134	11.39 ± 2.09	
Most used source of information regarding COVID-19			
Social media	128	11.05 ± 2.49	0.061 ‡
Google and search engines	48	11.87 ± 1.42	
Family, friends, neighbors	10	10.6 ± 2.22	
News channels	61	10.95 ± 2.46	
Ministry of health website	89	11.17 ± 2.16	
Scientific articles and research	93	11.68 ± 1.82	

SD: standard deviation; *: $p < 0.05$ is considered significant; †: T-Test; ‡: ANOVA; §: Mann-Whitney Test; ¶: Kruskal-Wallis Test.

Supplementary Tab. V. Parents' attitude and practices towards COVID-19 in children according to COVID-19 knowledge score.

	Knowledge score		
	N = 429	Mean ± SD	P-value
Parents 'attitude towards COVID-19 in children			
Do you agree that COVID-19 is a serious disease?			
Agree	366	11.45 ± 1.93	**0.014** ¶*
Disagree	47	10.70 ± 2.35	
I don't know	16	9 ± 4.76	
Are you worried about your child getting coronavirus?			
Yes	329	11.41 ± 2.08	**0.022** †*
No	100	10.84 ± 2.50	
Do you agree that COVID-19 will finally be successfully controlled?			
Agree	299	11.41 ± 2.18	0.063 ‡
Disagree	38	11.37 ± 2.12	
I don't know	92	10.80 ± 2.22	
Do you think that the pandemic will be controlled in Lebanon in the near future?			
Yes	257	11.27 ± 2.26	0.933 †
No	172	11.29 ± 2.09	
Do you think authorities should close educational centers (kindergartens, schools, and universities) to limit the spread of the disease?			
Yes	220	11.28 ± 2.23	0.984 †
No	209	11.28 ± 2.16	
Are you willing to vaccinate your kids when a vaccine will be available for them?			
Yes	287	11.42 ± 2.10	0.063 †
No	142	11.00 ± 2.36	
Parents 'practices towards COVID-19 in children			
In recent days, have you taken your children to any crowded place (> 10 people indoor, > 25 people outdoor)?			
Yes	140	10.97 ± 2.24	**0.043** †*
No	289	11.43 ± 2.16	
Have you asked your kids to wear a mask outside the house or when in presence with other people?			
Yes	338	11.36 ± 2.08	0.154 †
No	91	10.99 ± 2.54	

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Supplementary Tab. V. Parents' attitude and practices towards COVID-19 in children according to COVID-19 knowledge score.

	Knowledge score		
	N = 429	Mean ± SD	P-value
Do you teach your children to wash their hands with soap and water for 20 seconds frequently?			
Yes	409	11.27 ± 2.17	0.371 §
No	20	11.5 ± 2.66	
Do you teach your children to maintain an appropriate distance between them and other people?			
Yes	391	11.33 ± 2.09	0.094 †
No	38	10.71 ± 3.00	
Do you teach your children to avoid touching their eyes, nose and mouth?			
Yes	397	11.37 ± 2.13	**0.002** †*
No	32	10.12 ± 2.62	
Are you sending or willing to send your children to the school or to the nursery?			
Yes	284	11.29 ± 2.28	0.869 †
No	145	11.25 ± 2.02	

SD: standard deviation; *: $p < 0.05$ is considered significant; †: T-Test; ‡: ANOVA; §: Mann-Whitney Test; ¶: Kruskal-Wallis Test.

COVID-19

Childhood immunization coverage during the COVID-19 pandemic in the province of Siracusa, Italy

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Keywords

COVID-19 pandemic • Childhood immunization • Vaccine coverage • Vaccine-preventable diseases • Catch-up programmes

Summary

Introduction. *The COVID-19 pandemic has severely impacted routine immunization activities and a decline in vaccination coverage has been documented around the world. The aim of this study was to assess the impact of the direct and indirect effects of the COVID-19 pandemic on routine childhood vaccination coverage in the Province of Siracusa, Italy.*

Methods. *We compared 2020 and 2019 vaccination coverage by age group and vaccine type. Results were considered statistically significant at a two-tailed p-value ≤ 0.05.*

Results. *Our findings show that vaccination coverage rates for mandatory and recommended vaccinations decreased in 2020 compared with the previous year (range from -1.4% to -7.8%). Anti-rotavirus vaccination increased (+4.8%, as compared to 2019), while the reductions observed for polio vaccination (hexavalent) and human papillomavirus vaccination in males were not statistically significant. The reduction did not hit the population in the same manner, with the greater decreases observed for children aged > 24 months compared to the younger (-5.7% vs -2.2%) and for booster doses compared to the primary vaccinations (-6.4% vs -2.6%).*

Conclusions. *This study found that vaccination coverage of routine childhood immunisations was negatively affected during the COVID-19 pandemic in the Province of Siracusa. It is of huge importance to put in place some catch-up programs to ensure vaccinations at the earliest of individuals who missed immunization during the pandemic.*

Introduction

Childhood vaccination is one of the most important public health achievements in history and a cornerstone for the prevention of communicable infectious diseases. Routine immunizations of pregnant women, adults, elderly persons, patients with chronic conditions and higher risk, are also essential [1-5].

Although the direct health impact of the COVID-19 pandemic, caused by the new SARS-CoV-2 virus, on child health is generally low [6], the true impact on the paediatric population may lie in its indirect health impacts. The COVID-19 pandemic has severely impacted routine immunization activities and a decline in vaccination coverage has been documented around the world, regardless the economic status of the countries, rich and poor, developed and developing [7-9]. More than half of the countries in which data were available have reported moderate to severe disruptions, or total suspension of vaccination services during March-April 2020. Several countries postponed immunization campaigns in the first five months of the pandemic, including: measles vaccine, polio vaccine, meningococcal conjugated A vaccine, yellow fever vaccine, typhoid vaccine, cholera vaccine and tetanus-diphtheria vaccine [7-9]. According to WHO data, during the pandemic, global vaccine coverage (VC) has dropped from 86% in 2019 to 83% in 2020; an estimated of 23 million children under the age of one year did not receive basic vaccines, which is the highest number since 2009; the number of completely unvaccinated children increased by 3.4 million in 2020; only 19 vaccine introductions were reported in 2020, less than half of any year in the past two decades; 1.6 million more girls were not fully protected against human papillomavirus (HPV) in 2020, compared to the previous year [10, 11]. Immunization coverage has dropped also among adults [12]. The re-organization of health services on one hand, including the shift of health personnel to deal with increasing numbers of COVID-19 patients; the public health measures to mitigate the epidemic and the fear of contracting the infection on the other hand, have led to interrupt, delay and replan of a large number of vaccinations [13].

When immunization programs are stopped or interrupted for any reason, we may observe an increasing number of vaccine-preventable infections and related deaths, because of an increase in susceptible individuals to diseases that were controlled or even eliminated. Specifically, maternal and child health could be most affected by this problem, and this situation will represent a particular threat for low- and middle-income Countries for battling the pandemic alongside pre-existing challenges, including efforts to control vaccine-preventable diseases (VPDs) [14-16].

For this reason, interim guidelines warning about the risk of VPD outbreaks have been published, which could cause further pressure on health services [17-20].

Italy was the first country outside China to experience the impact of the COVID-19 pandemic and one of the worst-affected countries in the first months of the pandemic. The first case of SARS-CoV-2 infection was reported on 20 February and the disease quickly spread across the north of the country [21]. Italy adopted a generalized lockdown on March 12 and gradually resumed all activities from May 4 to June 15 [22].

The Italian vaccination policy provides for the following 10 mandatory routine immunisations for children aged 0-16: poliovirus, diphtheria, tetanus, hepatitis B, pertussis, *Haemophilus influenzae* type b, measles, rubella, mumps, and chicken pox (the anti-varicella – chicken pox – vaccine is mandatory only for children born from 2017 onwards). Furthermore, the vaccinations against human papillomavirus (HPV), meningococcus serotype B (Men B) and serotypes A, C, W135, Y (Men ACW135Y) are recommended in children and in adolescents, as well as herpes zoster and pneumococcus (PNC) for the population over 65 years [23, 24]. These vaccinations are offered actively and free of charge by the Italian National Health Service.

In this study, we aimed to assess the impact of the direct and indirect effects of the COVID-19 pandemic on routine childhood vaccine coverage in the Province of Siracusa, an area with 386,071 inhabitants situated in south-east of Sicily, Italy, according to different birth cohorts and vaccine types.

Material and methods

Vaccination coverage data were extracted from the official records of Epidemiology Unit of the Health Department of Provincial Health Authority of Siracusa, that routinely collects data on all administered vaccines. To estimate changes in vaccine coverage, we calculated absolute differences between 2019 and 2020 coverage rates.

We used the birth cohorts, population, target age group, number of doses and year of administration as showed in Table I. We used polio and measles vaccination as the usual proxy for the hexavalent (polio, diphtheria, tetanus, hepatitis B, pertussis, *Haemophilus influenzae* type b) and quadrivalent (measles, rubella, mumps and chicken pox) or trivalent (measles, rubella, mumps) vaccinations, respectively, since these vaccines are administered in six-in-one and four-in-one or three-in-one vaccine formulations in Italy. Data are reported for birth cohort and a complete vaccination cycle, regardless of the schedule adopted and the vaccine type administered. As for polio, measles, men B, men ACW135Y and PNC vaccination, we used the available data at 24 months of age (even though these vaccines are administered with different timing in the first two years of life according to Italian immunization) comparing vaccine coverage rates for the years 2019 (administered from January to December 2019 to the 2017 cohort) and 2020 (administered from January to December 2020 to the 2018 cohort).

Polio with diphtheria, tetanus, pertussis and measles with rubella, mumps (and chicken pox, not mandatory for children born before the 2017) vaccinations are boosted at 6, mandatorily. We used data on polio and measles vaccinations in 2020 (VC 2020) to the 2013 cohort (7 years old), as well as data on vaccinations administered through the year 2019 (VC 2019) to the 2012 cohorts (7 years old).

Vaccination against rotavirus is administered in the first year of life, therefore we compared vaccine coverage rates at the 12-month timepoint (VC 2019 for the 2018 cohort and VC 2020 for the 2019 cohort). Regarding anti-HPV vaccination, we used the full-cycle coverage for 14-year-old (2005 cohort in 2019, 2006 cohort in 2020) since it is offered during the 12th year of life.

We performed a statistical analysis at 12 months (for rotavirus vaccination; cohort 2018 and 2019) and 24 months (polio, measles, men B, men ACW135Y/men C vaccinations; cohort 2017 and 2018), 7 years (polio and measles booster doses; cohort 2012 and 2013) and 13 years (HPV; cohort 2006 and 2007) for mandatory and recommended vaccinations. The Chi-square test was executed on proportions for the years 2020 vs. 2019.

Analysis findings were considered statistically significant at a two-tailed p-value ≤ 0.05.

Results

The 2019 and 2020 level of vaccine coverage rates for mandatory and recommended vaccinations are reported in Table II and in Table III respectively. For each vaccine-preventable disease, cohort and year of administration, we reported the vaccine coverage, the number of vaccinated (in the numerator, extracted from official records of Epidemiology Unit) and the eligible population (in the denominator, according to Istat data, Italian National Statistical Institute).

With reference to the mandatory childhood immunisations, in 2020, 24-month coverage rates were 86.7% for polio (hexavalent vaccine), 87.2% for measles (quadrivalent vaccine), representing -1.4% (not statistically significant) and -3.8% decreases, respectively, as compared to 2019. By 7 years of age (booster doses), immunisation coverage was 77.3% for polio and 77.1% for measles, representing a -7.8% and -5.0%, respectively, compared to 2019 (Tab. II).

With reference to the recommended childhood immunisations, in 2020, 24-month coverage was 54.0% for Men B (-4.6% as compared to 2019), 61.7% for Men ACW135Y/C (-5.6% as compared to 2019), 83.5% for PNC vaccine (-2.4%, as compared to 2019), and 45.0% for rotavirus (+4.8%, as compared to 2019). Regarding HPV vaccination, in 2020, overall coverage was 41.7% (-4.3% compared to 2019), in female was 51.3% (-4.8%) and in male was 33.0% (-3.4%) (Tab. III).

Interestingly, we observed a significant increase for rotavirus vaccinations in 2020 compared to 2019 (+5.4%).

Tab. I. VDP, birth cohort, population, target group, number of doses and year of administration of vaccinations to assess the vaccine coverage.

VDP	Mandatory/ Recommended	Birth cohort	Eligible population§	Target age group	Number of doses	Year of vaccine administration (1st January - 31st December)
Rotavirus	Recommended	2018	3090	12 months	2*	2019
		2019	2989			2020
Polio, Measles, Men B, Men ACW135Y/Men C	Mandatory	2017	3155	24 months	3 for polio and 3 (or 4) for Men B; 1 for measles and Men ACW135Y/C	2019
	Recommended	2018	3090			2020
Polio, Measles	Mandatory	2012	3605	7 years	4 for polio; 2 for measles	2019
		2013	3408			2020
HPV	Recommended	2005	3909	14 years	2	2019
		2006	3890			2020

§ Data from www.demoistat.it. * The vaccination course of the vaccine used in the Province of Siracusa consists of two doses. VPD: vaccine-preventable disease. Men B, ACW135Y and C: *Neisseria meningitidis* serogroups B, ACW135Y and C; PNC: *Streptococcus pneumoniae*; HPV: human papillomavirus.

Tab. II. Vaccine coverage (VC) rates (%) registered for mandatory vaccinations, at 24 months and 7 years of age, stratified by vaccine type and year of administration, along.

With the percentage differences between the 2019 and 2020 rates in the Province of Siracusa.

Target age group	VDP	VC Rates (%) by Year of Vaccine Administration		% Difference (2020 *vs* 2019)	*p*-Value *
		2019	2020		
24 months	Polio	88.05 (2778/3155)	86.70 (2679/3090)	-1.4	0.11
	Measles	90.94 (2869/3155)	87.15 (2693/3090)	-3.8	< 0.001
7 years	Polio	85.10 (3068/3605)	77.26 (2633/3408)	-7.8	< 0.001
	Measles	82.14 (2961/3605)	77.11 (2628/3408)	-5.0	< 0.001

* Chi-square test (2020 vs 2019); VC: vaccination coverage; VPD: vaccine-preventable disease.

Tab. III. Vaccine coverage (VC) rates (%) registered for recommended vaccinations at 12 months, 24 months. and 14 years of age, stratified by vaccine type and year of administration, along with the percentage differences between the 2019 and 2020 rates in in the Province of Siracusa.

Target age group	VDP	VC Rates (%) by Year of Vaccine Administration		% Difference (2020 *vs* 2019)	*p*-Value *
		2019	2020		
12 months	Rotavirus	40.23 (1243/3134)	45.00 (1345/2988)	+4.8	< 0.001
24 months	Men B	58.61 (1849/3155)	54.01 (1669/3090)	-4.6	< 0.001
	Men ACW135Y Men C	67.29 (2123/3155)	61.68 (1906/3090)	-5.6	< 0.001
	PNC	85.86 (2709/3155)	83.50 (2580/3090)	-2.4	< 0.001
14 years	HPV	45.95 (1796/3909)	41.67 (1621/3890)	-4.3	< 0.001
	HPV females	56.12 (1059/1887)	51.30 (945/1842)	-4.8	< 0.01
	HPV (males)	36.45 (737/2022)	33.01 (676/2048)	-3.4	< 0.05

* Chi-square test (2020 *vs* 2019); Men B, ACW135Y and C: *Neisseria meningitidis* serogroups B, ACW135Y and C; PNC: *Streptococcus pneumoniae*; HPV: human papillomavirus; VC: vaccine coveragevaccination coverage; VPD: vaccine-preventable disease.

Discussion

Vaccine coverage of routine childhood immunisations was negatively affected during the COVID-19 pandemic in the Province of Siracusa. The reduction did not hit the population in the same manner, with the greater decreases observed for children aged > 24 months compared to the younger (-5.7% vs -2.2%) and for booster doses compared to the primary vaccinations (-6.4% vs -2.6%). Moreover, our data show that vaccine coverage rates for mandatory vaccinations decreased in 2020 compared with the previous year (range from -1.4 % to -7.8%), while recommended vaccinations ranged from +4.8% to -5.6%. Since the introduction of compulsory vaccination in 2017, the vaccine coverage progressively increased in Italy [25-27]. Nevertheless, during the pandemic, a significant drop in vaccinations coverage was observed [28-31]. According to a survey launched by the Ministry of Health, vaccination activity has slowed down throughout Italy, even if with regional differences [32-34]. The relocation of health personnel involved in this service to support the management of the pandemic is the most important reason for this slowdown (more than 33% throughout the national territory). In addition to this, about one out of four vaccination centres has recorded a reduction or even a suspension of vaccination activities because of the measures of social isolation and distancing. According to the survey, the reduction in vaccinations did not affect the entire population in the same manner, but mainly concerned the pediatric group aged > 1 year, to a lesser extent the adult population, because a priority was given to the basic courses and to the most susceptible groups during the emergency context. Above all, the immunization with the greatest decline in coverage rate among the pediatric population was that against HPV. To a lesser extent, a decrease was also observed for DTaP (polio booster dose) and men B immunizations.

A decline in immunizations could endanger the 90-95% vaccination coverage target that is necessary for herd immunity against diseases such as measles, mumps, and whooping cough. In such circumstances, an increased risk of resurgence of vaccine-preventable diseases that were controlled or eliminated in children who missed vaccinations during the pandemic is expected, thereby posing a twofold challenge to public health systems, with possible dramatic effects especially in the LMCI's countries [14, 35].

Despite a decrease in vaccine coverage rates, we did not register an increase in vaccine-preventable disease outbreaks in the Province of Siracusa in 2020. In the year 2020, 1 case of measles was reported compared to 3 cases in 2019; 6 cases of chicken pox in 2020 to 17 cases in 2019; no case of meningococcal and pneumococcal infection in 2020 vs 2 cases in 2019. Probably, at least in the short-term, the impact of the pandemic on possible vaccine-preventable disease outbreaks have been balanced by public health measures (personal protective equipment, hand hygiene, quarantine/isolation, physical distancing), which likely prevented the spread of other respiratory diseases as well. Similar data have registered in the rest of Italy, where no increase in outbreaks due to vaccine-preventable diseases has recorded [30, 36, 37]. Other countries reported a slight reduction in vaccine-preventable diseases rates [38-40].

Several factors are associated with the reduction in vaccine coverage in the Province of Siracusa, as the same in the rest of the world: public actions to contain the spread of infection (lockdown, isolation, quarantine and other infection control measures), relocation oh health personnel involved in vaccination activity to deal with the pandemic, and also parental concerns about potentially exposing their children to COVID-19 during well child visits [41-43].

Measure to prevent the spread of infections have been implemented in all vaccination centres of Provincial Agency of Health of Siracusa: physical distancing, environmental sanitation, room ventilation, wearing of the face masks, hand hygiene, telephone appointment, detection of body temperature, different time slots to increase availability, optimisation of spaces dedicated to vaccine administration and active search for new locations.

Our findings demonstrate that an attempt was correctly made to give priority to the infants and to primary cycles. As matter of fact, our data show that the effect of pandemic on vaccine coverage was less pronounced in infants compared to toddlers, since the medical staff of the vaccination centres of the local health authority of Siracusa prioritized age group over another within the childhood vaccinations with active call for these categories of patients.

Consistent with national data, we found an increase of vaccine coverage of anti-rotavirus vaccination [27, 30]. We hypothesize that this finding may be explained, at least in part, by the greater attention given to the infants, as mentioned above, and the fear of exposing children to the possible consequence of rotavirus infection, such as severe dehydration and hospitalization, in a critical period for the healthcare facilities.

The WHO recommends that all routine vaccinations be administered as scheduled, even during the COVID-19 pandemic. Routine immunization sessions should continue, using special measures and precautions, to the extent possible and as permitted within the local COVID-19 response context. This includes routine immunization for infants, children, adolescents, pregnant women, high-risk groups, and adult healthcare providers [44, 45]. Any interrupted immunization services should be resumed, and catch-up vaccinations offered as quickly as possible [46, 47].

Our findings are consistent with other available reports in Italy during the pandemic [30, 32], in which we observe similar outcomes for almost all vaccine coverage rates differences, even if with different magnitude, except for HPV vaccination among males and Men ACW135Y. Our data are also consistent with data reported for Sicily, that show similar trends in vaccine coverage rates reduction [27].

The main strength of our study is first its originality since, to the best of our knowledge, it is the only study

that assess the impact of COVID-19 pandemic on vaccine coverage at local level in Italy. In our opinion, this is very useful to better understand the reasons for the reduction in vaccine coverage in a specific local context and above all to establish tailored catch-up programs for missed vaccinations more effectively. The local data can also allow to evaluate the actual staff of the vaccination services, that even before the pandemic, were not rarely understaffed, and lacking in some skills, such an effective communication to a wider public in the complex environment surrounding vaccinations [48]. Increasing society complexity is presenting new challenges for vaccines, including vaccine hesitancy and misinformation of vaccine safety and effectiveness in the mainstream media and social media, which require specific skills. National policies that aim at halting the circulation of false information about vaccines on social media are welcome, but also solutions to improve the communication strategy locally are extremely important [49, 50].

Conversely, several limitations that merits discussion were detected in our study. To begin with, evaluating the vaccine coverage at 24 months, we did not analyse the potential delay in the administration of some vaccines, such as hexavalent or quadrivalent, which should be administered within the first year of life or at the beginning of the second year of life, respectively, according to the immunization calendar. Second, social determinants such level of the education, family income, social isolation, geographic location or ethnic minorities, were not evaluated due to insufficient data availability [51]. It is likely the COVID-19 pandemic has exacerbated the adverse effects of some social determinants on vaccination uptake behaviours *e.g.*, employment, poverty, healthcare access, food insecurity, education, etc. It's well known that these determinants are associated, among other things, with lower vaccine coverage rates [51, 52]. Third, vaccine hesitancy is one of the top threats to public health and while it is as old as vaccination itself, the nature of the challenge continues to shift with the social landscape [53]. Today, in the era of COVID-19, vaccine hesitancy and the "infodemic" it fuels are key drivers of under-vaccination across the globe [54-57]. In this study vaccine hesitancy has not been investigated.

Conclusion

Childhood vaccination remains paramount: all children should receive all scheduled vaccinations according to their age, with priority given for completion of all primary series vaccines, with no interruption of scheduled sessions [58]. Timely vaccination is key to maintaining population immunity against vaccine-preventable diseases, ensuring populations are fully protected against life-threatening illnesses as early as possible, and preventing large outbreaks of vaccine-preventable diseases, particularly for diseases such as measles for which a high coverage is required to prevent outbreaks.

It is vital to put in place a catch-up vaccination strategy to ensure vaccinations at the earliest of individuals who missed immunization during the pandemic, also with the involvement of primary care pediatricians in the direct administration of vaccination, going beyond any disparities in access driven by any social determinants, like education, income, ethnicity, location, social networks.

Our findings indicate that vaccine coverage of routine childhood immunisations was negatively affected during the COVID-19 pandemic in the Province of Siracusa, similar to what has been noted nationally and in other countries. Three mandatory and four recommended pediatric vaccinations slowed down during the epidemic waves in 2020; one mandatory vaccination and one recommended vaccination remain unchanged; lastly, one recommended vaccination increased significantly. These data are consistent with other available reports in Italy.

Further research is needed to follow-up the evolution of the vaccine coverage of the cohorts under investigation and the possible implications on spread of vaccine-preventable diseases.

Acknowledgements

The authors would like to thank all the health professionals involved in the routine immunisation activities in the Province of Siracusa.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

FC: conceptualization, methodology, statistical analysis, writing and original draft preparation.
FC, EDP, CR: acquisition of data.
FC, FB, EDP, MLC: formal analysis and interpretation of data.
FC, FB: writing, review and editing.
FC, EDP, MLC: supervision and project administration.
All authors have read and agreed to the submitted version of the manuscript.

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Received on April 24, 2022. Accepted on November 30, 2022.

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How to cite this article: Contarino F, Di Pietro E, Bella F, Randazzo C, Contrino ML. Childhood immunization coverage during the COVID-19 pandemic in the province of Siracusa, Italy. J Prev Med Hyg 2022;63:E513-E519. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2587

COVID-19

Role of the 1st booster dose of COVID-19 vaccine in the protection against the infection: A fundamental public health tool

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Keywords

COVID-19 infection • COVID-19 Vaccination • Booster dose • Seroprevalence • Prevention

Summary

Introduction. *The COVID-19 pandemic is having a huge impact on human health with high morbidity and mortality rates worldwide. Healthcare Workers (HCWs) are one of the most at risk categories to contract the infection. Effective anti-COVID-19 vaccines were approved in a very short time. Making the 1st booster dose is essential to induce a good protection against the infection.*
Methods. *We conducted a retrospective sero-epidemiological survey of already existing data concerning the antibody response of a HCWs sample vaccinated with the primary cycle and the 1st booster dose of the Pfizer-BioNTech COVID-19 mRNA vaccine and, specifically, after three weeks from the third dose of vaccination.*
Results. *In our analysis, after the primary cycle, a 95.15% efficacy was detected. Among the non-responders, women were significantly more frequent (69.56%). Moreover, we found a significant reverse correlation between the immune response and the age of the sample, especially in women. However, the 1st booster dose completely cancelled these differences.*
Conclusions. *Our data are perfectly in line with what has been declared by the conducted studies in terms of efficacy. However, it is important to highlight that people with only the primary cycle are at high risk to contract the COVID-19 infection. Therefore, it is necessary to not consider people vaccinated with the primary cycle completely risk-free and to stress the importance to perform the 1st booster dose.*

Introduction

The COVID-19 (Coronavirus Disease-19) pandemic with its huge impact on human health in terms of morbidity and mortality and on the environmental issues, shocked the community and gave a huge boost to the scientific research worldwide [1, 2]. The cause of this pandemic is the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), a new member of Coronavirus family (CoVs), responsible for high-risks pathological respiratory diseases [3]. This virus is surrounded by an external envelope containing a glycoprotein, called "spike" or "S" protein, forming spicules that allows it to recognize the cellular target [4].
Vaccination is undoubtedly one of the most effective preventive measures towards infectious diseases [5]. Traditionally, it takes between 4 to 15 years to develop a safe, efficacious, and cost-effective human vaccine. In comparison to these times, COVID-19 vaccine development has progressed at an unprecedented rate. On January 11, 2020, less than a month after the first documented cases in Wuhan, the complete viral genome sequence of SARS-CoV-2 was obtained [6]. Due to this crucial information, several laboratories and biotechnology companies globally have tried to produce an effective SARS-CoV-2 vaccine. Due to the knowledge obtained from previous vaccine development efforts against SARS and MERS, the initial step of target identification was remarkably facilitated as, for both SARS-CoV and MERS-CoV, the S protein had been demonstrated as the dominant antigen responsible for the production of neutralizing antibodies and an important target of protective T cell responses [7]. Several vaccine candidates for SARS-CoV-2 were then planned rapidly using the SARS-CoV-2 S protein as the primary immunogen.
mRNA vaccines are a new platform consisting of an mRNA, including a 5′ cap, regulatory elements in the 5′ and/or 3′ regions, a poly(A) tail, and modified nucleosides to increase RNA stability, that is elaborated to encode specific viral antigens and delivered by polymer-based or lipid nanoparticles [8]. Once entered into the cell cytoplasm, the mRNA is translated by ribosomes as an endogenous mRNA, with production of the antigen that is presented to the immune system. Two mRNA vaccines, Pfizer/BioNtech's BNT162b2 and Moderna/NIAID's mRNA-1273, received the Emergency Use Authorization (EUA) status from the U.S. Food and Drug Administration (FDA) and other countries [9, 10] among which that from the European Medicines Agency (EMA) for the European Union (EU) [11, 12]. Specifically, BNT162b2 is an mRNA-lipid

https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2742

nanoparticle-formulated vaccine encoding a membrane-bound, stabilized form of the full-length SARS-CoV-2 S protein [13]. mRNA-1273 encodes a prefusion stabilized form of the SARS-CoV-2 S protein and is delivered by lipid-encapsulated nanoparticles [14].

In natural infection, seroconversion for SARS-CoV-2 was described to occur 7–14 days after the onset of symptomatology, 100% within 19 days after clinical onset [15]. Several serologic investigations suggest that, in affected areas, SARS-CoV-2 infection has been acquired by a much higher number of persons compared to the number of infected people resulted positive to PCR analysis of nasopharyngeal swab specimens [15, 16].

In Italy, at 28 September 2022, from the beginning of the outbreak 22,567,577 cases were reported with a median age of 43 years and 173,368 deaths [17]. The vaccination campaign in Italy began on December 27, 2020. As of 28 September 2022, a total of 140,732,854 doses were administered (47,320,682 first doses, 49,975,928 second/single doses, 40,152,811 third doses). COVID-19 infection can be a problem especially for vulnerable and/or particularly at risk people such as people affected by comorbidities, obesity and pregnant women [18-20]. Among people particularly at risk to contract the infection, Healthcare Workers (HCWs) are surely one of the most exposed category. A meta-analysis assessed that the overall proportion of HCWs testing positive for SARS-CoV-2 was 8.7% among all enrolled subjects. Moreover, it has been reported that the values of seroprevalence among HCWs ranges from 0% to 45.3% [21]. These remarkable differences could be explained by different settings, observation period, and government strategies adopted with the aim of reducing viral transmission (e.g., lockdown, quarantine measures, etc.) [22]. In Italy, during the first wave of the infection, 421,521 (1.85% of the total reported cases) HCWs, of which 70.3% women and 29.7% men, with a median age of 47 years, have been reported to be infected since the beginning of the pandemic. In this category, 328 (0.2%) deaths were reported of which 226 (68.9%) were men and 102 (31.1%) were women with lethality rates of 0.6% and 0.1% in the two sexes respectively [23].

The purpose of this study was to evaluate the seroconversion rate of a population of HCWs vaccinated with the primary cycle and the 1st booster doses of COVID-19 mRNA vaccine, highlighting the role of the booster and the individual variables in the antibody response elicited by the vaccine.

Methods

Data collection

The sample was made up by HCWs of the Messina University Hospital "G. Martino", Italy, to whom the primary cycle and the 1st booster of BNT162b2 COVID-19 mRNA vaccine (Pfizer/Biontech) were administered. As exclusion criterion, a previous COVID-19 infection was considered. Therefore, people that stated to have contracted the infection and/or already underwent only a single dose of vaccine were excluded. Aiming to evaluate the efficacy of the vaccination cycle, we carried out a survey, in the period April-May 2022, evaluating the antibody response rate of the HCWs three weeks after the administration of the second dose of vaccine and three weeks after the administration of the 1st booster dose. To this aim, after obtaining the informed consent of all the participants including all the information about the study, we collected blood samples that were centrifuged at 4,000 rpm for 10 minutes and a CLIA (ChemiLuminescence ImmunoAssay) test (LIAISON SARS-CoV-2 S1/S2 IgG - DIASORIN S.p.A., Saluggia, Italia), consisting in a quantitative assay for the detection of IgG antibodies against S1/S2 antigens of SARS-CoV-2, was used. Specifically, values < 12 AU/ml were considered negative. The results were correlated with the individual variables (age and gender) to evaluate their potential role played influenced the immune response.

Statistical analyses

Descriptive statistics were used to find the percentages. Correlations were determined using the standard Pearson correlation coefficient. Significance was assessed at the $p < 0.05$ levels. All analyses were performed using Prism 4.0 software.

Results

The characteristics of the sample, concerning the total number of people, their gender, occupation and hospital areas, are shown in Table I.

The immune response to the primary vaccination cycle was 95.15% with a mean antibody response of 214.62 AU/mL (min 3.8; max ≥ 400). Dividing according the gender, the mean antibody response was 224.53 AU/mL (min 3.8; max ≥ 400) in men and 205.27 AU/mL (min 3.8; max ≥ 400) in women. To the 1st booster does the immune response was 100% (68.75% of the sample reached the maximum value ≥ 400) with a mean antibody response of 352.21 (min. 251; max ≥ 400).

According to the antibody titre of the primary cycle, we divided the sample in four groups, specifically <12 = no response, 12-99 = low response, 100-299 = intermediate response and > 300 = high response, in order to better characterised the different responses to the vaccine evaluating for each group the role played by some individual variables such as age and gender (Fig. 1).

The figure shows that 4.85% of the sample was negative to the antibody search. Among these negative people, women were significantly more frequent than men with percentages of 69.56% and 30.44% respectively ($P < 0.05$). In general, about these non-responder people, the mean age was 46.26 ± 10.81, specifically 51.43 ± 11.59 in men and 44.88 ± 9.61 in women. Moreover, 78.48% of the entire sample shows an intermediate-high response, with an average age of 46.76 ± 12.62. Specifically, 61.29% were women and 38.71% were men, with a mean age of 46.33 ± 12.58 and

Tab. I. Personal details and features of the sample.

Total sample 480		
	Men	**Women**
Absolute Number (%)	286 (59.58%)	194 (40.42%)
Average Age (±SD)	45.97 ± 12.39 (min 25; max 67)	48.01 ± 12.01(min 25; max 67)
Occupation (%)		
	Physicians	39.23%
	Nurses	36.92%
	Technicians	6.15%
	Administrative personnel	4.62%
	Biologists	3.08%
	Pharmacists	3.08%
	Others	2.31%
Hospital areas (%)		
	Medical	36.93%
	Surgical	19.32%
	Emergency	9.09%
	Services	34.66%

Fig. 1. Statistical correlation between the immune response and the age of the sample.

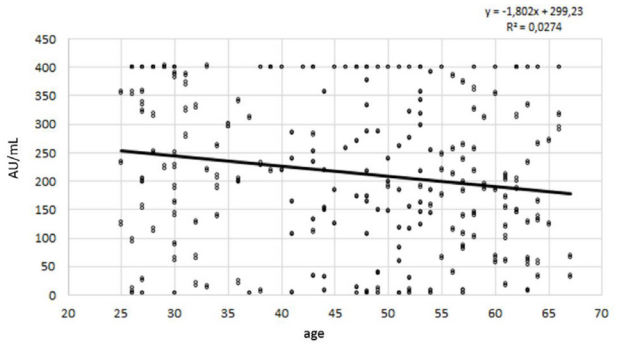
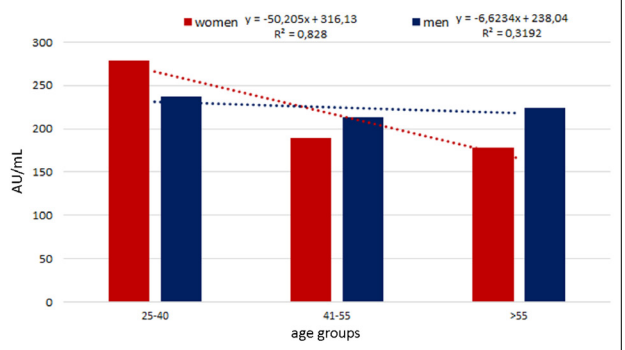


Fig. 2. Different antibody response according to gender and age groups.



47.44 ± 12.66 years, respectively. For the three groups of responders, there were no significant statistical differences by gender and age.

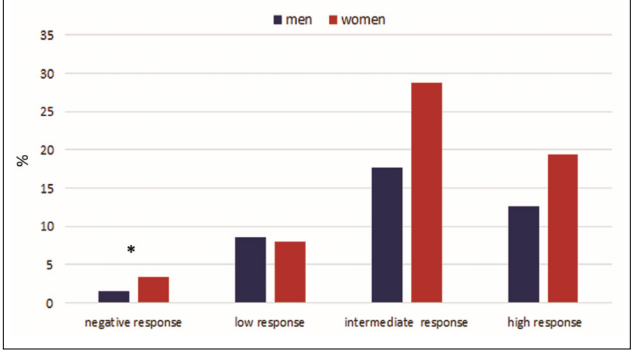
A significant reverse correlation ($P < 0.05$) was found between the immune response and the age of the sample (Fig. 2).

No correlation was found between immune response and gender. However, dividing according the gender, this significance was found only for the women group (Fig. 3).

As shown by the figure, an important percentage decrease (35.97) was found in the immune response between the youngest and oldest women while in men such percentage decrease was 5.59. Moreover, among men, a slight percentage increase (4.74%) was found in the oldest compared to the second group.

In the first age group the immune response was higher in the women with a percentage increase of 17.78 compared to men. An opposite result was found in the others two age groups in which the response was higher

Fig. 3. Percentage results of antibody response levels divided per gender.



in men with a percentage increase of 11.39 and 20.12 in the two age groups respectively.

No statistical correlation between the individual

variables and the immune response was observed after the 1st booster dose.

Discussion

HCWs are surely one of the most important categories at risk to contract COVID-19 [24, 25] and infections in general due to the exposure with potential infected people during their working activity [26, 27]. For this reason, according to the current Italian National Vaccination Plan, it is important to protect these at high risk people with the active offer of some strongly recommended vaccinations [28]. This issue applies also and above all concerning the COVID-19 infection. According to a recent meta-analysis of studies evaluating the positivity of SARS-CoV-2 antibodies on HCWs after natural infection, an overall result of 8.7%, ranging from 0% to 45.3%, was found [21].

Indeed, the occurrence of nosocomial transmission of SARS-CoV-2 has been reported, highlighting the necessity for HCWs of a strict adherence to infection control measures in order to protect themselves and avoid the transmission to inpatients and the onset of nosocomial outbreaks [29]. In this light, vaccination is undoubtedly the cornerstone of the control measures. Data from phase 3 clinical trials showed a 95% efficacy for the prevention of the infection at 7 days after the second dose of the BNT162b2 vaccine [30].

Unfortunately, vaccine hesitancy is an attitude more and more present in general population, linked to several wrong beliefs about vaccines among which fear of potential side effects and lack of trust towards health providers are the most declared [31]. This attitude is even present among HCWs, as showed by previous studies [32]. However, some reviews reported in this category a high rate of acceptance of COVID-19 vaccination [33, 34].

In our study, the antibody response of HCWs to vaccine was closely similar to that reported for general population [17]. After primary cycle, a significant correlation was found between the immune response and age especially in women. Specifically, the response decreased with the increasing of the age suggesting the important role played by the physiological process of immunosenescence [35]. The immune changes linked to the senescence explain the higher severity of some viral and bacterial infections (e.g., influenza, herpes zoster, pneumococcal disease) among elderly compared to younger individuals, and of the onset of more acute and long-term sequelae [36]. Moreover, in this category of people, vaccine responses are often lower and frequently failing to induce long-term immunity, placing these individuals at risk for subsequent disease [37]. These findings in elderly people have been largely linked to the failure of the adaptive immune response. Specifically, in elderly a lower antibody response is elicited by diphtheria [38], hepatitis A [39], Hepatitis B [40] and pneumococcal polysaccharide (PPV23) [41] vaccinations.

However, this result was more marked in women compared to men and this could be explained by the presence, in aged women, of some variables influencing negatively the antibody response. Particularly, it has long been proven that, in women, menopause could negatively impact on the immune system and the response to vaccination. Previous evidences showed that in postmenopausal and with surgical menopause women, a reduced number of total lymphocytes, mainly B and CD4+ T lymphocytes, is present and that the CD4+/CD8+ ratio and the numbers of circulating B cells are decreasing, while NK cells are increasing [42]. These changes in immune system could explain the difference found between genders in our study. On the contrary, in younger group, the response was higher in women compared to men. This result can be explained by the difference existing between sexes in the antibody production. It has been reported that females produce more elevated circulating levels of antibodies than males following the positive influence exerted on the humoral immune responses by estrogens [43, 44]. On the other hand, androgens play a very important role in modulating negatively the immune responses by affecting both the innate and the adaptive immune system (immunosuppressive action) [45]. These hormonal differences can account for the discrepancies between females and males found on the onset of different kind of diseases among which autoimmune diseases, but also in response to infectious diseases and vaccination [46].

It is important to emphasize that the 1st booster dose completely annulled the amount of non-responders to the primary cycle even if no statistical correlation was found between individual variables and immune response probably because the majority of the sample (68.75%) had a response ≥ 400 AU/mL and, therefore, hypothetical correlations were masked by this limit. Therefore, it is important to highlight the essential role played by the 1st booster dose in the complete protection against COVID-19 infection. This is important not only for HCWs but especially for general population. Indeed, it has been estimated that about 20% of general population in Italy has not yet received the 1st booster dose and is, therefore, at risk to get the infection with more severe clinical outcomes [47].

Conclusions

In conclusion, our data are perfectly in line with what has been declared by the conducted studies in terms of vaccine efficacy. Considering that HCWs are at first line in the fight against COVID-19 and, therefore, at high risk to contract and, eventually, spread the infection in nosocomial settings, it is important to highlight that, even if only a very little portion of the sample did not produce antibodies after the primary vaccination cycle, this risk was completely cancelled by the 1st booster dose. Moreover, individual variables as age and gender played an important role in the immune response to the primary cycle putting potentially at risk to get the infection and to have negative clinical outcomes more vulnerable

people. However, the 1st booster dose produced a good immune response in all the sample independently from the individual variables. This finding is valid also for the general population on which the importance of the 1st booster dose should be stressed through a general and correct information.

Conflict of interest

The authors declare no conflict of interest.

Funding

None.

Ethics approval

The study has been performed in accordance with the Declaration of Helsinki and has been approved by the Ethics Committee of the University Hospital "G. Martino", Messina, Italy (protocol number 1860 of 05/10/2022).

Authors' contributions

Conceptualization: ADP, SC and DLG. Methodology: AF and GV. Formal analysis, data curation and writing - original draft: GV and AF. Resources: AB and AL. All Authors revised the manuscript and gave their contribution to improve the paper. All authors read and approved the final manuscript.

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Received on October 14, 2022. Accepted on November 29, 2022.

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How to cite this article: Calimeri S, Lo Giudice D, Buda A, Laganà A, Facciolà A, Di Pietro A, Visalli G. Role of the 1st booster dose of COVID-19 vaccine in the protection against the infection: A fundamental public health tool. J Prev Med Hyg 2022;63:E520-E526. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2742

HEALTH PROMOTION

Health literacy in Mediterranean general population

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Keywords

Health literacy • Prevention • Public health

Summary

Introduction. *Health literacy refers to "the ability to obtain, process, and understand basic health information and access health services in order to make informed choices." In essence, being able to acquire, understand, and use information for one's own health.*
Methods. *Observational study through the administration of a face-to-face questionnaire conducted between July and September 2020 on 260 individuals residing between Calabria and Sicily, aged between 18 and 89 years. Questions related to education, lifestyle (alcohol, smoking, and physical activity). Multiple-choice questions to assess health literacy and conceptual skills, ability to find information on health topics and services, use of preventive medicine especially vaccinations, and ability to make decisions about one's own health.*
Results. *Of 260, 43% were male and 57% female. The most represented age group is between 50 and 59 years. Forty-eight percent of respondents had a high school diploma. 39% smoke and 32% habitually consume alcoholic beverages; only 40% engage in physical activity. Ten percent had a low level of health literacy, average 55%, and adequate 35%.*
Conclusions. *Given the importance of adequate HL on health choices and on individual and public wellbeing, it is essential to expand the knowledge of the individual, through public and private information campaigns and with an increasing involvement of family physicians, who are fundamental in training and informing their patients.*

Introduction

Health literacy is gaining critical importance in public health. Since its introduction in the 1970s, the concept gradually expanded and continues to expand [1].
The World Health Organization during the Ninth Global Conference on Health Promotion defined health literacy as the ability of individuals to "gain access to, understand and use information in ways that promote and maintain good health" for themselves, their families and their communities" [2-3].
It is considered a determinant of health, as it is proven to influence healthy lifestyles, adherence to treatment, and appropriate access to health services, providing the foundation upon which citizens are able to play an active role in improving their health [4]. WHO supports the development of appropriate action plans to promote health literacy considering it an evolving concept, not just a personal resource; in fact, higher levels of health literacy within the population produce social welfare. Health Literacy is fundamental to patient empowerment, that is, a process through which people can gain greater control over decisions and actions that affect their health (World Health Organization. Regional Office for Europe, 2012) [5].
Health literacy can be considered a factor that affects several aspects of patient care ranging from the use of preventive medicine to the adequate control of chronic diseases to mortality itself.
Poor health literacy is, therefore, related to a lower quality of life for patients and increased costs for the health care system [6].
A systematic review of the literature evaluates the association of low levels of health literacy with several health outcomes by correlating them with a higher probability of emergency room access and hospitalizations and in the elderly population with worse overall health status resulting in increased mortality [7].
The level of health literacy is also correlated with greater/lesser awareness of health-related risk factors [8-9]. The available evidence suggests that more people have limited health literacy than is often assumed. According to population data from the US, nearly half of the American adult population may have difficulties in acting on health information [10]. In Europe, findings from the recent European Health Literacy Survey indicate that 12% of the people surveyed have inadequate general health literacy, and 35% have problematic health literacy [11-12]. Although the prevalence of problematic health literacy varies widely between countries (between 2% inadequate health literacy in the Netherlands versus 27% in Bulgaria) and between groups within populations, it is clear that health literacy is not just a problem of a small minority [13].
In Italy, studies related to functional health literacy are few, a study on the general population states that 11.5% of the Italian population has a high probability of having

a limited level of health literacy, it is also pointed that the elderly, the less educated and the poorer have a higher probability of having a limited or inadequate level of health literacy [14].

Eurostat has analyzed the frequency with which European citizens ask for a consultation to primary care physicians, with 75% having done so in the last year and women going more frequently. As for Italy, it is sixth to last in terms of people who have never visited a primary care physicians, but it is in first place in terms of the percentage of people who have seen a general practitioner between one and two times in a year. In light of this, we also asked about the frequency of visits with their family doctor highlighting the communication and health information received.

Despite the enormous implications of inadequate health literacy, knowledge of health literacy in the general population and how health literacy impacts health behavior and health status remain scarce [15-16]. Considering the above, the aim of our study was to evaluate the levels of health literacy in a sample of the general population residing in Calabria and Sicily.

Materials and methods

An observational study was conducted, after obtaining informed consent from respondents, by administering anonymous face-to-face questionnaires to a sample of 260 patients. Participants were selected from primary care physicians' offices of some municipalities in the provinces of Calabria and Sicily: Reggio Calabria, Cosenza, Messina and Catania. The sample was stratified by age, sex, and level of schooling. Inclusion criteria were as follows: age between 18 and 89 years and Italian language. Exclusion criteria included cognitive impairment, severe psychiatric illness, and end-stage disease. The research was conducted for a three-month period from June 1 to September 30, 2020. Questions were asked about education level, also assessing habits and lifestyles regarding, alcohol consumption, cigarette smoking habit and physical activity. An analysis of health-specific literacy and conceptual skills was conducted through multiple-choice questions, assessing the ability to find information on health topics and services and evaluating the use of preventive medicine particularly vaccinations. Also assessed were the ability to clearly express questions and opinions, analyzing risks and benefits, and finally, being able to make decisions related to one's own health. As far as the relationship with the family doctor is concerned, among European citizens, women go to their family doctor more frequently. The chi-squared test and p-value were used to assess statistical significance.

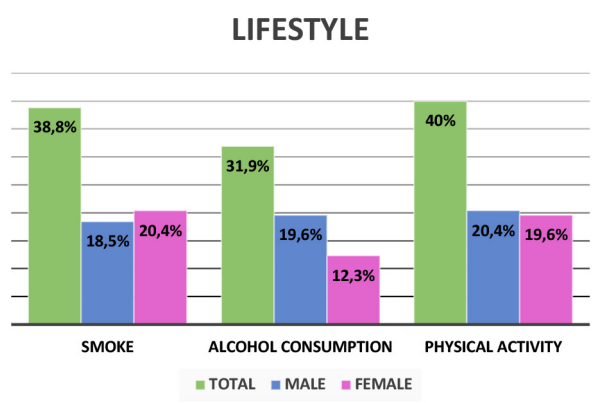
Results

A total of 260 subjects between 18 and 89 years of age responded to the questionnaire (mean age 49.30 SD 16.14). The most represented age is between 50 and 59 years with 27% of responses, among them there is a significant gender difference with 21.7% males and 78.3% females (chi-square 20,261; $p < 0.001$). Forty-three percent of respondents were male while 57% were female. At least 48% of all respondents had a high school diploma; among women, 24% had a bachelor's degree, while among men only 13% had a bachelor's degree. Twenty percent of respondents are retired, among women 22% are housewives and 27% of men are retired, it is not possible to assess a statistically significant correlation between occupation and gender (Tab. I).

Tab. I. Sample representation by age, education, occupation.

		Total (N = 260)	Male (N = 112; 43%)	Female (N = 148; 57%)
Age	18-29	(45/260) 17%	(19/112) 17%	(26/148) 18%
	30-39	(33/260) 13%	(17/112) 15%	(16/148) 11%
	40-49	(45/260) 17%	(22/112) 20%	(23/148) 16%
	50-59	(69/260) 27%	(15/112) 13%	(54/148) 36%
	60-69	(33/260) 13%	(18/112) 16%	(15/148) 10%
	70-79	(32/260) 12%	(20/112) 18%	(12/148) 8%
	80-89	(3/260) 1%	(1/112) 1%	(2/148) 1%
Studies	Elementary school	(17/260) 7%	(9/112) 8%	(8/148) 5%
	Lower middle school	(67/260) 26%	(32/112) 29%	(35/148) 24%
	High school	(126/260) 48%	(57/112) 51%	(69/148) 47%
	Graduation	(50/260) 19%	(14/112) 13%	(36/148) 24%
Work	Unemployed	(39/260) 15%	(19/112) 17%	(20/148) 14%
	Freelancer	(41/260) 16%	(23/112) 21%	(18/148) 12%
	Retiree	(51/260) 20%	(30/112) 27%	(21/148) 14%
	Public employee	(56/260) 22%	(23/112) 21%	(33/148) 22%
	Private employee	(20/260) 8%	(10/112) 9%	(10/148) 7%
	Student	(21/260) 8%	(7/112) 6%	(14/148) 9%
	Housewife	(32/260) 12%	0%	(32/148) 22%

Fig. 1. Lifestyle, gender differences.



Among those who responded to the questionnaire, 39% smoke and 32% habitually consume alcoholic beverages and only 40% engage in physical activity. Evaluating statistical significance in relation to gender, we found that a highly significant correlation with alcohol consumption (chi-square = 16.777; $p < 0.001$) with males who drink more than females; a slightly significant correlation with physical activity (chi-square = 4.395; $p < 0.036$) with males engaging in more physical activity than females; in contrast, there were no significant differences related to smoking habit (chi-square = 1.332; $p = 0.248$) (Fig. 1). It is not possible to assess a statistically significant correlation between lifestyle variables and age and education level.

Questions were then asked regarding basic concepts and common notions of what the health terms are most frequently encountered in daily life. Terms such as drug package insert, contraindications, posology, but also the concept of over-the-counter medication or the use of antibiotics, were not always answered correctly, as shown in Table II.

Another section of the questionnaire investigated the knowledge in the field of prevention and in particular on vaccines and even more the fear for the same. In this case, 40% of subjects said they were afraid of the side effects of the vaccine, 44.6% do not know whether the vaccine is or is not the cause of autism as well as 45% do not know the possible correlation with an increased risk of developing allergies. Furthermore 43.5% of respondents admitted that in their opinion doctors do not provide enough information on the side effects of the vaccine (Tab. III).

By assigning a value of 0 to incorrect or missed responses and 1 to correct responses, it was possible to obtain ranges to assess the level of health literacy (HL), with a minimum total of 1 and a maximum of 10. On our sample of 260 individuals, the mean score obtained was 6.47 (SD 2.12). Statistical significance between the mean score and several parameters was then assessed. Considering the mean HL score obtained by males and females, the female gender has a higher score than males slightly significant Pvalue 0.046. The different occupation slightly significantly affects comparing the results obtained by public employees compared to students with a post-hoc Pvalue 0.040, where students have a higher average HL parameter value than public employees. Educational qualification highly significantly affects pvalue post-hoc 0.001, relating the mean of values obtained by high school graduates to those with only an elementary degree. In contrast,

Tab. II. Percentage of correct answers to definitions of common health terms.

	Correct Answer Total (n = 260)	Correct Answer Male (n = 112; 3%)	Correct Answer Female (n = 148; 57%)
What is the meaning of the term "bugiardino" (alias package insert)?	(214) 82%	(85) 76%	(129) 87%
What are over-the-counter medications?	(219) 84%	(92) 82%	(127) 86%
Are antibiotics drugs for treatment of…?	(192) 74%	(72) 64%	(120) 81%
What are contraindications?	(139) 53%	(60) 54%	(79) 53%
What does the posology represent?	(210) 81%	(85) 76%	(125) 84%
What is a vaccine?	(209) 80%	(85) 76%	(124) 84%

Tab. III. Questions related to vaccine knowledge.

Total	Yes	No	Don't know	No answer
The side effects of vaccinations worry me	(105) 40%	(107) 41%	(48) 18%	0%
Vaccines are important because they prevent diseases that can have even serious effects	(203) 78%	(24) 9%	(33) 13%	0%
Substances in vaccines are dangerous to humans	(46) 17,7%	(103) 39,6%	(110) 42,3%	(1) 0,4%
Doctors often fail to provide information about the side effects of vaccines	(113) 43,5%	(66) 25,4%	(79) 30,4%	(2) 0,8%
Autism could be caused by vaccinations	(51) 19,6%	(91) 35%	(116) 44,6%	(2) 0,8%
Vaccinations increase the risk of allergies	(40) 15%	(103) 40%	(117) 45%	0%

* Percentage on the total of those who answered the questionnaire.

there is no correlation between HL value and age pvalue 0.124. Finally, the correlation between voluptuous habits, physical activity with the HL parameter obtained on average from the sample was evaluated. There was no significant correlation between smoking (p value 0.084) and alcohol consumption (p value 0.163) and HL. But regarding physical activity the correlation is highly significant with pvalue 0.001 those who do physical activity have a higher mean HL than those who do not (Tab. IV).

Finally, the role of the general practitioner in communication and information with their patients and the frequency with which they visit was explored (Fig. 2).

When asked if the doctor's instructions and prescriptions on illnesses are always understandable, 70% answered yes, 59% not always and often unclear for 23%. In case of lack of clarity, only 24% ask the general practitioner for further clarification, 8% prefer to turn to a friend or acquaintance who practices medicine, 7% discuss it in the family, 3% ask the pharmacist for advice and 5% turn to the web.

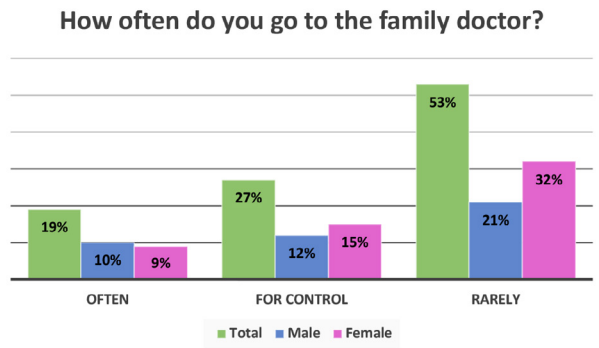
With regard to information obtained via the web, 13% stated that they always resort to it after having spoken with their doctor, whereas 32% do so only a few times. Among those who make use of information obtained from social networks and medical websites, 17% do so to better understand their disease, 26% to learn more and, finally, 4% to know what to do. 16% use the web constantly to obtain information about their health and of these, 18% do not seek discussion with their doctor while 23% do so only sometimes.

87% of those who responded to the questionnaire, said they follow the instructions of the doctor for the treatment and use of drugs, but only 33% have ensured that they follow the directions of the doctor or pharmacist regarding the timing and mode of treatment, 39% do not trust either the directions of the doctor or the pharmacist and 25% follow the prescriptions only sometimes. The 12% of the subjects, stop taking drugs and antibiotics as soon as they feel better, without following the prescribed times and do it on their own initiative, without asking for the advice of the doctor.

Tab. IV. Relationship between average HL value and behavioral variables.

Behavioral variables			P-value
Physical activity (No)	Average	6,09	
	Median	6,00	
	DS	2,21	
	Lowest value	1,00	
	Max value	10,00	
	IQR	3,00	
Physical activity (Yes)	Average	7,05	0.001
	Median	7,00	
	DS	1,85	
	Lowest value	1,00	
	Max value	10,00	
	IQR	2,00	
Alcohol consumption (No)	Average	6,5989	
	Median	7,0000	
	DS	2,07052	
	Lowest value	2,00	
	Max value	10,00	
	IQR	3,00	
Alcohol consumption (Yes)	Average	6,2048	0.162
	Median	6,0000	
	DS	2,21282	
	Lowest value	1,00	
	Max value	10,00	
	IQR	3,00	
Smoke (No)	Average	6,65	
	Median	7,00	
	DS	2,00	
	Lowest value	2,00	
	Max value	10,00	
	IQR	3,00	
Smoke (Yes)	Average	6,19	0.084
	Median	6,00	
	DS	2,28	
	Lowest value	1,00	
	Max value	10,00	
	IQR	3,00	

Fig. 2. Representation of the frequency with which subjects visit their general practitioner.



Conclusion

From our survey has emerged a general lack of awareness of what are the terms that are most commonly encountered in everyday life about their health and care as well as a general distrust of prevention especially towards vaccines. The age group most represented in our survey is over 50 years old and 47% of them have a level of education that does not exceed a secondary school diploma. They are mainly housewives and retired people. Sixty percent of our sample does not engage in physical activity, and it is females who do less than men. On the other hand, men consume alcohol and drink significantly more than women, with significant gender differences. In our study, we stratified the responses of the subjects so that we could obtain three macro-categories, based on the formulation of correct or incorrect responses: those

who have a substantially low, medium, and adequate level of functional health literacy. Of the total, 10% have an evidently low level and of these, 6% are males and 4% females; 55% have a medium-intermediate level, (25% are males and 30% females) and 35% have an adequate level (12% are males and 23% females). Compared to the national data where 63.9% of the sample has an adequate level of health literacy, our sample has an adequate HL much lower than the national average, almost halved; we are in line, however, regarding the high probability of having a limited level of literacy [14]. We also observed how belonging to the female gender affects a higher HL value, as does student status and degree, where greater education also implies greater knowledge of the terminology and meaning of common health terms. There is no correlation between basic health knowledge and age. Interesting, however, is the correlation between physical activity and HL, based on the data obtained it would seem that those who practice physical activity have a greater awareness of their health and risk factors, showing more basic health knowledge. It is interesting to point out that 19% of our sample goes frequently to the family doctor, among them most are over 50 years old and are women; 7% and 23% often or not always understand what they are told by the doctor and 10% of them do not have enough confidence in the general practitioner to follow his prescriptions or directions on health. In addition to the barriers that low health literacy creates in the context of the clinical encounter, low health literacy also reduces the likelihood that people will access the health care system in a timely manner and understand the importance of the many risk factors such as smoking, alcohol, diet, lack of physical activity, and infectious agents [17-23] and understand how not following doctor's prescriptions in the time/dose of antibiotics gives rise to antibiotic resistance (AMR) is important drivers of increased morbidity and mortality rates resulting in rising healthcare costs. Antibiotic resistance is multifactorial and may be favored by inappropriately prescribed antibiotics or due to erroneous dosages, by empirical therapies in which broad-spectrum antibiotics are used in the absence of adequate diagnostic procedures. WHO recommends that antibiotics be used only when prescribed by a certified health care professional and in accordance with the prescription and dosage [24-25].

It is therefore essential that health promotion includes concerted efforts to raise levels of health literacy from early childhood through adulthood, taking advantage of all means of communication, media campaigns, and all living and working environments such as schools of all levels. It becomes important and indispensable for the entire health care community to make a concerted effort to guide and transmit health education that is not limited to the mere transmission of information but to educate the patient so that he or she reaches an optimal level of health literacy. In addition, it would be appropriate to involve all healthcare professionals and especially the network of family physicians, the only ones who really come into contact with women and men throughout their lives, who often show little interest in prevention, especially with regard to the importance of vaccination in general, as shown by previous studies [26-27].

Even today, universal health literacy precautions need to be recommended to facilitate a better match between people's needs and the services and information offered through the health care system and to provide understandable and accessible information to all patients, regardless of their literacy or education level. This includes avoiding medical jargon, breaking down information or instructions into small, concrete steps, limiting the focus of a visit to three key points or activities, and assessing comprehension [28-30].

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare no conflict of interest.

Ethical approval

Not required.

Authors' contributions

Writing, data processing and commentary: VA, VLF.
Statistical calculation: GT.
Data collection: CC, FM, RP.

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Received on January 25, 2022. Accepted on November 09, 2022.

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How to cite this article: La Fauci V, Trimarchi G, Ceccio C, Mazzitelli F, Pappalardo R, Alessi V. Health literacy in Mediterranean general population. J Prev Med Hyg 2022;63:E527-E532. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2485

HEALTH PROMOTION

Russian subject-level index of multidimensional deprivation and its association with all-cause and infant mortality

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Keywords

Deprivation Index • Mortality • Population Census • Russia

Summary

Background. *Social and environmental inequalities in public health are recognized as global problems of our time. From the point of view of the theory of deprivation, social and environmental determinants identified as deprivation indicators, which help to detect health inequality. Indices are one of the most practical and powerful tools for measuring the level of deprivation.*
Objectives. *The aims of our study are (1) to develop a Russian derivation index to measure the levels of deprivation and (2) to analyze its associations with total and infant mortality.*
Material and methods. *Deprivation indicators were obtained from the Federal State Statistics Service of Russia. All mortality data were taken from the official website of the Federal Research Institute for Health Organization and Informatics of Ministry of Health of the Russian Federation from 2009 to 2012. Principal components analysis with varimax rotation was used to (1) select suitable deprivation indicators and (2) create the index. A Spearman's correlation was run to determine the relationship of deprivation with all-cause and infant mortality. Ordinary least squares (OLS) regression was used to assess the relationship between deprivation and infant mortality. Development of the index and statistical analysis were carried out using R and SPSS software.*
Results. *There is not a statistically significant correlation between deprivation and all-cause mortality. OLS regression showed a significant relationship between deprivation and infant mortality ($p = 0.02$). For every one-unit increase in the index score, infant mortality rate increases by about 20%.*

Background

The World Health Organization (WHO) definition of health are based on the same principles: "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". It follows that for the prosperous existence of a person, the external environment plays an essential role, the factors of which are defined as determinants.
According to WHO, "the social and environmental determinants of health are the full set of social and physical conditions in which people live and work, including socioeconomic, demographic, environmental and cultural factors, along with the health system" [1]. It is difficult to single out and classify all the determinants. Social determinants conditionally include the socioeconomic status (SES), race and ethnicity, cultural and linguistic characteristics, housing conditions and social support. SES is reflected by education, income level, employment status and professional affiliation. Separately, it is necessary to highlight environmental determinants, which include noise levels, access to green spaces, air pollution, drinking-water quality and sanitation, weather extremes and flooding.
According to WHO, social and environmental inequalities in public health are recognized as global problems. Environmental risk factors account for 23% of all deaths in the world and 20% of the total burden of disease, measured in disability adjusted life years (DALYs). For example, risk factors such as outdoor and indoor air pollution are responsible for 25 and 26% of the total burden of stroke, respectively, and 24 and 18% of the total burden of cardiovascular diseases, the leading causes of global death. Overall, environmental risk factors account for 42% of the total burden of stroke and 35% of the total burden of coronary heart disease [2]. Cancer is the cause of about 30% of all premature deaths from noncommunicable diseases among adults aged 30-69 [3]. About 19% (12-29%) of all cancers were estimated to be attributable to the environment [4].
From the point of view of the deprivation theory, we can identify social and environmental determinants as deprivation indicators, which help to detect health inequality. The theory was developed in the second half of the XX century by the English sociologist Peter Townsend [5]. Townsend defined deprivation as "the lack of resources to sustain the diet, lifestyle, activities and amenities that an individual or group are accustomed to or that are widely encouraged or approved in the society to which they belong". Currently, the deprivation theory is a theoretical basis for assessing the impact of differences in living conditions on individual and public health.
One of the most practical and powerful tools for measuring deprivation both at the individual and

population levels are deprivation indices [6, 7]. The main advantage of using the index instead of separate indicators is the assessment of problems and mechanisms of health inequality in more depth, which would provide an opportunity to draw competent conclusions to develop and target strategies for improving public health in the future.

If we look at the problem of health inequality in Russia, in fact this phenomenon is associated with the transformation of social attitudes that Russian society underwent in the early 90s of the last century due to a change in the political paradigm in the country. In the Soviet period, there were approximately equal living and work conditions as well as access to health care therefore the obvious socio-economic inequality of society was not observed. With the country's transition to a market economy, the commercialization of all spheres of society's life began to be actively pursued, resulting in a significant gaps and inequities in the quality of life of the various population groups "stratification of society". In conditions of socio-economic stratification of society, differences began to appear in the distribution of fertility, morbidity, all-cases and infant mortality across the regions [8, 9].

The aim of our study is to develop a Russian derivation index (RDI), taking into account the peculiarities of the geographical, industrial, ecological, and socio-economic characteristics of the regions, for the analysis and quantitative assessment of the problem of social and environmental inequality in health. An analysis of its associations with total and infant mortality was carried out to evaluate predictive validity of the index [10].

Materials and methods

Data sources

Data were obtained from official statistical publications of the Federal State Statistics Service of Russia (Rosstat) and the All-Russian Census of Population for 2010. The census took place from October 14th to 25th and covered the 83 federal subjects. The federal subject is the first-order administrative level divisions in Russia. The 83 federal subjects comprise various different types of unit; these are viewed as administratively equal, though some enjoy significantly more autonomy than others: specifically there are 46 oblast', 21 republics, 9 kray,4 autonomous okrug, 2 cities of federal significance and 1 autonomous oblast'. The study of the deprivation of areas was carried out at a level of subjects of federation due to the possibility of obtaining the most complete information about the socio-economic situation and the state of the environment. All data are available on the official website of Rosstat (https://rosstat.gov.ru/).

Selection of variables

The selection of indicators was carried out in two stages. At the first stage, a total 58 indicators were selected (the full list of indicators can be obtained from the corresponding authors upon request) in accordance with the theory of deprivation and taking into account the socio-economic and environmental characteristics of the country, as well as the previous experience of constructing similar indices in other countries.

At the second stage, principal components analysis (PCA) was used to (1) select suitable deprivation indicators and (2) create the index.

Statistical analysis

PCA is subject to the same restrictions as regression, so the distributions of each variable were checked for normality [11, 12]. To evaluate normality of variables we used SPSS-generated histograms and normal Q-Q plots. If data were nonnormal, natural and 10 log transformations were applied to increase normality [13]. To eliminate the indicators the following criteria are used (1) the indicators have no significant loadings, (2) even with a significant loading, the indicators 'communality is less than 0.50, (3) the indicators have a cross-loading (more than one significant loading) [14]. A component loading of 0.40 and over is significant [15].

The factorability of the indicators was examined using Bartlett's test of sphericity and the Kaiser-Meyer-Olkin (KMO) test. Bartlett's test of sphericity evaluates the studied data for the possibility of their compression with a significant result: the null hypothesis assumes that the variables are orthogonal, not correlated. P-value less than the significance level suggests that PCA can be performed. KMO test measures sampling adequacy for the complete model. KMO values less than 0.60 indicate the sampling is not adequate [16].

The steps taken were:

1. selection of the set of variables to be used;
2. calculation of the correlation matrix for all variables involved in the analysis;
3. extraction of factors by the method of principal components;
4. selection of a suitable number of factors using a scree test and the Kaiser rule – components with an eigenvalue greater than one;
5. varimax rotation of components to create a simplified structure.

A Spearman's rank-order correlation was run to determine the relationship between deprivation and all-cause mortality. All-cases mortality were age-standardized by the direct method. For standardization, used the standardized European population (1976).

In addition, Spearman's correlation and ordinary least squares (OLS) regression were used to assess the relationship between deprivation and infant mortality. The dependent variable is infant mortality rate and the independent variable is the index scores. Infant mortality rate is log-transformed. All mortality data were taken from the official website of Federal Research Institute for Health Organization and Informatics of Ministry of Health of the Russian Federation (CNIIOIZ) from 2009 to 2012 (https://mednet.ru/).

To carry out PCA, the SPSS Statistics Base 22.0 (IBM Corporation New Orchard Road Armonk, NY 10504) statistical software package was used. Spearman's rank

correlation and OLS regression were run using the cor. test and lm functions in R. The significance level was set at 0.05.

Results

Development of the deprivation index

The final index includes 17 deprivation indicators (Tab. I). KMO coefficient = 0.79, Bartlett's test of sphericity was significant ($\chi 2$ (136) = 1557.56 p < 0.001). Only the first three components displayed eigenvalues greater than 1, and the results of scree test suggested that only the first three components were meaningful. Therefore, only the first three components were retained for rotation. Combined, components 1, 2 and 3 accounted for 73.5% of the total variance. Deprivation indicators and factor loadings are presented in Table II. In interpreting the rotated factor pattern, an indicator was said to load on a given component if the factor loading was 0.40 or greater for that component, and was less than 0.40 for the other. Using these criteria, five indicators were found to load on the first component, which was subsequently labelled the social deprivation component. The first component explains 24.8% of the total variance and includes the following indicators: living in crowded households, children under age 5 years old, children +3, unemployment rate, and phone. Five indicators were found to load on the second component, which was subsequently labelled the economic deprivation component. The second component explains 24.6% of the total variance and includes indicators: stove heating, no hot water supply, no sewerage system, not central sewerage system, low income. Seven indicators were found to load on the third component, which was subsequently labelled the environmental deprivation component. The third component explains 24% of the total variance and includes indicators: dead forest, fire forest incidence, environmental crime, transport-related emissions, and emissions from stationary sources: NO_2, SO_2, CO. A variable with a positive loading indicates a negative association to the component.

Finally, all components are aggregated into the deprivation index according to the following equation:

$$RDI = w_1 \text{ (factor 1 score)} + w_2 \text{ (factor 2 score)} + w_3 \text{ (factor 3 score)}$$

Tab. I. Definitions of deprivation indicators.

Domain	Variable	Description	Data source
Family structure / Demographics	Children +3	Percentage of families with 3 and more children (ages 0-18)	Census 2010
	Children under 5 years old	Children ages 0-4 as a percentage of total population	Census 2010
Housing	Stove heating	Percentage of households with stove heating	Census 2010
	No hot water supply	Percentage of households without heat water supply	Census 2010
	No central sewerage system	Percentage of households with toilets emptying into a cesspit	Census 2010
	No sewerage system	Percentage of households without sewage system	Census 2010
	Overcrowded	Percentage of households (individual (single-family) houses, individual and communal apartments) with > 5 persons	Census 2010
Communication	Phone	Percentage of households with telephone	Census 2010
Income and Wealth	Low income	Percentage of people below a low income threshold in the total population	Regions of Russia. Social and Economic Indicators – 2011
	Unemployment rate	Population 15 or older unemployed	Labour and Employment in Russia – 2011
Air quality	NO_2	Nitrogen dioxide (thousand tons) from stationary sources	Environment Protection in Russia – 2012
	SO_2	Sulphur dioxide (thousand tons) from stationary sources	Environment Protection in Russia – 2012
	CO	Carbon monoxide (thousand tons) from stationary sources	Environment Protection in Russia – 2012
	Transport-related emissions	Air emissions from vehicle (thousand tons)	Environment Protection in Russia – 2012
Natural disaster	Fire forest incidence	The number of fire forest incidence (unit)	Environment Protection in Russia – 2012
Green space	Area of dead forest	The area of dead forest (hectares)	Environment Protection in Russia – 2012
Crimes	Environmental crimes	The number of recorded environmental crimes	Environment Protection in Russia – 2012

Tab. II. Component loadings and communalities based on a principal components analysis with varimax rotation for 17 variables.

Variables	Component			Communality
	Social deprivation	Economic deprivation	Environmental deprivation	
Children +3*	**0.910**	0.176	-0.261	0.928
Children under 5 years old*	**0.821**	0.344	-0.053	0.796
Unemployment rate**	**0.698**	0.243	-0.272	0.620
Phone*	**-0.826**	-0.186	0.198	0.756
Overcrowded	**0.888**	0.007	-0.347	0.908
Stove heating	0.295	**0.798**	0.097	0.732
No hot water supply	0.299	**0.906**	-0.006	0.910
No sewerage system	0.237	**0.926**	0.008	0.913
No central sewerage system	0.387	**0.836**	-0.117	0.862
Low income	-0.165	**0.665**	-0.217	0.517
Area of dead forest*	-0.299	0.328	**0.556**	0.506
Fire forest incidence*	-0.263	0.294	**0.699**	0.644
Emissions from stationary sources:				
NO_2*	-0.221	-0.299	**0.863**	0.883
SO_2*	-0.121	-0.099	**0.774**	0.624
CO*	-0.073	-0.180	**0.843**	0.749
Transport-related emissions*	-0.107	-0.343	**0.629**	0.524
Environmental crimes*	-0.334	0.218	**0.686**	0.629

Extraction method: Principal component analysis; Rotation method: Varimax with Kaiser normalization. Loadings larger than .40 are in bold.
* Natural log transformation: new variable = ln (1+old variable). ** Log 10 transformation: new variable = log10 (old variable).

Where w_k - weight which is calculated by dividing the percent of variance accounted for by k_{th} - principal component by the cumulative percentage of variance accounted for by all preceding principal components whose eigenvalues are 1 or greater; factor *j* score - regression factor score that is the actual value for each region on the underlying components in a particular row of data.

RDI scores were calculated for the 83 federal subjects. Moreover, the scores were divided into four quantiles (1Q, 0% -25%; 2Q, 25% -50%; 3Q, 50% -75%; 4Q, 75% -100%), where the first quantile (1Q) is the least deprived area and the fourth quantile (4Q) is the most deprived area (Tab. III). The distribution of RDI scores is shown in Figure 1.

Validation of the deprivation index

There was a positive correlation between deprivation and infant mortality, which was statistically significant (r_s = 0.31, p = 0.003). Regression model confirmed a significant relationship between deprivation and infant mortality (p = 0.02). For every one-unit increase in the value of the index, infant mortality rate increases by about 20%. The R^2 value was 0.108 thus 11% of the variation in infant mortality can be explained by the model containing only deprivation.

There is not a statistically significant correlation between deprivation and the age-standardized mortality rates (both sex, females and males) (Tab. IV).

Discussion

When selecting indicators for the index, economic, environmental and social issues were taken into account. The index includes socio-economic and environmental indicators due to the fact that a complex two-stage method base on conceptual (theory about deprivation) and empirical (previous experience with indicators, used PCA) approaches was used.

Russia is the largest country in the world, covering over 17,125,191 square kilometres. The largest federal subject of Russia is the Republic of Sakha (Yakutia),

Tab. III. Mean index score by quantile.

Quantile	Number of federal subjects	Mean	SD	95% CI
1 – the least deprived	20	-0.687	0.268	(-0.813, -0.562) (-0.262, -0.176) (0.042, 0.170) (0.616, 0.921)
2	21	-0.219	0.094	
3	21	0.106	0.140	
4 – the most deprived	21	0.768	0.335	

SD: standard deviation; CI, confidence interval.

Fig. 1. Region-level deprivation across Russia.

Tab. IV. Spearman's rank correlation between deprivation and the age-standardized mortality rate.

Variable	r_s	P - value
Total population	0.15	0.164
Females	0.21	0.051
Males	0.08	0.462

with a total area of 3,083,523 km^2 and a population of 958,528 people; the smallest federal subject is St. Petersburg with an area of 1,403 km^2 and a population of 4,879,566 people. Our study showed that generally the most deprived regions are industrial with poor ecological conditions [17] such as Chelyabinsk, Kurgan, Sverdlovsk, Tyumen, Omsk Oblasts, and Sakha and located in Ural and the Western Siberia. Less deprived regions such as Voronezh, Ivanovo, Yaroslavl, Moscow Oblasts, and Moscow located in European part of Russia. Our study, unlike other similar ones [18, 19], was carried out at large area level because of the full dataset of the census and other indicators is publicly available only at a level of subjects of federation (the largest territorial-administrative unit of the country).

In our study, there is no the relationship between deprivation and overall mortality, unlike other similar studies that used indices to measure deprivation. Choi et al. [20] estimated an association between the most deprived population and all-cause mortality. The study found that all-cause mortality increased by 23% (RR: 1.23, 95% CI 1.16 to 1.30) in the most deprived population compared to the least deprived one. Deprivation was determined using the index that consists of no house ownership, no passenger car, poor house environment, single household, low level of education, male unemployment, divorced or separated, elderly people, female-headed variables. McCartney et al. [21] estimated the association between all-cause mortality and deprivation between four time periods (1981-1983, 1990-1993, 2000-2002, 2010-2012). Deprivation was determined using the Carstairs index, which consists of four indicators: male unemployment, overcrowding, low social class, and lack of car ownership. The study found that the mortality ratios among the population of England, Wales and Scotland aged 35-79 years were higher in more deprived areas without significant gender differences. Kraftman et al. [22] assessed the dependence of the all-cause mortality on deprivation in 2003 and 2017. In 2003, the mortality from all causes among adult increased by 1.4 times in the more deprived area, and in 2017 the mortality increased by 1.6 times. Simultaneously, all-cause mortality among women living in the most deprived areas was 1.3 times higher in 2003 and increased 1.5 times by 2017. To determine deprivation level, the Index of Multiple Deprivation 2015 (IMD) was used, including domains related to income, employment, education, crime, environmental and housing conditions as well as living environment. Pearce et al. [23] created an environmental deprivation index consisting of the following indicators: air pollution, average UV radiation, green space, average annual ambient temperature, and established a positive association of all-cause mortality (Incidence Rate Ratio (IRR) = 1.14) with the most deprived area.

In our study along with other similar studies, deprivation is significant associated with infant mortality. However, unlike our study, they generally used indices that formed only from socio-economic indicators. Yun et al. [24] developed a deprivation index that includes the following indicators: unemployment rate, low social class, lack of car ownership, overcrowded housing, married status, family structure, and low education level. Furthermore, they established that the risk of infant mortality increased by 26% (Hazard Ratio (HR):1.261, 95% CI 1.199 to 1.326) among the most deprived population compared to the least deprived one. Padilla et al. [25] also analyzed the association between infant mortality and deprivation between two time periods (2002-2005 and 2006-2009). The study showed that infant mortality was higher in more deprived census tracts than in less deprived ones. The deprivation index included five domains: family structure, immigration status and mobility, occupation and income, education and housing conditions. Guildea et al. [26] established that risk of infant death increased

by 53% (RR: 1.53, 95% CI 1.35 to 1.74) in the most deprived areas compared to the least deprived ones. To measure deprivation level, they used Townsend index that included unemployment rate, car ownership, owner occupation, and overcrowding variables.

Similarly, socioeconomic inequality in health outcomes have been observed around the world. Pathirana et al. [27] conducted a systematic review and found that low level of education was associated with a 64% increased odds of multimorbidity (summary Odd Ratio (OR): 1.64, 95% CI 1.41 to 1.91). Another systematic review [28] investigated the relationship between stroke survival and socio-economic inequality in China. It was found that both low level of education (a pooled Relative Risk (RR): 3.07, 95% CI 1.27 to 7.45) and low per capita income (the pooled RR: 1.58, 95% CI 1.50 to 1.65), as well as rural status (the pooling RR: 1.47, 95% CI 1.37 to 1.58) increase the risk of death from stroke. Kim et al. [29] reviewed studies which analyzing the relationship between income and obesity. The result of the meta-analysis demonstrated that lower income is associated with obesity (OR: 1.27, 95% CI 1.10 to 1.47; RR: 1.52, 95% CI 1.08 to 2.13).

Cohort studies conducted in Asia and Australasia [30] showed that low level of education increased the risk of mortality from all causes by 56% (HR: 1.56, 95% CI 1.38 to 1.76) in Asia and by 14% in Australasia (HR 1.14, 95% CI 1.05 to 1.23). Furthermore, low level of education increased the risk of mortality from cardiovascular diseases by 78% (HR: 1.78, 95% CI 1.42 to 2.23) in Asia and by 20% (HR: 1.20, 95% CI 1.04 to 1.38) in Australasia as well as increased the risk of mortality from cancer by 39 % (HR: 1.39, 95% CI 1.15 to 1.69) in Asia.

Only few studies have analyzed the relationship between deprivation and infant mortality using indices formed from environmental indicators. For instance, Genowska et al. [31] created index, which consists of total particle pollution, sulfur dioxide, nitrogen oxides, industrial waste, and untreated industrial waste water variables and found that an increase in index of 1 SD was related to an increase in the expected infant mortality rate of 16 (95 % CI 2 to 30) per 100,000 live births.

Strengths and limitations

Strengths of the study is firstly using deprivation indicators from open access datasets that makes the data aggregation transparent. Moreover, it allows researchers to trace the entire process of transform primary indicators and to restore the original data. Secondly, the index includes both socio-economic and environmental characteristics that allow analyzing the multifaceted nature of factors influence on health. Furthermore, our methodology of development of the index allows including many more different variables (not only socio-economic ones as in many indices) and avoiding overloading indicator systems. Limitations to the study should be noted. Our study did not take into account possible confounders that could affect the results [32]. For instance, when studying the relationship of deprivation with overall mortality, there are not individual – level information on age, behavioral risk factors (alcohol, smoking use, physical activity), and when studying the relationship with infant mortality, there are not information on infant sex and gestational age as well as maternal age, behavioral characteristics and morbidity. Nakaya et al. [33] applied two regression models to estimate the relationship all-cause mortality with deprivation. First model adjusted by age, sex, and public health centre district and showed that the most deprived neighborhoods have 1.144 times higher (95% CI 0.987 to 1.326) HR for all-cause mortality compared with the least deprived ones. Second model adjusted by age, sex, public health centre district, histories of diabetes and hypertension, and body mass index and demonstrated that the most deprived neighborhoods have about 1.160 (95% CI 1.001 to 1.344) times higher HR for all-cause mortality compared with the least deprived ones. Calling et al. [34] analyzed the relationship between deprivation and mortality of the preterm infant. The index included low education, low income, unemployment rate, and social benefits. Two logistic models were used: (1) adjusted for maternal age and (2) adjusted for infant sex, gestational age, small for gestational age, maternal age and maternal marital status. First model showed that OR for mortality in preterm infants born in the most deprived neighborhoods was 1.33 (95% CI 1.12 to 1.58) times higher compared to preterm infants born in the least deprived ones. Second model showed that there is not statistically significant result when comparing the most deprived areas with the least deprived ones (OR: 0.99, 95% CI 0.82 to 1.20).

Conclusion

The study assessed the relationship the level of deprivation with all-cause and infant mortality and showed that there is a statistically significant relationship between deprivation and infant mortality, whereas there is not a link with all-cases mortality.

RDI require further study. We will continue to analyze the relationship of deprivation with health behaviors and outcomes. Evidence will be obtained from the Epidemiology of Cardiovascular Risk Factors and Diseases in Regions of the Russian Federation study (ESSE-RF) [35]. ESSE-RF is a large cross-sectional multicenter population-based study conducted in 2012-2014, covering 13 federal subjects of Russia, differing in climatic, geographic, economic, and demographic characteristics. Data were obtained from questionnaires administered face-to-face, by a brief physical examination, and fasting venous blood samples. Dataset of ESSE-RF study will be used to increase opportunities for high-quality research and analysis of the impact of deprivation on health in Russia, taking into account possible confounders. Also, in the future, it seems necessary to create an index using the methodology from this study to measure the level of deprivation at a small area level.

Overall, we sought to create an easy-to-calculate and interpret index, which implies its use both in the practical activities of public health specialists and policymakers. As far as we are aware, this is the first deprivation index characterizes the level of physical environmental and socio-economic deprivation of Russian regions. Moreover, it makes it possible to carry out comparative regional assessments of inequality in relation to population health. The research findings demonstrate the need for further study of the impact of deprivation on health both at the population and individual level in order to a more in-depth study of the mechanisms of the development of the social gradient of health.

Acknowledgements

None.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

All authors discussed the results and contributed to the final manuscript.

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Received on January 30, 2022. Accepted on November 10, 2022.

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How to cite this article: Zelenina A. Russian subject-level index of multidimensional deprivation and its association with all-cause and infant mortality. J Prev Med Hyg 2022;63:E533-E540. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2498

HEALTH PROMOTION

What do young people know about HIV? Results of a cross sectional study on 18-24-year-old students

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Keywords

Students • HIV knowledge • HIV perception • HIV prevention

Summary

Introduction. *Increasing people's knowledge of transmission, prevention, early diagnosis, and available treatments is a key step toward HIV control; it means setting the conditions for empowerment and enabling individuals to make aware choices about the prevention strategy best suited to their needs. This study aims to identify unmet needs on HIV knowledge among freshman students.*
Methods. *A cross sectional study was carried out at the University of Cagliari, which is an Italian public state university. Data were collected by means of an anonymous questionnaire; the final sample included 801 students.*
Results. *Results offer a detailed picture of students' knowledge and perceptions of HIV. Several topics deserve to be better understood by students, but the main gaps relate to the pre-exposure prophylaxis and the decreased likelihood of sexually transmitting HIV due to early treatments. Students' vision of the quality of life of people living with HIV was negatively affected by perceiving as relevant the effects of HIV on physical health or on sexual/affective domains, while conversely, it seemed positively affected by knowing that current treatments are useful for counteracting physical symptoms and decreasing the possibility of transmitting HIV.*
Conclusion. *Being aware of the potential benefits of current therapies could favour a less negative view, in line with the current state of the beneficial effects of HIV treatment. Universities are a valuable setting to bridge the HIV knowledge gap and thus also contribute to tackling stigma and actively promoting HIV testing.*

Introduction

Currently, in the field of HIV, numerous benefits are ensured from the diagnostic and therapeutic advancements. Since 2000, the epidemiological trend suggests a positive evolution of HIV management. The global incidence decreased from 2.7 million in 2000 to 1.5 million in 2020, while AIDS related death decreased from 1.4 million in 2000 to 680.000 in 2020, and the prevalence of people living with HIV increased from 25.5 million in 2000 to 37.7 million in 2020 [1].
Although progress in HIV testing and treatment has reduced the disease's spread and improve affected people's health and well-being, HIV is still a serious public health issue, at the foreground of the public health agenda. Further reducing the possibility of transmission, promoting the early diagnosis, improving the access and coverage of effective HIV antiretroviral therapy, and contrasting stigma are the milestones to achieve HIV control [2-7].
At the community level, the lack of knowledge and the subsequent misconceptions about HIV not only foster stigma and discrimination but are also among the main barriers to primary and secondary HIV prevention. Low perceived risk of HIV and fear of HIV diagnosis are frequent reasons for late testing [8,9]. Other barriers can be related to difficulties accessing health care services, specifically for migrants and black and minority ethnic populations and for those who are socioeconomically underprivileged. Language and religion, as well as taboos about discussing sexual behaviors and identities further highlight the cultural barriers, along with racism, discrimination, and isolation [10, 11]. Although knowledge is not the only factor that affects an individual's behaviour, it is certainly an important part of making conscious choices [12]. People should be able to identify potentially risky behaviours, and they should know all existing opportunities to manage the risk in those situations; they also should be aware of the benefits of early diagnosis which, in combination with current treatments, allows people living with HIV to have a good quality of life [12-15]. Some studies indicate that the 15-24 age group is the most at risk of contracting HIV and the least worried about incurring risky behaviour [16-19]. Monitoring young people's knowledge of transmission, prevention, early diagnosis, and available treatments is a key step toward HIV control [12, 14-24].
In the context of Italy, it is reasonable to assume that young people's knowledge about HIV is limited. In fact, ministerial teaching programs for secondary schools do not include sex education, and institutional communication on this topic is occasional and mainly

focused on condom use. This study aims to identify unmet needs on HIV knowledge among Italian students aged between 18 and 24 years, a crucial target for HIV control. In Italy, the incidence of new diagnoses of HIV infection, had increased until the second half of the 1980s, gradually declined in the 1990s, stabilised from 2000 to 2010, and since 2010 it has shown a decreasing trend again. Currently, Italy has an incidence of newly diagnosed with HIV of 4.2 per 100,000 residents, ranking among the nations that are slightly below the average value of European Union countries, which is equal to 4.7 cases per 100,000 residents. In 2019 the highest incidence of HIV was observed among people aged 25-29 (10.4 new cases per 100,000 residents) and 30-39 (9.8 new cases per 100,000 residents). However, the analysis of time trends suggests that the 15-24 age group should be given careful consideration. In fact, temporal trend data disaggregated by age group highlight that the incidence decrease is clear in the age groups above 25, while in the 15-24 age group, substantial stability was observed from 2012 to 2017. Additionally, Italian data show that in 2019, 58.7% of people newly diagnosed with HIV were diagnosed late (CD4 < 350 cells/μL) [25]. In line with these observations, the present study aims to achieve the following objectives:

- assessing knowledge of HIV transmission, prevention and testing;
- assessing the perceived benefits of early diagnosis and current treatments;
- exploring students' conception of HIV, perceived quality of life of early diagnosed people, and beliefs about the consequences of HIV in daily life;
- exploring the association between the envisioned quality of life of early diagnosed people and knowledge/misconceptions of HIV.

Methods

This study was carried out in 2019 at the University of Cagliari, which is an Italian public state university with six faculties: medicine, biology, science, engineering, economics and law, and humanistic/humanities. The study was carried out through the administration of a questionnaire to freshman students in the 18-24 age group of the different faculties; it involved 18-24-year-old freshman students to ensure that their knowledge and perceptions of HIV were not influenced by the subjects studied during the university classes or affected by other experiences. The investigation was authorised by the Vice Rector for Training Programs and by the deans of the six faculties of the university. The University Ethics Committee assessed the questionnaire and concluded that formal approval was not necessary because only non-sensitive data were collected.

Data were collected by means of an anonymous questionnaire administered by the researchers in the classrooms at the beginning of the lectures, through a previous agreement with tutors and lecturers. To guarantee students total anonymity, tutors and lecturers were not involved in the questionnaire administration or subsequent collection. Before administering the questionnaires, the researchers specified that the survey would focus on HIV knowledge and perceptions, no identifying data would be collected, the results of the survey would be published only in aggregate form, and participation in the survey was voluntary (those who did not wish to participate could return the questionnaire not completed). To minimise the risk of potential bias, students were not notified in advance of the study.

Knowledge of transmission, prevention, and consequences of being diagnosed with HIV, the perception of implications of early diagnosis and current therapies, and the envisioned quality of life of a person with an early HIV diagnosis were explored through an ad hoc questionnaire. The questionnaire, available on request, included questions on the main sociodemographic data (age, gender, attending biological/medical courses *vs* other courses), one open-ended question asking respondents to write the first word that comes to mind when they hear the term HIV, and subsequently, several closed questions on the following topics:

- knowledge of the main biological outcome of HIV: sporadic immune deficiency crises *(yes or no),* high fever *(yes or no)*, infertility *(yes or no)*, chronic loss of immune defences *(yes or no)*;
- knowledge of infection transmission routes: handshake *(yes or no)*, sweat *(yes or no)*, shared use of needles for injections, piercings or tattoos *(yes or no)*, breastfeeding *(yes or no)*, semen *(yes or no)*, saliva *(yes or no)*, vaginal secretions *(yes or no)*, tears *(yes or no)*, coughing *(yes or no)*, blood *(yes or no);*
- knowledge of protection from HIV: condom *(yes or no)*, birth control pills *(yes or no)*, oral sex *(yes or no)*, pre-exposure prophylaxis *(yes or no)*;
- knowledge of the minimum time required for diagnostic testing after possible/suspected exposure to HIV: 16 days *(yes or no)*, 30 days *(yes or no)*, 90 days *(yes or no)*;
- knowledge of services to carry out the test in the shortest possible time: general practitioner *(yes or no)*, emergency department *(yes or no)*, diagnosis centre without a general practitioner's prescription *(yes or no)*, pharmacy *(yes or no)*;
- perceived consequences of early HIV diagnosis: improving the effectiveness of therapy *(yes or no)*, worsening quality of life because it provides awareness of the disease before the symptoms *(yes or no)*;
- perception of potential benefits of current HIV therapies: counteracting symptoms *(yes or no)*, decrease in the likelihood of sexually transmitting HIV *(yes or no)*, increase in life expectancy *(yes or no)*, possibility of undergoing post-exposure prophylaxis *(yes or no)*;
- envisioned quality of life of a person with HIV diagnosed at an early stage: worse than people without HIV (from here defined as poor) or comparable to that of people without HIV (from here defined as good) (*only one answer*);

- perceived HIV impact on different domains of the life of a person living with HIV: effects of the disease on physical health *(very relevant, quite, a little, not at all)*, effects on the sexual/affective domain *(very relevant, quite, a little, not at all)*, effects on the emotional/psychological domain *(very relevant, quite, a little, not at all)*, social stigma *(very relevant, quite, a little, not at all)*, discrimination in the workplace *(very relevant, quite, a little, not at all)*.

Data were analysed using descriptive analysis and are expressed as relative frequencies with 95% confidence intervals. Gender differences, as well as differences between students attending biological/medical courses and those attending other courses, were assessed through chi square tests. A multivariate logistic regression analysis was performed to explore factors that affect the students' envisioned quality of life of people with an early diagnosis of HIV. An envisioned good quality of life *vs* a poor one was the dependent variable. The following factors were included as independent variables: gender, being aware that current therapies counteract symptoms (*yes vs no*), being aware that current therapies decrease the possibility of transmission (*yes vs no*), being aware that current therapies increase life expectancy (*yes vs no*), being aware that early diagnosis improves the effectiveness of therapy (*yes or no*), thinking that early diagnosis worsens quality of life due to awareness of the disease before the symptoms (*yes or no*), perceiving very relevant effects of HIV on physical health (*very relevant vs quite/a little/not at all*), perceiving very relevant effects of HIV on the sexual/affective domain (*very relevant vs quite/a little/not at all*), perceiving very relevant effects of HIV on the emotional/psychological domain (*very relevant vs quite/a little/not at all*), perceiving it as a very relevant social stigma (*very relevant vs quite/a little/not at all*), perceiving it as very relevant to discrimination in the workplace (*very relevant vs quite/a little/not at all*). Non-significant associated variables (p value ≥ 0.05) were consecutively deleted from the logistic model, and at each round the goodness of fit of the model was assessed through the likelihood statistic. The final regression model includes only significantly associated variables.

Results

A total of 871 questionnaires were administered, but 10 were excluded from the analysis because they were not completed, and additional 60 were excluded because the respondents' age was greater than 24 years old. The final sample included 801 university freshmen aged between 18 and 24; 48.3% (95% CI 44.9-51.8%) were attending the first year of a biological/medical course. Regarding gender, 57.6% of the respondents defined themselves as women, 41.9% defined themselves as men, and 0.5% indicated "undefined gender".

Regarding knowledge about the main biological outcome of HIV, respondents had to give a yes/no answer for each of four listed possibilities. The results revealed students' uncertainty on this item: the chronic loss of immune defences was indicated by 85.4% (95% CI 82.9-87.8%) of interviewees, the sporadic immune deficiency crises by 68.3% (95% CI 65.1-71.5%), the high fever by 53.8% (95% CI 50.4-57.3%), and infertility by 10.9% (95% CI 8.7-13.0%). Only 7.0% of respondents properly (95% CI 5.2-8.8%) indicated yes for "chronic loss of immune defences" and no for the other listed possibilities.

Knowledge of the transmission routes of HIV is illustrated in Table I.

Most students recognised the role that blood (96.1%), shared use of needles (94.4%), semen (91,4%), and vaginal secretions (85,0%) can play in the transmission of infection. Conversely, the possibility of virus transmission through breastfeeding, indicated by 30.6% of respondents, appears considerably less well known. Regarding the ways in which HIV cannot be transmitted, most students were aware that transmission cannot occur through handshake (95.0%), tears (92.1%), sweat (84.3%), and cough (82.6%), but only 64.2% know that saliva cannot transmit the virus. Overall, 14.0% of respondents (95% CI 11.6-16.4%) correctly identified all the ways in which the virus can be transmitted and all the ways in which it cannot be transmitted.

Concerning the knowledge on tools and strategies to prevent HIV, almost all interviewees identified condoms (98.5% CI 97.7-99.3%); pre-exposure prophylaxis was indicated by only 20.8% (CI 18.0-23.7%) of respondents. The awareness that the contraceptive pill does not protect

Tab. I. Knowledges on the transmission routes of HIV.

Item: transmission of HIV		Relative frequencies of correct answers %	95% Confidence Interval
Routes through which HIV can be transmitted	Blood	96.1	94.8-97.5
	Shared use of needles (piercings…)	94.4	92.8-96.0
	Semen	91.4	89.4-93.3
	Vaginal Secretions	85.0	82.5-87.5
	Breast milk	30.6	27.4-33.8
Routes through which HIV cannot be transmitted	Handshake	95.0	93.5-96.5
	Tears	92.1	90.3-94.0
	Sweat	84.3	81.7-86.8
	Cough	82.6	80.0-85.3
	Saliva	64.2	60.8-67.5

Tab. II. Knowledge on diagnostic tests for HIV.

Item: test for HIV		Relative frequencies of answers %	95% Confidence Interval
How long a person should wait to get tested for HIV after suspected exposure	16 days	14.2	11.8-16.7
	30 days	28.8	25.7-32.0
	90 days	27.5	24.4-30.6
Where a person should go to get tested for HIV	NHS Diagnostic Centre	56.8	53.4-60.2
	General Practitioner	67.8	64.6-71.0
	Emergency Department	48.7	45.2-52.2
	Pharmacy	18.5	15.8-21.2

against HIV is widespread (90.6% CI 88.6%-92.7%), while understanding that limiting oneself to oral sex does not avoid the risk of HIV infection seems to be slightly less prevalent (70.8% CI 67.6-73.9%). Only 14.0% of the respondents (CI 11.0-16.1%) showed comprehensive knowledge of both the ways to avoid infection and the ways that do not protect against the risk of HIV.

The results of students' knowledge on diagnostic tests are shown in Table II.

Only 14.2% of students believed that it is possible to get tested from 16 days after a potential risky exposure; the possibility to be tested from 30 and 90 days after the risk exposure was known by 28.8% and 27.5% of the students, respectively. Overall, 5.7% of students (CI 4.1-7.4%) correctly indicated all three time intervals.

Regarding HIV testing services to go to in case of need for testing at the earliest possible time, 56.8% of students were aware of the possibility of going to National Health System diagnostic centres without a GP's prescription. General practitioners in Italy do not routinely provide this service, but the possibility was indicated by 67.8% of students; the emergency department was indicated by 48.7% and pharmacies by 18.5%.

Concerning the knowledge/perception of the implications of early HIV diagnosis, the idea that early diagnosis improves the effectiveness of therapy was shared by 78.8% (CI 75.9-81.6%) of students, while the idea that it worsens the quality of life because it provides awareness of the disease before the symptoms was shared by 15.0% (CI 12.5-17.5%).

The analysis of answers given to the question on the knowledge/perception of HIV treatments highlights that 84.4% (CI 81.9-86.9%) of students thought that the current therapies increase life expectancy; 65.3% (CI 62.0-68.6%) knew that treatments are useful for counteracting symptoms, and 53.4% (CI 50.0-56.9%) that treatments decreased the possibility of sexually transmitting HIV. The existence of post-exposure prophylaxis was known by 67.4% (CI 64.2-70.7%).

To explore freshmen's conception of HIV, the questionnaire included an open-ended question asking for the first word/thought that comes to mind when they hear the term HIV.

The transmission of the virus through sexual intercourse or by blood, was the first thought that 43.3% (CI 37.4-45.6%) of respondents associated with the term HIV. A further 32.2% (CI 27.0-34.7%) of interviewees thought at first glance about the consequences of the transmission; among these, approximately one-fifth referred to a general immune system deficit, while the remaining identified HIV with AIDS or wrote words such as "*incurable disease*", "*fear*", "*suffering*" or "*death*". Only 15.0% (CI 11.4-17.3%) of the students when faced with the term HIV thought about the possibilities of prevention; most of these answers referred exclusively to primary prevention and mentioned condoms, but some were related to secondary/tertiary prevention mentioning "*current therapies that prevent HIV from becoming AIDS*". In 5.5% (CI 3.4-7.1%) of the responses, the term HIV was associated with famous people who have died of AIDS or with men who have sex with men (quoted as "*homosexuals*"), sex workers (quoted as "*prostitutes*"), and people with substance use disorders (quoted as "*junkies*"). Finally, 1.6% (CI 0.5-2.6%) of the interviewees thought about the misinformation existing on the subject, a further 1.8% (CI 0.7-2.9%) thought about the existing prejudices, and 0.5% (0-1.1%) thought about decreasing the spread of the infection.

The quality of life of a person with early diagnosed HIV was envisioned as potentially good by 57.3% of interviewees (CI 53.9-60.7%).

The perceived impact of HIV on different life domains of people living with HIV are shown in Table III.

A large proportion of students stated that the effects on the affective/sexual domain (83.8%) and on the psychological/emotional domain (79.8%) were very relevant. The rate of students who considered it very relevant to the effects on physical health was 65.7%; social stigma was perceived as a very relevant effect by 47.8%, while discrimination in the workplace was perceived as very relevant by 31.3% of students.

Overall, the knowledge/perception of the explored items showed a substantial overlap between men and women, and between students attending biological/medical courses and students of other courses. The only relevant differences relate to the following: the existence of pre-exposure prophylaxis, which was more known by men (21.6% *vs* 15.0%, p value 0.02); the impossibility of HIV transmission through sweat, which was more known by women (92.4% *vs* 86.6% p value 0.01); the possibility of going to the National Health System diagnostic centres without a GP's prescription to be tested for HIV, which was more known by women (66.1% *vs* 55.5% p value < 0.01) and the existence of post-exposure prophylaxis, which was more known by students attending biological/medical courses (74.6% *vs* 60.6% p value < 0.01).

Tab. III. Prevalence of students who perceive the impact of HIV in different life domains of people living with HIV as very relevant.

Domains	Prevalence of students who perceive a very relevant impact %	95% Confidence Interval
Sexual/affective domain	83.8	81.2-86.3
Emotional/psychological domain	79.8	77.0-82.6
Physical health	65.7	62.4-69.0
Social stigma	47.8	44.4-51.3
Employment discrimination	31.3	28.1-34.5

With regard to the association between the envisioned quality of life of early-diagnosed people and the knowledge/perception of HIV topics, the multivariable logistic regression analysis revealed that some of the explored independent variables were not significantly associated. More specifically, perceiving as very relevant the effects of HIV on the emotional/psychological domain, the social stigma, and the discrimination in the workplace were not significantly associated with students' envisioned quality of life of people with an early diagnosis of HIV. Additionally, these variables do not show confounding effects; therefore, they were deleted from the model. The final logistic model, highlighting factors significantly affecting the students' perspectives is shown in Table IV.

The probability of envisioning a good quality of life 1.45-fold higher in women than in men. It was 1.75-fold higher in students who knew that current treatments are useful for counteracting symptoms than in students who did not know this; it was 1.96-fold higher in students who knew that current treatments decrease the possibility of transmitting HIV than in student who did not know it. Conversely, the probability of envisioning a good quality of life was approximately halved in students thinking that early diagnosis worsens the quality of life because it gives awareness of the disease before the symptoms (OR 0.48), and in students perceiving a relevant effect of HIV on physical health (OR 0.61) or on the sexual/affective domain (OR 0.55).

Discussion

Increasing knowledge about HIV protection, testing, and treatments is one of the strategies to support HIV control. This study provides a snapshot of young students' knowledge and perception of HIV, providing insights to strengthen prevention efforts. The results highlight several topics that deserve to be better understood by young people.

Overall, awareness of the potential consequences of HIV appears to be limited; more than half of the students indicated both chronic and sporadic loss of immune defences as consequences of the infection, showing that they have confused ideas on this aspect. Regarding primary prevention of HIV, our results show that knowledge of the main transmission routes was widely spread among students. The only exception was breastfeeding, which was recognised as a potential virus vector by only one third of the sample, in line with the findings of other studies [15, 16, 23]. This lack of knowledge may be affected by the young age of the respondents, for most of whom breastfeeding is not an issue in their daily lives. In turn, almost all students appeared to be aware of the possibility of transmission through semen, vaginal secretions, and sharing needles. However, the answers given by respondents on HIV protection suggest some shortcomings. All respondents knew that condoms protect against the virus, but approximately 1/3 of them believed that the virus cannot be transmitted during oral sex, a misconception found in other studies focused on students [21-24]. These results are consistent with the institutional information disseminated in Italy in the period preceding our survey [26-29]. Between 2017 and 2019, the campaign "*With HIV you cannot joke, protect yourself and others*" was implemented with the main focus on condom use; it was directed at a young target population and used an ironic style, but did not clarify that condoms use is appropriate in any type of

Tab. IV. Factors affecting the probability of envisioning a good quality of life for people with early diagnosis of HIV.

Factors		Odds Ratio	95% Confidence Interval	p value
Gender	Men	1	-	0.03
	Women	1.45	1.04-2.00	
Knowing that current treatments are useful for counteracting symptoms	No	1	-	0.003
	Yes	1.72	1.21-2.47	
Knowing that current treatments decrease the possibility of transmitting HIV	No	1	-	< 0.0001
	Yes	1.96	1.41-2.72	
Thinking that early diagnosis worsens the quality of life due to awareness of the disease before the symptoms	No	1	-	0.001
	Yes	0.48	0.31-0.74	
Perceiving as very relevant the effects of HIV on physical health	No	1		0.01
	Yes	0.61	0.43-0.87	
Perceiving as very relevant the effects of HIV on the sexual/affective domain	No	1	-	0.02

sexual intercourse, whether vaginal, anal, or oral. Future communication should focus on safer sex education and clarify any type of sexual practices and other concomitant factors that could increase the risks of transmission.

The lack of knowledge on the existence of pre-exposure prophylaxis was common in our sample; indeed, only 1/5 of students knew it. Sometimes people choose not to use condoms for various reasons, even though they know that condoms protect against HIV [30-31]. In these circumstances, if people are highly-exposed or generally at higher risk, pre-exposure prophylaxis could be the appropriate strategy to enhance protection, but it is necessary to raise awareness about it [14, 32, 33]. Lack of knowledge is among the barriers that need to be overcome to advocate the implementation of official prophylaxis policies and pre-exposure prophylaxis availability [12, 32-34]. Furthermore, it is important to advocate the availability of post-exposure prophylaxis and its use within the timeframe of 24-hours up to 72-hours following a risk of transmission, as this could prove to be fundamental in preventing the contraction of HIV [35]. Regarding HIV secondary prevention, although the results revealed that most students recognised the role of early diagnosis in improving the effectiveness of therapies, a remarkable lack of knowledge of when and where to get tested emerged. In Italy, the HIV test has rarely been the subject of institutional communication campaigns, and the last campaign, prior to this study, was conducted in 2010 [28, 29]. Obviously, the high percentages of wrong answers on the HIV testing do not necessarily indicate that people would not be able to find this information if they needed it. However, in a context such as Italy, where half of the population has an inadequate level of health literacy, namely, inability to navigate the health care system, this information should be disseminated in an active and approachable way [36]. Concerning the knowledge of benefits from early HIV treatments, the most noteworthy result in terms of unmet information needs was that only half of the students were aware of the decreased likelihood of sexually transmitting HIV. Although this information has spread over time, a knowledge gap still exists, especially at the general community level [37]. To counteract stigma and discrimination, the benefits of "Treatment as Prevention" should be fully recognised, not only by people living with HIV and their potential sexual partners, but also by the general population.

Students' overall views and perceptions of HIV confirmed the existence of misconceptions and a lack of knowledge. The word HIV recalls the possibility of prevention for only a minority of students. In approximately a quarter of the interviewees, the term HIV evokes mental associations that suggest the existence of stigma and stereotypes towards the infection or the affected people. It is noteworthy that the term HIV call forth words such as "*homosexuals*" or "*prostitutes*" in students' mind. This suggests that the narrative about HIV is still negative and that people living with HIV are still stigmatized. It seems that for some students, the risk of HIV transmission concerns specific groups of people rather than behaviuor that anyone could engage in. Reducing stigma is crucial to making a difference in the HIV prevention.

Almost half of the respondents believed that the quality of life of a person with an early HIV diagnosis is poor. Their vision of the quality of life of people living with HIV was negatively affected by perceiving as relevant the effects of HIV on physical health or on sexual/affective domains, while conversely, it seemed positively affected by knowing that current treatments are useful for counteracting physical symptoms and decreasing the possibility of transmitting HIV. These findings, therefore, support the hypothesis that being aware of the potential benefits of current therapies could favour a less negative view, in line with the current state of the beneficial effects of HIV treatment. According to the current literature, fear of being diagnosed with HIV is one of the individual barriers to accessing testing; fear, in turn, is influenced by misconceptions that still exist about HIV [37-40].

However, currently, HIV is no longer synonymous with AIDS, and the quality of life in people diagnosed and treated in the early stages, can be comparable to that of the general population. Raising awareness of these topics could contribute to reduce fear and encourage HIV testing, with a positive impact on early diagnosis and, consequently, on the control of HIV [37-40].

The present study offers a detailed picture of unmet needs about HIV information among freshman students attending an Italian public state university. Some limits should be recognised. The study is monocentric, although the students attending the University of Cagliari come from different Italian regions, especially in courses with restricted access because access rankings are nationwide. Only university freshmen were eligible to participate in this study to avoid the risk of information bias due to the subjects studied in biological/medical courses. Referring the results to all university students and more generally to young people who have graduated from college should be done with caution because potential bias cannot be ruled out with certainty. However, the main findings are in line with other HIV knowledge studies, so it is reasonable to assume that the impact of this potential bias is limited.

Conclusion

Information obtained from first-year university students could be useful for implementing prevention interventions tailored to young people. Bridging the knowledge gap is a complex task that requires striking a balance between alerting people about HIV's seriousness and reassurance about the current outcomes of early diagnosis. These two approaches seem to be at odds with each other, but both play a crucial role in HIV control. Future communications in university settings should emphasise that people living with HIV can envision a better life expectancy as it is now a chronic and manageable condition, provided it is diagnosed early

and treatment is started early [41-42]. At the same time, the communications should not diminish the seriousness of HIV, and should continue to promote primary prevention tools. Providing comprehensive knowledge on all these aspects means setting the conditions for empowerment and enabling individuals to make aware choices about the prevention strategy best suited to their needs [12]. Universities are a valuable setting to bridge the HIV knowledge gap and thus also contribute to tackling stigma and actively promoting HIV testing. Health topics, such HIV prevention and control, could be embedded into university culture, processes and policies, and the potential benefits would affect not only students but also the communities to which those students belong and on which they have an impact [43, 44].

Authors' contributions

Conceptualization: CS, MP, LC; study design: CS, PC; Literature search: AL; data collection and management: LF, data analysis: CS, AM; writing original draft: CS, AM. Review and editing: CS, AM, AL, LF, MP, LC, PC. All authors have read and agreed to the published version of the manuscript.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Received on March 30, 2022. Accepted on November 9, 2022.

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How to cite this article: Mereu A, Liori A, Fadda L, Puddu M, Chessa L, Contu P, Sardu C. What do young people know about HIV? Results of a cross sectional study on 18-24-year-old students. J Prev Med Hyg 2022;63:E541-E548. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2555

HEALTH PROMOTION

Effect of sexual enrichment program on the sexual satisfaction of pregnant women in Iran: A randomized clinical trial

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Keywords

Training program • Sexual satisfaction • Pregnant women • Clinical trial • Iran

Summary

Background. *To improve the sexual satisfaction of pregnant women, there needs to be a culturally appropriate sex education program. This study aimed at determining the effectiveness of a sexual enrichment program on the sexual satisfaction of pregnant women.*

Methods. *This single-blind randomized clinical trial was conducted on 61 pregnant women aged 18 to 35 years old with low-risk pregnancies and gestational ages of 14 to 32 weeks, who had referred to three healthcare centers in Mashhad. The participants were randomly assigned to two groups of control (n = 31) and intervention (n = 30) based on a table of blocks of four. The intervention group, in addition to receiving routine pregnancy training, participated in six one-hour sessions of a sexual enrichment program held on a weekly basis, while the control group received only the routine pregnancy healthcare. Larson's sexual satisfaction questionnaire was used to assess the sexual satisfaction of pregnant women prior to the study and two weeks after the intervention. Comparison of mean scores between and within the two groups was performed using SPSS software (version 21) using independent and paired t-tests.*

Results. *After the intervention, there was a significant difference between the mean sexual satisfaction scores of the two groups (p = 0.02). Comparison of the differences between the mean sexual satisfaction scores of the intervention group before and after the intervention indicated a significant change (p = 0.009), while in case of the control group this change was not significant (p = 0.46).*

Conclusion. *A sexual enrichment program can be effective in improving the sexual satisfaction of pregnant mothers.*

Introduction

Sexual satisfaction is considered an important component of sexual health, a sexual right and an outcome of sexual well-being [1]. Sexual dissatisfaction of the couples accounts for 80% of marital conflicts and disagreements, and it causes many psychological disturbances and an increased number of infidelity [2].

Women's sex life is affected by pregnancy. Due to multiple physical and psychological changes which occur during pregnancy, there might also be fluctuations in sexual relations of the couple, including feelings, sexual desire, the frequency of intercourse and sexual satisfaction [3, 4]. The prevalence of sexual problems in non-pregnant women is between 30% and 46%, but during pregnancy, it reaches 57-75% [5-8]. The prevalence of sexual dysfunctions in the first trimester of pregnancy is 46.6%, in the second trimester it is 34.4%, and in the third trimester, it reaches 73.3% [5, 9]. Various reports also indicate a gradual decline in sexual desire and satisfaction throughout pregnancy [10, 11]. According to a study by Lee and colleagues (2002) in Taiwan, the frequency of intercourse decreases from the first to the third trimester [12].

Although there are no specific reasons for limiting sexual activity in pregnancy, and the use of safe, hygienic and non-violent methods is innocuous [3], sexual issues are often overlooked during pregnancy, and couple's information is often based on superstition and false beliefs [13, 14]. In some cases, the misconceptions and inadequate information of couples about sexual relationships during pregnancy and the negative attitudes toward these issues lead to the decrease or cessation of sexual relationships, which in turn results in a reduced emotional and affectionate relationships on the part of the husband and it also causes anxiety and lower self-confidence for the mother [15]. Research shows that women due to some reasons such as fear of injury to the fetus, abortion, premature rupture of the amniotic sac, preterm delivery, infection, painfulness of the intercourse, and discomfort due to large abdomen avoid sexual relationships during this period [16-18]. This will cause confusion and disagreement among the couples [19] exactly at a time when they need to be closer to each other more than any other time. Since women refrain from sexual relationship during this time, violence in couples' relationships often begins or worsens during pregnancy [15] and men experience the first sexual

relationship outside the family during the pregnancy of their wives [15, 20].

Though pregnancy can be the beginning of marital conflicts and sexual discontent, it is also a good time to create a strong sense of intimacy and mutual commitment [11, 10]. According to Lee (2002), sexual activity during pregnancy improves self-identity, empowers sexual relations, strengthens marital bonds, and reinforces the value of sexuality [12]. Since during pregnancy women have more emotional needs, their sexual orientation declines, which in many cases is rooted in their misconceptions and their beliefs, proper education and counseling can be helpful to lower the problems [21]. Through sexual counseling, people acquire the necessary information and knowledge about sexuality and form their attitudes, beliefs, and values [19]. Research has already confirmed the effect of educational interventions on the sexual performance of couples. In a study by Heidari and colleagues, it was found that the educational program had an impact on sexual performance and satisfaction of pregnant women, and therefore, the researchers concluded the effectiveness of sex education for pregnancy [5].

The sexual enrichment program is one of the educational and counseling programs on women's sexual satisfaction. Sexual enrichment enhances couples' current sexual relationship, and leaves no need for relationships outside of the family, and provides the couples with complete spiritual relief. In this counseling method, the couple are advised to have realistic and positive expectations. These expectations help to increase sexual satisfaction and intimacy, and intimacy in turn for each side creates a sense of the importance of the other side [22].

Despite the importance of sexual relations in pregnancy, and the emphasis of the previous studies that sexual issues should be an important part of prenatal care [23], not only such information on how couples should manage sexual life and meet sexual needs in pregnancy is not provided to couples [5, 24-29], but also during pregnancy, the couples are not provided with information and education on sexual health [5, 30, 31]. Therefore, a culturally appropriate sexual education program is required to improve the sexual satisfaction of pregnant women. Since the framework of sexual enrichment program is easy to implement, and since no study exists on this issue, it seems necessary to conduct the current study. This study aimed at determining the effectiveness of the sexual enrichment program on the sexual satisfaction of pregnant women.

Methods

Study design

This study was a single-blind randomized clinical trial with two groups. It was registered in the Iranian Registry of Clinical Trials (registration code: IRCT2016022526757N1) and is reported based on the CONSORT statement 2010 checklist**.**

Participants

This randomized clinical trial with two parallel groups (intervention and control groups) was conducted from August 2016 to February 2017 in Mashhad, Iran, on 61 pregnant women. Participants were 18 to 35-year-old women with gestational ages of 14 to 32 weeks who also had other characteristics including being healthy and at low-risk pregnancies; having singleton pregnancies; without embryonic anomalies; having no sexual problems before the pregnancy; having no medical and obstetric problems (including diabetes, hypertension, heart disease, history of drug use, placenta previa, cerclage); having no history of primary and secondary infertility; having no midwifery problems in previous pregnancies (including abortion, stillbirth, preterm labor, fetal anomalies) and having no psychological problems either themselves or their husbands. The participants and their husbands were required not to have a history of alcohol and drug abuse, and they were required to have at least elementary school education. Having no history of previous marriage or a lawsuit and a divorce request were the other inclusion criteria. Exclusion criteria also included the occurrence of medical and obstetric problems during the study, and failure to attend all educational sessions or failure to complete the questionnaires.

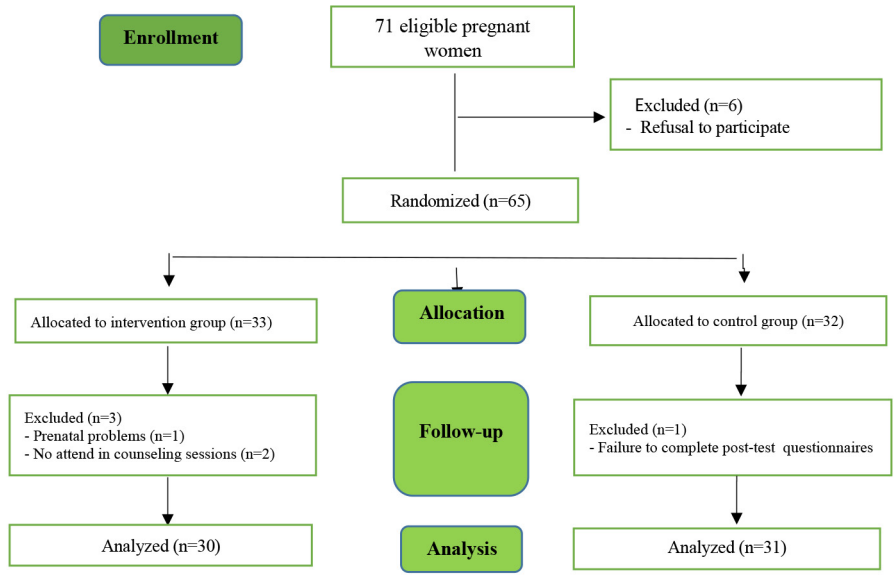
Based on Fatehizadeh's study [32] and taking into account the mean difference formula, a confidence interval of 95% (α = 0.05), and a test power of 90% (β = 0/10), the minimum sample size was estimated to be 30 in each group, and with the inclusion of 10% of sample dropout, a total of 65 people were selected to take part in the study.

To select the participants, among the five health centers of Mashhad city (from number 1 to 5), three health centers (health center number 1, 2 and 5) were selected through cluster sampling. Then, a comprehensive health service center was selected from each of the centers through cluster sampling (Bahar, Shahid Fatiq and 17 Shahrivar). Subsequently, using the registry book of pregnant women, eligible women (71 women) were listed. Of these, 65 consented to participate in the study.

Randomized blocks size of 4, was used to randomly assign samples to each of the intervention and control groups. In this way, first six possible states of the blocks were listed (AABB, ABAB,ABBA, BBAA, BABA, BAAB). Then, each block was assigned a number from 1 to 6. One number (between 1 and 6) was randomly selected and individuals were assigned to the (A) and (B) based on the respective block, and this continued until the sample size was completed.

33 people were assigned to the intervention group and 32 people were assigned to the control group. Of these, 3 people in the intervention group (1 due to prenatal problems and 2 because of unwillingness to attend the counseling sessions for personal reasons) and 1 in the control group (due to failure to complete post-test questionnaires) were excluded from the study (Fig. 1).

Fig. 1. Flowchart of the study.



Procedures and measurements

After extracting the names of qualified pregnant women from health records, they were contacted by telephone and the willing ones were invited to participate in the study. After obtaining written consent from the participants, all members of both groups completed the Larsson Sexual Satisfaction Questionnaire. Then, the intervention group, in addition to routine healthcare, received sexual counseling sessions. Considering the appropriate number of people for group counseling and also based on the suggested time and the possibility of participants attending the counseling sessions, the intervention group was divided into 3 group counseling groups (8, 10, and 12 people).

Sexual enrichment counseling and education classes were held in form of six weekly one-hour sessions for each group in the healthcare center. The training was conducted by one of the researchers (a graduate student), who is a midwife trained in sexual counseling. Meetings included group discussions, question and answer, slideshow, assignment setting and checking the previous session's tasks. Educational content was developed based on existing books [33], then using the judgment of specialists in sexology (as well as taking into account the educational needs of pregnant women and the Iranian culture), the content was modified. The control group received only routine pregnancy care. Two weeks after the intervention, the two groups completed Larson's Sexual Satisfaction Questionnaire again.

To maintain blindness in studying the outcome (sexual satisfaction), after determining which group the pregnant mother was assigned to, a code was assigned to her and based on that, a guide card with a code was given to her. Two weeks after the sixth session, each mother received the Larsson Sexual Satisfaction Questionnaire based on the code and the card she had, while the researcher was not aware to which group the participant belonged. The content of the sessions of the enrichment program is presented in Table I.

The Larsson Sexual Satisfaction Questionnaire was designed and developed by Hudson in 1981 [34]. This Questionnaire has 25 items on a five-point Likert scale which ranges from 1 (Never) to 5 (Always) [35]. All items except items 1, 2, 3, 10, 12, 13, 16, 17, 19, 21, 22 and 23 are scored in reverse. The minimum score on this scale is 25, and the maximum score is 125. A score of 25-50 indicates sexual dissatisfaction, a score of 51-75 indicates low sexual satisfaction, a score of 76-100 indicates average sexual satisfaction, and a score of 101-125 is interpreted as high sexual satisfaction. The questionnaire was completed before the intervention and then two weeks after the sixth session by both groups.

The reliability of the questionnaire in Larson's study was confirmed with Cronbach's alpha of 0.91 [35]. Bahrami and colleagues (2016) examined the face and content validity of the questionnaire and reported a Cronbach's alpha reliability of 0.93 [36].

Data analysis

Data were analyzed using SPSS software (Version 21). The assumption of the normality of the data distribution was checked through Kolmogorov-Smirnov test and paired t-test and independent t-test were used as the appropriate tests to compare the quantitative variables in two groups and the chi-square test was used for comparing the qualitative variables in two groups. A p-value less than 0.05 ($P < 0.05$) was considered statistically significant.

Results

The average age of the participants in the intervention and control groups was 27.69 ± 5.33 and 30.29 ± 5.32

Tab. I. How to implement the sexual enrichment program.

First Session 1. Welcoming and establishing rapport with the participants, introducing session norms, number of meetings and instructing how to complete the questionnaires 2. Giving the pretest 3. Explaining the sexual enrichment program and its purpose 4. Explaining the importance of the sexual relationship in pregnancy and its impact on the husband's sense of security and support
Second Session 1. Introducing false beliefs and inhibitors of sexual relationships in pregnancy 2. Familiarity with sexual and reproductive system changes during pregnancy 3. The appropriate method of intercourse in pregnancy and cases of its prohibition 4. Teaching the first type of touching (affectionate) and assignment setting
Third Session 1. Reviewing the previous meeting and checking assignments and talking about the experience of relaying the contents to the spouse 2. Teaching the second type of touching (sensual) and assignment setting
Fourth Session 1. Reviewing the previous meeting and checking assignment and talking about the experience of relaying the contents to the spouse 2. Teaching the third type of touching (playful) and assignment setting
Fifth Session 1. Reviewing the previous meeting and checking the assignment and talking about the experience of relaying the contents to the spouse 2. Teaching the fourth type of touching (erotic) and assignment setting
Sixth session 1. Reviewing the previous meeting and checking assignment and talking about the experience of relaying the contents to the spouse 2. Teaching the fifth type of touching (intercourse) and emphasis on the practice of learned touches. 3. Instructing how to generalize the training into everyday life 4. Emphasizing the repetition of skills for their stabilization

years, respectively. In terms of education level, 53.4% and 54.8% of the participants in the intervention and control groups had below high school diploma education, respectively. In terms of employment status, the majority of participants in the intervention (66.7%) and control (77.4%) groups were housewives.

There was no significant difference between the two groups in terms of the main characteristics such as occupation, education, kinship with husband, age difference with husband, husband's occupation, husband's education, type of housing, age, marriage age, Distance to previous pregnancy and gestational age (Tab. II).

In both groups 88.1% of the participants were multigravidae and there was no significant difference between the two groups. Moreover, 84.7% of pregnancies were planned and 96.2% of the participants were satisfied with the fetal sex, and the two groups were not significantly different in this regard.

Prior to the intervention, the mean sexual satisfaction scores in intervention and control groups were 113.17 ± 25.06 and 110.74 ± 22.88, respectively and there was no significant difference between the groups ($p = 0.69$). However, after the intervention, the results of the independent t-test showed a significant difference between the mean sexual satisfaction scores of the two groups ($p = 0.02$). The results of paired t-test also showed a significant difference between the mean sexual satisfaction scores before and after the intervention in the intervention group ($p = 0.009$), but this difference was not significant in the control group ($p = 0.46$). Another independent t-test comparing the mean differences between the two groups before and after the intervention also showed a significant difference between the two groups ($p = 0.01$) (Tab. III).

Regarding the frequency of different types of touch per week in the intervention group, affectionate touch had the most frequency and the intercourse touch was the least frequent (Tab. IV).

Discussion

The present study showed that sexual enrichment program can be effective in increasing the sexual satisfaction of pregnant women. Since the sexual enrichment program in the present study focused on reformulating the attitudes of participants towards sexual activity in pregnancy and providing the knowledge required for engagement in healthy sexual relationships, the resulting enhancement of participants' sexual satisfaction seems reasonable. In other words, training women and increasing their information reduces fear and therefore, improves their sexual satisfaction. This finding was consistent with reports of previous studies on the positive role of education of pregnant women in the improvement of their sexual performance and sexual satisfaction [5, 25, 28, 37-40].

Therefore it is recommended that couples are well educated to understand changes in sexual function

Tab. II. Comparison of demographic and midwifery characteristics of the participants in two groups of intervention and control.

Variable	Intervention group (n = 30)	Control group (n = 31)	P value
Qualitative variables			
Occupation Housewife Working Student	 8 (26.7) 20 (66.7) 2 (6.7)	 7 (22.6) 24(77.4) 0 (0)	0.83
Education Below high school diploma Diploma or Bachelor's Mater's or higher No answer	 16 (53.4) 10 (33.3) 3 (10) 1 (3.3)	 17 (54.8) 12 (38.7) 1 (3.2) 1 (3.2)	0.6
Kinship with husband Yes No No answer	 7(23.3) 22 (73.4) 1 (3.3)	 11(35.5) 20 (64.5) 0	0.4
Age difference Husband is older Wife is older The same age No answer	 25 (83.3) 5 (16.7) 0 (0) 0 (0)	 24 (77.5) 5 (16.1) 1 (3.2) 1 (3.2)	0.75
Husband's occupation Employee Self-employed No answer	 8 (26.7) 21 (73.3) 1 (3.3)	 10 (32.2) 21 (67.74) 0	0.76
Husband's education Below high school diploma Diploma or Bachelor's Master's or higher No answer	 18 (60) 8 (26.7) 1 (3.3) 3 (10)	 16 (51.6) 14 (45.2) 0 (0) 1 (3.2)	0.4
Housing Owned Rented Others	 11 (36.7) 18 (60) 1 (3.3)	 10 (32.3) 18 (58.1) 3 (9.7)	0.13
Quantitative variables	**Mean ± SD**	**Mean ± SD**	
Age Marriage age Distance to previous pregnancy (month) Gestational age before intervention (week)	 27.69 ± 5.33 2.79 ± 1.65 39.25 ± 41.45 22.86 ± 3.62	 30.29 ± 5.32 2.79 ± 1.65 75.23 ± 47.4 24.42 ± 3.27	0.06 [a] 0.1 [b] 0.06 [a] 0.08 [a]

SD: Standard Deviation; [a] Independent-samples t test; [b] Mann whitney test.

Tab. III. Comparison of sexual satisfaction scores before and after the intervention in the two groups.

Groups	N	Befor intervention	After intervention	Difference	Paired T- test
Intervention	30	113.17 ± 25.06	120.50 ± 16.51	7.3 ± 14.35	p = 0.009
Control	31	110.74 ± 22.88	109.16 ± 22.03	1.58 ± 11.99	P = 0.46
T- test		P = 0.69	P = 0.02	P = 0.01	

SD: Standard Deviation.

Tab. IV. Frequency of different types of touch in the intervention group.

Variables	Mean ± SD	Min.	Max.
Affectionate touch	3.58 ± 1.95	1	7
Sensual touch	1.65 ± 2.79	1	7
Playful touch	1.91 ± 2.69	1	8
Erotic touch	1.69 ± 2.19	1	8
Intercourse touch	1.44 ± 1.66	0	7

SD: Standard Deviation.

during pregnancy [41]. Many studies have emphasized that sexual education during pregnancy can reduce the fear and concern of the couples, and as a result, they can continue their close and intimate relationships and sexual activity during pregnancy [42-45].

A decrease in sexual satisfaction may cause a decrease in the mental comfort of pregnant women, a disturbance in the process of pregnancy, childbirth and postpartum. Therefore, there is an obvious need for sexual counseling during pregnancy [46]. In other words, a normal sex life during pregnancy is the key to becoming parents [47].

Although in terms of the impact of educational programs on the sexual satisfaction of pregnant women the present study is in line with many other ones, it is unique because it focused on a sexual enrichment program where the false beliefs and misconceptions of the participants were recognized and through using five types of touches and providing the participants with materials and appropriate ways of sexual relationship during pregnancy, their sexual satisfaction was improved.

The findings of this study are also inconsistent with the report of Wannakosit and Phupong (2010) in which there was no significant difference between sexual behavior and sexual satisfaction of pregnant women in the control and intervention groups after sex education. The reason for this difference might be the demographic characteristics of the participants and the content and manner of implementation of the program. In the present study, six one-hour weekly sessions were held using a special educational program, while in the study conducted by Wannakosit and Phupong, the participants were trained in a 20-minute class [48].

Concerning the five-fold touches in the intervention group (affectionate touch, sensual touch, playful touch, erotic and intercourse touch), the findings showed that affectionate touch had the highest frequency and sexual touch was the least frequent. The results of the research indicate that even those who, for any reason, had had no sexual activity or full sexual intercourse and had often used non-sexual touches and had maintained warm and intimate relationships with their spouses, reported higher sexual satisfaction than what they reported before the intervention and compared to what the control group reported. This finding implies that sexual satisfaction does not necessarily mean full intercourse, a point which has also been emphasized in the protocol of the sexual enrichment and is, in fact, one of the strengths and novelties of the present study. During these emotional relationships, women are more likely to feel protected and experience more calmness and comfort during pregnancy. Evidence strongly suggests that non-genital sexual behavior is important for stimulation, pleasure, and orgasm of many people. According to Galinsky (2012), there is a positive relationship between sexual touch and satisfaction with emotional relationships. She also reported that people who do not engage in sexual touch during sexual intercourse are more likely to suffer from arousal, erection, and orgasm disorders [49].

Although the participants in the study were only pregnant women and their spouses did not participate in the training sessions, based on the implementation guidelines of the enrichment program which recommend participants to transfer information to their partners, the sexual enrichment program could increase the sexual satisfaction of the pregnant women. Heidari and colleagues (2017) also reported no significant differences in sexual functioning and sexual satisfaction of pregnant women who participated in their education programs with their spouses and received a training booklet and those who were participated in the training classes by themselves but had studied the booklet along with their spouses. The researchers concluded that if pregnant women who receive the sexual education have a good relationship with their partner, they can easily exchange educational topics with them while their spouses may not take part in the classes, a finding which is in line with the current study [5]. In line with the present study, Ghasemi Moghadam and colleagues (2012) also reported that the overall marital satisfaction in the experimental group was more than the control group and concluded that the sexual enrichment program could increase marital satisfaction even when husbands did not participate in the enrichment program [50].

Despite the fact that some previous studies have argued that increasing sexual behavior during pregnancy requires the care and understanding of the couples [48] and therefore they recommend that husbands should also participate in the sexual education programs for pregnant women [51, 52, 25, 26], since the implementation guidelines of the sexual enrichment program requires women to do some assignments and confer the information with their husbands, the obligation of husbands' attendance in training sessions can be ignored, taking into account time and occupational inconveniences that this obligation might bring about.

The results of this study showed that sexual enrichment program can be effective in increasing the sexual satisfaction of pregnant women, even in the absence of their husbands in educational classes. Therefore, the sexual enrichment program can be used as a simple user-friendly academic framework by health personnel, especially midwifery counselors, in healthcare centers to help women solve their sexual problems in particular pregnancy situations.

Limitations

Among the limitations in implementing the study was that pregnant women due to pregnancy problems were reluctant to attend the counseling classes. Furthermore, it was not possible to predict the health condition of healthy pregnant women either and some of them because of prenatal problems could not attend the sessions and withdrew from the study. Another limitation was that the researchers could not guarantee the participants' commitment to do the assignments and exercises. Sexual satisfaction of pregnant women requires mutual cooperation of the couple, therefore, absence of attendance spouses in counseling sessions are one of the limitations of the study.

Conclusion

The results of the study showed that the sexual enrichment program could impact on the sexual satisfaction of pregnant women. After conducting additional studies with similar methodology and larger sample size, if the findings of this study are confirmed, the integration of this program is suggested as a simple, practical and cost-effective intervention in the prenatal care system.

Ethics Approval

Before launching the study, the proposal of the study was approved of by the Ethics Committee of Shahroud University of Medical Sciences (Ethical code No: IR.SHMU.REC.1395.39) and it was registered in the Iranian Registry of Clinical Trials (Code: IRCT2016092930048N). Then after obtaining written permission from the concerned authorities, the researchers were introduced to the research environments. Informed written consents were also obtained from all participants.

Acknowledgment

The present study was supported by Shahroud University of medical sciences as a MSc Thesis. We hereby acknowledge the research deputy for grant.

Conflict of interest statement

The authors report no conflict of interest.

Authors' contributions

FBG, AMN, AK, ZM, FHT: Study conception and design.
FBG, AMN: Acquisition of data.
FBG, AMN, AK, ZM, FHT: Analysis and interpretation of data.
FHT, FBG: Drafting of manuscript.
FHT: Critical revision. All authors have read and approved the final manuscript.

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Received on May 23, 2022. Accepted on October 13, 2022.

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How to cite this article:Barvanloo-Golmohamadi F, Motaghi Z, Keramat A, Nazari AM, Hadizadeh-Talasaz F. Effect of sexual enrichment program on the sexual satisfaction of pregnant women in Iran: A randomized clinical trial. J Prev Med Hyg 2022;63:E549-E556. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2610

HEALTH PROMOTION

An epidemiological profile of women suffering from urinary incontinence residing at one of the cities of western India: A mixed method approach study

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Keywords

Urinary Incontinence • ICIQ • Quality of Life • Treatment-seeking behavior

Summary

Introduction. *Urinary incontinence (UI), a discomforting condition is predominantly seen in women. Affected women are forced to modify their lifestyles to alleviate symptoms and associated complications.*
Objectives. *To find the prevalence, determinants and association of UI with Socio-demographic, obstetrical, gynecological and personal history and its impact on quality of life.*
Methods. *Research was conducted with a mixed method approach (quantitative and qualitative assessment) among women residing in urban slum of Ahmedabad city, India. Sample size calculated was 457. The study was conducted in urban slums served by one of the Urban Health Centre (UHC) of Ahmedabad city. A modified pre-evaluated standard questionnaire developed by International Consultation on Incontinence Questionnaire (ICIQ) was used for quantitative part. Qualitative part consisted of Focused Group Discussions (FGD) which was carried out amongst the women in batches of 5-7 per discussion at the nearest anganwadi center.*
Results. *Prevalence of UI was found to be 30% among study-participants. A statistical significant relation was seen between the presence of UI and age, marital status, parity, past history of abortion, and occurrence of urinary tract infection (UTI) in last year ($P < 0.05$). Comparison of severity of UI by calculating ICIQ score showed statistical significant relation of same with age, occupation, literacy, socioeconomic status, and parity ($P < 0.05$). More than 50% of women suffering from UI were having chronic constipation, reduced daily sleep, and diabetes. Only 7% of the total women suffering from UI had consulted doctor for their problem.*
Conclusion. *Prevalence of UI was found to be 30% in study participants. Sociodemographic factors like age, marital status and socio-economic class were found to have statistical significant effect on existing UI at the time of interview. ICIQ categories of UI were found to be influenced statistically with age, occupation, literacy, socio-economic classe, parity and obstetric factors like place of delivery and facilitator of delivery. Majority of participants (93%) had never consulted doctor for various reasons/ myths like perception that it shall resolve on its' own, Belief that it is an age-related normal phenomenon, shyness to discuss issue with male doctors/members of family and financial reasons.*

Introduction

India is going through a transition phase in the pattern of health and disease profile of the population. The spectrum of health/disease status, in general, is getting widened with inclusion of non-communicable diseases and health-conditions other than communicable diseases. Urinary incontinence (UI) among post-menopausal females is one such health-related issue that is a part of submerged portion of iceberg in epidemiological profile of India. UI is one of priority health issues recognized by World Health Organisation. It is defined by international continence society as "a complaint of involuntary loss of urine [1]. It is a common and perilous medical condition severely affecting daily life activities of affected women. The UI may be divided into three broad categories: urge, stress incontinence, and mixed variety. The most common etiology for UI includes increasing age, increasing parity, vaginal deliveries, obesity, pelvic surgery, diabetes mellitus, depression, constipation, chronic respiratory problems as well as caffeine and alcohol [2, 3].

Urge incontinence is a condition characterized by frequent urination during day or night and a sudden urge to urinate, with urinary leakage. A person may sometimes not be able to make it to the bathroom in-time with associated leakage. This condition is caused by spontaneous bladder spasms which can result from dietary factors (bladder stimulants-caffeine or alcohol), increased fluid intake, drug side effects, urinary tract infection/cancer, and/or nerve dysfunction (associated with nerve trauma, diabetes, multiple sclerosis, or spinal cord injury). Primary treatments for overactive bladder include behavioral interventions and medications [4].
Stress incontinence is characterized by urinary leakage during physical activities which increases intra-abdominal pressure including coughing, sneezing, exercising, lifting, and laughing. It can result from a variety of conditions including vaginal childbirth, aging, and injury to the pelvic floor muscle levator ani which in turn can lead to urethral hypermobility that manifests as urinary incontinence. As this is an anatomic condition, primary treatment may involve pelvic floor exercises

and/or minimally invasive surgery. [5]the involuntary loss of urine, is a common health condition that may decrease quality of life. Ten to twenty percent of women and up to 77% of women residing in nursing homes have urinary incontinence, yet only 25%seek or receive treatment.

Observations

Mixed incontinence is a condition in which the patient experiences symptoms of both stress and urge incontinence.

Women suffering from UI reframe their lifestyles to avoid social and sexual activities. Urge incontinence was associated with more mental distress, practical inconveniences, and social restrictions than stress incontinence [6].

The prevalence of UI and treatment-seeking behavior is comparatively a very less explored field of research in India. With numerous confining factors such as the non-availability of female doctors in the periphery, shyness, fear of surgery, lack of money, dependency on husbands and belief that it is a natural consequence of aging [7], women tend to avoid reporting this problem. Prevalence of UI ranges from 8-45% in different studies in India [8, 9].

So, with this background, research with mixed method approach (both quantitative and qualitative) to assess determinants, impact on quality of life, and treatment-seeking behavior for UI among females residing in urban slums, Ahmedabad was planned. The objectives of the study were: a) to determine prevalence of urinary incontinence and its determinants. b) To assess severity of UI in women and its association with various risk factors. c) To study Treatment seeking behavior and impact on quality of life of UI in focal group discussions (FGDs) by Qualitative approach.

Methodology

After necessary approval by institutional ethical committee, study was carried out from October 2020 to March 2021. For quantitative research part of study, following methodology was followed:

Based on previous study carried out by, Biswas et al. [3] in West Bengal province of India, the prevalence of UI was found to be 28% (27.7%). According to this data, estimated sample size calculated by 4pq/l2 with 15% allowable error gave an approximate sample size of 457. Multi-stage sampling technique was applied for selection of study area and study participants.

In current study, inclusion of women who were 45 years of age or above was done. This age limit was kept considering previous research carried out by Quiroz et al. [10] and Khan et al. [11] who concluded respectively that there is an association between age and numerous pelvic floor disorders in post-menopausal women and an association between years spent in menopause and presence of urinary incontinence.

The study unit was considered as one of the selected areas of Ahmedabad city, India. The smallest health-administrative unit at city level is Urban Health Center (UHC) which is managed by Municipal Corporation. One of the UHC catering to the population of 71,480 was selected randomly from list of total UHCs serving Ahmedabad city. The area served by selected UHC was divided into 7 regions comprising the various numbers of *Chawls* (a cluster of the urban slums)/society/areas in each region for further sampling. To represent all regions of UHC, four *chawls*/societies/areas were selected from each region using simple randomization, comprising a total number of 28 (7 x 4 = 28) chawls/societies/areas.

Within *chawls*/society/areas, house numbers provided by Municipal Corporation were used. A specific house number was selected randomly by currency note method. Starting from that house, participants were included from consecutive households. A total of 17 women above 45 years were taken as subjects. If ≥ 1 woman above 45 years were residing in same house-hold, all were included in study. Thus, total 476 (17 x 28) subjects were selected for study (larger than calculated sample size).

Informed oral consent of participants was taken before interviewing them. They were interviewed face to face using a standard questionnaire. The modified pre-evaluated standard questionnaire developed by International Consultation on Incontinence Questionnaire - Urinary Incontinence short form (ICIQ-UI SF) [12] was used in current study. It was modified according to regional requirements and by adding relevant questions about socio-demographic profiles. It was validated by a pilot study (results of which were excluded from final data collection/analysis). The questionnaire included following information: socio-demographic data, socioeconomic status, gynaecological and obstetric history, personal relevant medical history, questions regarding UI (with Impact on quality of life and Treatment seeking behavior), and another co-existing medical history if any. The socioeconomic status of the family was obtained according to the Modified Prasad's Classification [13] which is based on monthly per capita income calculated by using the CPI-IW (Consumer Price Index - Industrial worker) provided by the Labour Bureau of India for the month of October 2020 [14]. The score of ICIQ was assessed on a scale of 0-21. Score ranges were 1-5 (slight), 6-12 (moderate), 13-18 (severe) and 19-21 (very severe). Question items were Frequency of urinary incontinence, Amount of leakage, Overall impact of urinary incontinence, and Self-diagnostic items [10, 12].

Height was measured by regular measuring tape and weight was noted by using manual weighing machine and analyzed to calculate BMI (Body Mass Index). The responses during personal interview were recorded by investigator directly in Google forms, data were exported to excel sheet and analyzed by chi-square test and correlation tests for significance with IBM SPSS (Statistical Package for the Social Sciences) version 26 for Windows.

Exclusion criteria considered in quantitative part were: Closed house at the time of visit, No women above 45

years of age were available, Consent not given, and Patients with leakage of urine from sites other than urethra. For Qualitative research part of study, women having urinary incontinence were individually contacted later on for FGD after completion of the quantitative part. Exclusion criteria for qualitative research part were: participants who did not give oral consent, who could not be contacted due to currently not living at the same place and who were unable to travel to place of FGD due to various reasons like old age/ co-morbidities/ Job timings and participants who died due to various reasons (co-morbidities/ COVID-19) in period between quantitative and qualitative research part.

FGD was carried out amongst the women in batches of 5-7 women per discussion at nearest possible place where privacy was maintained. Besides investigators, two female social workers remained present in each FGD. The timings and schedule of FGD were kept flexible by keeping into consideration working hours and feasibility of attending each session for participants. FGD was carried out in a separate and quiet room for better audio recording and taking notes. Participants were made to sit in a circle for ease of discussion and communication. All possible due care was taken to create an environment where open and healthy discussion could be done. Before starting discussion, participants were oriented to whole process of FGD and most influential person in the group was assigned as a leader for that FGD. Role of the leader was to encourage her peers (other participants) to share their experiences. Various aspects regarding UI were discussed in FGD such as risk factors, symptoms, impact on quality of life, lifestyle modifications, and treatment-seeking behavior. All sessions were audio-recorded and subsequently analyzed. After the end of each FGD, participants were also counseled to consult doctors.

Result

The quantitative part of the study

Of total 476 study participants, 143 (30.04%) women were suffering from UI. Mixed incontinence was the most common type of UI (63, 44.06%) found in study participants (Fig. 1).

Of total participants affected with UI, majority were in the 61-65 years of age-group. Of total working participants, nearly one-third (19, 32.20%) had UI. On assessing role of various socio-demographic characteristics in participants with UI, it was revealed that age, marital status, and socio-economic class were statistically significantly associated with existing UI (Tab. I).

Participants were divided as per suggested categories of ICIQ as described in methodology. Among women with UI (143), 38, 72 and 33 had respectively very severe, severe and moderate UI as per ICIQ classification of same. The categorical distribution as per ICIQ was found to have a significant statistical association (for all p-value < 0.05) with age, literacy, occupation, and socio-economic status (Tab. II).

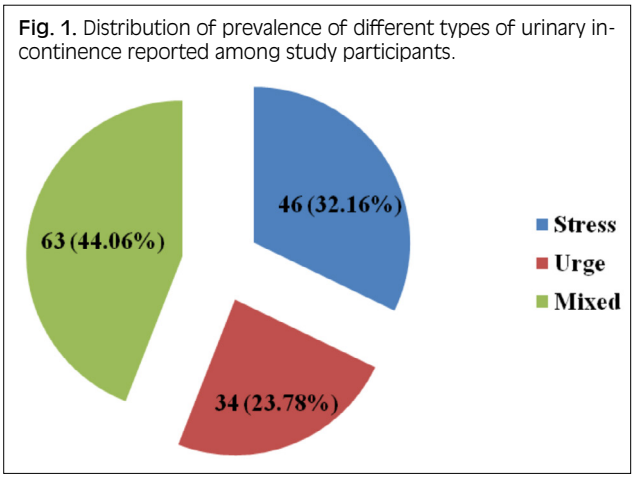

Fig. 1. Distribution of prevalence of different types of urinary incontinence reported among study participants.

The obstetric profile is considered to be one of the prime factors responsible for occurrence of UI among females; the same was assessed among study participants which revealed that parity of ≥ 3, history of abortion, and Number of UTI episodes in past 1 year had a statistically significant association with existing UI. Other obstetric factors like age at time of first delivery, place of delivery, type and facilitator for delivery, history of prolonged labor (> 20 hours for primigravida and > 14 hours for multigravida) [13], and history of previous pelvic surgeries did not reveal any statistically significant association with UI (Tab. III).

On comparing the impact of parity on ICIQ categorization of UI, a total of 44 women had parity < 3 (16, 20, and 8 had moderate, severe, and very severe UI respectively) while among women with ≥ 3 parity (n = 99), 17, 52 and 30 women had moderate, severe and very severe UI respectively. The difference was found statistically significant with a $\chi 2$ test statistic of 6.849 and P value = 0.032 (Tab. IV).

On assessing the relationship between ICIQ score and BMI (Body Mass Index) of women suffering from UI, a positive correlation was observed. The slope of the line is 0.524 (r = Karl Pearson's correlation coefficient = 0.524, *p*-value = 0.000, $+0.5 \leq r < +1$) indicating a moderate correlation between ICIQ score and BMI (Fig. 2).

On assessing comorbidities among women suffering from UI, it was found that constipation (105, 73.42%), decreased/disturbed sleep (83, 58.04%), diabetes (78, 54.54%), hypertension (45, 31.46%), and chronic cough (25, 17.48%) were co-existed (multiple responses allowed). In context to tobacco exposure, tobacco chewing (36, 25.17%), Active smoking (7, 4.89%), Passive smoking (44, 30.76%), and snuffing (28, 19.58%) were reported among participants with UI (Multiple responses allowed).

Asking about treatment-seeking behavior revealed that out of total women with UI (n = 143), 10 (7%) had consulted doctor for single or multiple times while the remaining 93% had never consulted doctor for various reasons/myths like perception that it shall resolve on its' own (90, 62.93%), belief that it is an age-related

Tab. I. Association between various socio-demographic variables with Urinary Incontinence (n = 476).

Variables		UI Present (%)	UI Absent (%)	Total	χ2 test statistic	p-value
Age (in completed years)	45-50	42 (25.45)	123 (74.55)	165	17.50	0.003
	51-55	38 (40)	57 (60)	95		
	56-60	30 (27.27)	80 (72.73)	110		
	61-65	25 (43.10)	33 (56.90)	58		
	66-70	2 (7.69)	24 (92.31)	26		
	> 70	6 (27.27)	16 (72.73)	22		
Occupation	Working	19 (32.20)	40 (67.80)	59	0.15	0.699
	Non-working	124 (29.74)	293 (70.26)	417		
Marital Status	Married	73 (25.44)	214 (74.56)	287	13.46	0.003
	Unmarried	0 (0)	5 (100)	5		
	Divorced	0 (0)	4 (100)	4		
	Widowed	70 (38.89)	110 (61.11)	180		
Type of Family	Nuclear	39 (28.06)	100 (71.94)	139	1.708	0.425
	Three Generation	53 (33.97)	103 (66.03)	156		
	Joint	51 (28.18)	130 (71.82)	181		
Literacy	Literate	58 (26.98)	157 (73.02)	215	1.753	0.186
	Illiterate	85 (32.57)	176 (67.43)	261		
Socioeconomic Status	Class 2	16 (38.10)	26 (61.90)	42	76.50	< 0.0001
	Class 3	48 (23.65)	155 (76.35)	203		
	Class 4	142 (65.44)	75 (34.56)	217		
	Class 5	4 (28.57)	10 (71.43)	14		

Tab. II. Association between various categories of ICIQ and socio-demographic variables (n = 143).

Variable		ICIQ Categories (score: 0-21)			Total	χ2 test statistic	p-value
		Moderate (6-12) (%)	Severe (13-18) (%)	Very Severe (19-21) (%)			
Age (in completed years)	45-50	14 (33.33)	21 (50)	7 (16.67)	42	23.09	0.01
	51-55	8 (21.05)	22 (57.89)	8 (21.05)	38		
	56-60	4 (13.33)	20 (66.67)	6 (20)	30		
	61-65	4 (16)	7 (28)	14 (56)	25		
	66-70	0 (0)	1 (50)	1 (50)	2		
	> 70	3 (50)	1 (16.67)	2 (33.33)	6		
Occupation	Working	2 (10.53)	16 (84.21)	1 (5.26)	19	10.231	0.006
	Non-working	31 (25)	56 (45.16)	37 (29.84)	124		
Literacy	Literate	21 (36.21)	28 (48.28)	9 (15.52)	58	11.861	0.002
	Illiterate	12 (14.12)	44 (51.76)	29 (34.12)	85		
Socio-economic Status	Class 2	5 (31.25)	9 (56.25)	2 (12.50)	16	16.177	0.012
	Class 3	19 (39.58)	19 (39.58)	10 (20.83)	48		
	Class 4	9 (12)	42 (56)	24 (32)	75		
	Class 5	0 (0)	2 (50)	2 (50)	4		

normal phenomenon (74, 51.74%), shyness to discuss issue with male doctors/members of family (56, 39.16%) and financial reasons (5, 3.49%), (Multiple responses allowed).

Qualitative part result

Each FGD consisted of 5-7 participants. A total number of 10 such FGDs were conducted. For sake of maintaining anonymity of each participant, they were given numbers to describe various qualitative variables. All recordings of FGDs were saved and coded separately which yielded following.

In-depth discussion classified based on selected themes relevant to UI.

Knowledge of risk factors contributing to symptoms

While some Women were aware of medically proven risk factors of UI, some were unsure of symptoms. For instance, when asked, "What do you think caused this condition?"
FGD1 (Sr. No. 2) answered: "I think it is caused by chronic tobacco use".
FGD3 (Sr. No. 14) answered: "I think it was caused by frequent infections in my genital tract".

Tab. III. Association of Urinary Incontinence with obstetric and other relevant details of study participants (n = 476).

Variables		UI Present (%)	UI Absent (%)	Total	χ2 test statistic	p-value
Parity	< 3	44 (23.66)	142 (76.34)	186	**5.924**	**0.014**
	≥ 3	99 (34.14)	191 (65.86)	290		
Age at First Delivery	≤ 18	33 (29.73)	78 (70.27)	111	1.754	0.416
	19-30	110 (30.47)	251 (69.53)	361		
	> 30	0 (0)	4 (100)	4		
Place of last Delivery	Home	84 (31.46)	183 (68.54)	267	1.348	0.509
	Hospital	59 (28.50)	148 (71.50)	207		
	Others*	0 (0)	2 (100)	2		
Who performed the last delivery	Doctor	50 (29.41)	120 (70.59)	170	0.601	0.740
	Nurse	11 (25.28)	32 (74.42)	43		
	Others**	82 (31.18)	181 (68.82)	263		
Type of last Delivery	Vaginal	135 (31.03)	300 (68.97)	435	2.367	0.124
	Caesarean	8 (19.51)	33 (80.49)	41		
History of Prolonged Labour	Yes	39 (36.45)	68 (63.55)	107	2.696	0.1
	No	104 (28.18)	265 (71.82)	369		
History of abortion	Yes	61 (35.67)	110 (64.33)	171	**4.026**	**0.044**
	No	82(26.89)	223 (73.11)	305		
History of Pelvic operation	Yes	71 (29.96)	166 (70.04)	237	0.002	0.964
	No	72 (30.13)	167 (69.87)	239		
Number of episodes of UTI in past 1 year	0	69 (21.04)	259 (78.96)	328	71.866	**< 0.0001**
	1	19 (27.54)	50 (72.46)	69		
	1-2	49 (69.01)	22 (30.99)	71		
	3-5	6 (75)	2(25)	8		

*Places other than Home or Hospital or during transit in vehicle. ** Dai or other local ladies or spontaneous.

Tab. IV. Association between various categories of ICIQ and Gynaecological/ obstetrical variables (n = 143).

Gynecological/obstetrical history		ICIQ Score			Total	χ2 test statistic	p-value
		Moderate (%)	Severe (%)	Very Severe (%)			
Parity	< 3	16 (36.36)	20 (45.45)	8 (18.19)	44	**6.849**	**0.033**
	≥ 3	17 (17.17)	52 (52.53)	30 (30.30)	99		
Age at First Delivery	≤ 18	10 (30.30)	13 (39.40)	10 (30.30)	33	2.218	0.329
	19-30	23 (20.91)	59 (53.64)	28 (25.45)	110		
Place of last Delivery	Home	14 (16.67)	43 (51.19)	27 (32.14)	84	**6.03**	**0.049**
	Hospital	19 (32.21)	29 (49.15)	11 (18.64)	59		
Who performed the delivery	Doctor	15 (30)	24 (48)	11 (22)	50	**9.947**	**0.041**
	Nurse	5 (45.45)	6 (54.55)	0 (0)	11		
	Others	13 (15.85)	42 (51.22)	27 (32.93)	82		
Type of last Delivery	Vaginal	30 (22.22)	68 (50.37)	37 (27.41)	135	1.396	0.497
	Caesarean	3 (37.50)	4 (50)	1 (12.50)	8		
History of Prolonged Labour	Yes	8 (20.52)	18 (46.15)	13 (33.33)	39	1.262	0.532
	No	25 (24.04)	54 (51.93)	25 (24.04)	104		
History of abortion	Yes	13 (21.31)	30 (49.18)	18 (29.51)	61	0.517	0.772
	No	20 (24.39)	42 (51.22)	20 (24.39)	82		
History of Pelvic operation	Yes	16 (22.54)	36 (50.70)	19 (26.76)	71	0.023	0.988
	No	17 (23.61)	36 (50)	19 (26.39)	72		
Number of episodes of UTI in past 1 year	0	19 (27.54)	35 (50.72)	15 (21.74)	69	2.638	0.852
	1	4 (21.05)	10 (52.63)	5 (26.32)	19		
	1-2	9 (18.37)	24 (48.98)	16 (32.65)	49		
	3-5	1 (16.67)	3 (50)	2 (33.33)	6		

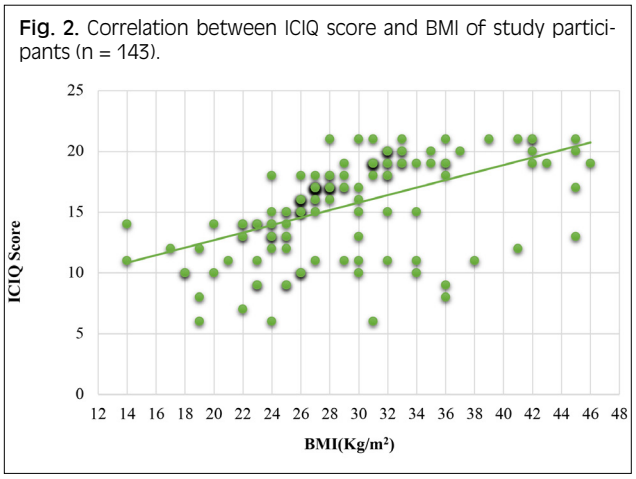

Fig. 2. Correlation between ICIQ score and BMI of study participants (n = 143).

FGD5 (Sr. No. 29) answered: "I don't know what caused this. It started gradually and worsened over time."
When asked about medical history, Sr. No. 29 said she was diagnosed with diabetes a few years back. She was explained that it may be cause of her symptoms and was advised regular monitoring of blood glucose and referred to hospital after FGD.

Unavoidable risk-factors

All women in FGDs were provided with knowledge of common risk-factors. Further discussion was done with some women who couldn't avoid those risk-factors.
The most common was multiple parity. For instance,
FGD 5 (Sr. No. 27) said: "I have 5 children, this led to constant injury and laxity of my genital-tract, what can I do now"? She was given knowledge about different physiotherapeutic exercises to decrease frequency of symptoms and referred to doctor.
Other commonly unavoidable things were household chores and work that required heavy lifting. FGD6 (Sr. No. 34) said "I am a fruit seller. Constant heavy lifting of baskets and pulling a fruitcart is all I do the whole day. It's the only source of income for my family".
FGD9 (Sr. No. 54) said "I am the only woman in house. I constantly work in kitchen where I left heavy boxes from storage room, and I do all cleaning of house along with broom-stick". Both of these women were referred to hospital. They were advised that they'll be started on medications, and if medications show no improvement, surgery may be indicated.

Variation of symptoms according to weather/ work activity/UTI

Women were also asked about what things aggravate their symptoms.
FGD4 (Sr. No. 15) answered: "Drinking coffee before going to bed results in frequent waking up and going to bathroom".
FGD10 (Sr. No. 57) said: "frequency of symptoms increases when I am in stress". She was diagnosed with anxiety disorder a few years back. She drinks excessive water during anxiety attacks. She was advised to consult a psychiatrist. FGD9 (Sr. No. 54) said "During winter season, symptoms of urge incontinence increase a lot". This was also said by a majority of women during that FGD.

Varied Symptoms for similar risk factors

Many women had similar types of risk factors but symptoms varied in them. For instance, FGD 5 (Sr. No. 27) and FGD 4 (Sr. No. 20) both have 5 children but ICIQ score in earlier was higher. She underwent delivery of all children at home which may have led to improper management of labor while FGD4 (Sr. No. 20) underwent delivery of all her children in hospital.

Non-medical measures taken to avoid the incontinence

Preventive measures being taken by affected women on a day-to-day basis were also discussed. FGD1 (Sr. No. 3) answered "I stop drinking water 2 to 3hours before going to sleep".
FGD8 (Sr. No. 48) answered "I constantly wear an adult diaper when I am at home to prevent my clothes from getting spoiled".
FGD 3 (Sr. No. 14) answered "I ask my son/husband to do all the heavy lifting for me".

Efforts taken to avoid social embarrassment

While majority of women avoided social gatherings and functions, some assorted to various tedious and cumbersome measures like drinking less water and wearing diapers whenever going out of the house. FGD9 (Sr. No. 52) said "I live in a very old house, our bathroom/ toilet is located outside inbackyard. Usually, I spoil my clothes by the time I reach there on time, so I have shifted my bed and all my stuff to room nearest to bathroom/toilet." It was noticed by observers that many old women resorted to this measure.

Reasons for not consulting the doctor

FGD2 (Sr. No. 10) answered "This problem started when I was pregnant and I hoped it will stop after delivery, but I continued. I considered it as side-effect of pregnancy. "It was explained to her that during pregnancy, pressure from her gravid uterus on her bladder may have caused symptoms and during labor, injury may have occurred in genital tract. She was advised to consult a specialist.
FGD6 (Sr. No. 34) said "My mother hadsame problem; even my mother-in-law hadsame problem. It's a normal phenomenon. We have to deal with it." It was explained to her that it can be avoided by proper management and treatment.
Many old women were dependent on their sons to take them to hospital and due to unavailability of time and/ or money; they had to resort to non-medical measures.

Missing out on daily chores/activities

It ranged from missing social gatherings to permanently leaving their job.

FGD1 (Sr. No. 6) and FGD7 (Sr. No. 44) wasa school teacher and office clerk respectively, due to frequent exacerbation of symptoms, they had to resign from their jobs.

Impact on mental health

Majority of women faced daily anxiety to avoid embarrassment. While younger women were more prone to mental health issues, older women avoided getting out as much as possible. FGD4 (Sr. No. 20) said "Earlier I used to be very anxious while going out. I used to take extra pair of clothing with me. But for the past 1.5 years, I avoid going out as I am retired, and my son earns for daily living".

Discussion

In India, there are lots of social barriers and misconceptions regarding reproductive and/or sexual health in general which include UI. It is a subject that is still not talked about or discussed in public and women appear not to be aware of how exactly to address issue.

Present study reported prevalence of UI to be 30% with mixed incontinence to be the highest (63/143). A similar study conducted by Singh et al. [17] reported a prevalence of 21.8% while Bodhare et al. [18] in Telangana, India reported a prevalence of 10% for UI.Both of these studies may have different prevalence as they were conducted at different areas and different settings. A study conducted in China by Lan Zhu et al. [18] reported highest prevalence of Stress UI.

Present study reported significant association of existing UI with age and marital status ($p < 0.05$). Also, a significant association was seen based on age, occupation, literacy, and socioeconomic status and ICIQ scores among women having UI ($P < 0.05$). A study conducted by Singh et al. [17] in India also reported association of increasing age with UI. A study conducted at Nigeria by Abiola et al. [20] showed that Increasing age has a positive correlation with ICIQ score.

Present study demonstrated a significant difference between ICIQ scores among women (suffering from UI) with < 3 children and women having ≥ 3 children ($P < 0.05$). Saadia [21] conducted by Al-Badr [22] among Saudi women showed a significant association between a history of previous gynecological surgery (like abortion) and the presence of UI.

A moderate correlation was seen between BMI and ICIQ scores in present study. Palms et al. [23] conducted a study in Brazil where correlation between BMI and overactive bladder was assessed which revealed that women with BMI ≥30 presented a significantly higher score for ICIQ than women with a lower BMI (18.5-24.9).

Present study found that a high number of women suffering from UI had co-morbidities like constipation and diabetes mellitus. Maeda et al. [24] in their research found that functional constipation is related to moderate to severe overactive bladder symptoms (OAB) and to OAB with urinary incontinence. Nazaal et al. [25] in their research conducted amongst Palestinian women founda high prevalence of UI among women suffering from diabetes (43.2%).

In context to treatment-seeking behavior, the current study observed that 7% of affected women had consulted doctor. A study conducted by Singh et al. [26] in North India showed that 20% of women had consulted a doctor for their problems. Same reasons like "consideration of UI as normal and shyness" were provided in that study.

Possible Limitations of study

Social Desirability bias

In present research, it was observed that some women may still be denying presence of UI despite presence of female social worker.

Recall Bias

Respondents may have faced problems recalling number of UTIs in past one year. Many old women did not remember their age correctly.

For many women, problem of UI aggravated significantly during winter season, so ICIQ score may change over the months. This may have created the confounding bias. Cold weather being confounding factor.

There was a time lag between quantitative and qualitative data collection due to existing COVID pandemic which in turn may have resulted some lost to follow up participants.

Current study could not separate the risk factors for different types of UI (stress UI/ Urge UI/ Mixed UI).

Conclusion

The revealed prevalence of UI among study participants was 30% and mixed incontinence was the most common reported variety. Sociodemographic factors like age, marital status and socio-economic class were found to have statistical significant effect on existing UI at the time of interview. ICIQ categories of UI were found to be influenced statistically with age, occupation, literacy, socio-economic class parity and obstetric factors like place of delivery and facilitator of delivery. Other important factors which impacted existing UI with statistical significance were parity, history of abortions and number of episodes of UTI in past 1 year. Majority of participants (93%) had never consulted doctor for various reasons/myths like perception that it shall resolve on its' own, Belief that it is an age-related normal phenomenon, shyness to discuss issue with male doctors/members of family and financial reasons.

Acknowledgements

We would like to express our gratitude towards Director of GCS Medical College, Dr Kirti Patel as well as Dean of GCS Medical College, Dr Yogendra Modi for allowing us to conduct this research. Also, we would like to thank

faculty of Department of Community Medicine, GCS Medical College for their constant help and guidance.

Authors' contributions

VRD designed the methodology of the cross-sectional study and provided intellectual support. KS and PK collected the data for the study and carried out the data analysis. KS and PK wrote the manuscript and VRD did the final editing. All authors reviewed the final manuscript.

Conflict of interest statement

The Authors declare no conflict of interest.

Financial support

The study was applied for and approved by ICMR – STS grant (Indian Council of Medical Research – Short Term Studentship) ID- 2020-06417 which is an endeavour to support research being conducted by medical student from Central Government, India.

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Received on October 17, 2022. Accepted on November 29, 2022.

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How to cite this article: Sharma K, Khandhedia P, Dave VR. An epidemiological profile of women suffering from urinary incontinence residing at one of the cities of western India: A mixed method approach study. J Prev Med Hyg 2022;63:E557-E565. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2773

HEALTH PROMOTION

Vaccine hesitancy among Ukrainian refugees

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Keywords

Ukraine • Vaccine hesitancy • Refugees

Summary

Background. *On February 2022, Russia invaded Ukraine. Beyond Poland, Romania, Russia, several refugees reached Italy also. In the past, several factors contributed to low vaccination coverage in Ukraine and the occurrence of epidemic outbreaks. The purpose of our study was to analyze the main characteristics of Ukrainian refugees who accessed the Rozzano Vaccination Center (Italy), and the attitude towards proposed vaccinations.*
Methods. *In March-July 2022, we conducted a cross-sectional study on Ukrainian refugees under the age of 18. On the basis of their vaccination certificates or antibody dosages, the doctor proposed to the parents (or legal guardians) any vaccinations to be carried out on the basis of the Italian childhood vaccination schedule. Refused or accepted vaccinations were registered and the data exported for statistical analysis. COVID-19 vaccination was excluded from the analysis.*
Results. *27 refugees missed the appointment, so 79 Ukrainian refugees have been included in the study. Females represented the 51.90% of patients; the average age was 7.11 (sd 4.92) years. The most refused vaccinations were: HPV, MMR and men C. Significant differences due to age were found for Men C and Chickenpox acceptance.*
Conclusions. *The efforts made to ensure complete care and to promote vaccination among refugees, offering them a complete evaluation of the vaccination status and the possibility of being vaccinated for free, seem to be insufficient to convince most refugees to get vaccinated.*

Introduction

War causes an enormous amount of deaths and disabilities around the world. It destroys families, communities and cultures, divert scarce resources, disrupts the social infrastructure that supports health. It forces people to leave their homes and to become internally displaced persons or refugees who have fled to other countries [1].
According to UNICEF, about forty percent of partially vaccinated or unvaccinated children live in partially or wholly conflict-affected countries. These children are often the most vulnerable to outbreaks of diseases such as measles and polio, which can cause death or severe disability.
Children in conflict-affected areas lose basic vaccinations due to the failure – and sometimes deliberate destruction – of vital health services [2].
On February 24, 2022, Russia launched a full-scale military invasion of Ukraine. Since then, millions of Ukrainians have fled their homes in search of refuge, especially in neighboring countries such as Poland, Romania and Russia [3].
Italy also welcomed thousands of Ukrainian refugees whose main destinations were the biggest Italian cities such as Milan, Rome, Naples and Bologna [4].
At the end of March 2022 (30th) the Italian authorities had announced that so far about 71,940 Ukrainian refugees had entered the country, of which 37,082 women, 6,661 men and 28,197 minors. About 3,000 Ukrainian refugees had reached Italy every day since the war began.
By the end of April 2022, almost 100,000 Ukrainian refugees arrived in Italy, most of them women and children. Exactly 97,912 people fleeing the war in Ukraine arrived in Italy, of which 50,612 women, 11,833 men and 35,467 minors [4].
Before the war, vaccination rates in Ukraine were among the lowest in Europe. Childhood vaccination coverage has steadily fallen below the WHO target thresholds required to establish herd immunity for some of the most serious diseases. In 2021, 20% of children in Ukraine were not fully vaccinated against measles and 13% were not protected against poliovirus; this percentage is likely to have increased due to the conflict [5].
Likewise, vaccination coverage against COVID-19 has been poor; by February 2022, less than 35% of the general population had received two doses of the vaccine, compared to an average of 65% in the rest of Europe [5].
Several factors have contributed to the low prevalence of vaccination in Ukraine, including widespread hesitancy about the vaccines, fueled in part by social media campaigns that have served to spread vaccine misinformation and undermine public trust in Ukrainian authorities [6].
The World Health Organization (WHO) defined the vaccine hesitancy as a behavior, influenced by a number of factors including issues of confidence (do not trust vaccine or provider), complacency (do not perceive a need for a vaccine, do not value the vaccine), and convenience (access) [7].
Wavering confidence has been compounded by problems

https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2774

with vaccines provision and disruption of immunization services related to the COVID-19 pandemic.
Due to low vaccination coverage, Ukraine has recently experienced vaccine-preventable disease outbreaks. In 2017-2020, Ukraine reported over 115,000 measles cases and 40 measles-related deaths, representing the largest epidemic in Europe in over a decade [8].
An outbreak of type 2 poliovirus was confirmed in 2021. The poliovirus was isolated from over 20 children, two of whom suffered from acute flaccid paralysis [8]. A mass vaccination campaign in response to this outbreak began in February 2022, but was ultimately halted by the Russian invasion, putting Ukraine's children at risk.
The risk of further vaccine-preventable disease outbreaks has been heightened by the conflict. Ukraine has experienced widespread disruption of health services, including immunization programs. Most internally displaced people flee to rural areas or small towns in Ukraine, which do not have the adequate infrastructure to run disease surveillance programs or vaccination campaigns [9].
Most families who have fled Ukraine include young children, the elderly (aged > 60), or people with chronic illnesses, and many are temporarily housed in crowded shelters. There is therefore a risk that crucial doses of vaccines will be missed or delayed.
The risk of epidemic outbreaks of vaccine-preventable diseases in the structures responsible for welcoming migrants, led the Italian Ministry of Health to provide instructions to the Health Authorities to manage the migratory phenomenon [10], indications that have then been declined in regional and local instructions.
The purpose of our study was therefore to analyze the main characteristics of the Ukrainian refugees who accessed the Rozzano Vaccination Center (Milan, Italy), analyzing some socio-demographic data and the attitude towards proposed vaccinations (acceptance or refusal).

Methods

The so called Azienda Socio Sanitaria Territoriale (ASST, translated as Territorial Social and Health Authority) Melegnano e della Martesana tries to respond to the multiple needs of daily life of the citizens who live and work in certain areas of the metropolitan city of Milan. It is present in the territory with: 6 hospitals, 14 territorial clinics, 23 social and health structures.
Vaccinations are administered in eleven vaccination centers (Rozzano, Melegnano, San Giuliano M., San Donato M., Peschiera Borromeo, Melzo, Gorgonzola, Pioltello, Segrate,Trezzo d'Adda). A clinic dedicated to travel medicine is active in Rozzano and Melzo.In the period March-July 2022, a cross sectional study was conducted in Rozzano Vaccination Center (VC).
In response to regional and ministerial indications, the strategic direction of ASST Melegnano Martesana has organized a specific path for taking charge of Ukrainian refugees.
At the beginning of March 2022, a single point for managing migrants was instituted, with the following registration to the national health service (giving them a Straniero Temporaneamente Presente "STP" code, translated as Temporarily Present Foreigner), the execution of a rapid antigenic nasopharyngeal swab for COVID and a complete clinical anamnesis. At the end of the visit, the refugees were then assigned an appointment in Rozzano vaccination center.
On the day of the appointment, the responsible doctor, with basic Ukrainian language knowledge, assessed patients' vaccination status (by evaluating the vaccination certificates in the original language or antibody dosages). Then the doctor recorded the vaccinations in the software used in the Lombardy Region (called Siavr), and proposed to the parents (or legal guardians assigned by the court) any vaccinations to be carried out on the basis of the Italian childhood vaccination schedule. The vaccinations carried out or refused have been registered in Siavr as per regional indications.
The software, connected to the registry, made it possible to obtain information such as the age and sex of the patient.
All the collected data were then exported in an Excel sheet for statistical analysis.
Percentages, means and standard deviation were calculated from the collected data. The Shapiro Wilk test was performed to evaluate the normality of the continuous variables. The Mann - Whitney test was then applied. Odds ratios were calculated to understand the relationship between vaccination refusal and gender. Data were organized and processed by Stata® SE software, version 12.1 (StataCorp, College Station, Texas, USA). The significance level was set at $p < 0.05$.
The study was conducted in a totally anonymous way and approved by the Health Direction of the ASST Melegnano Martesana (Vizzolo Predabissi, Milan, Italy).

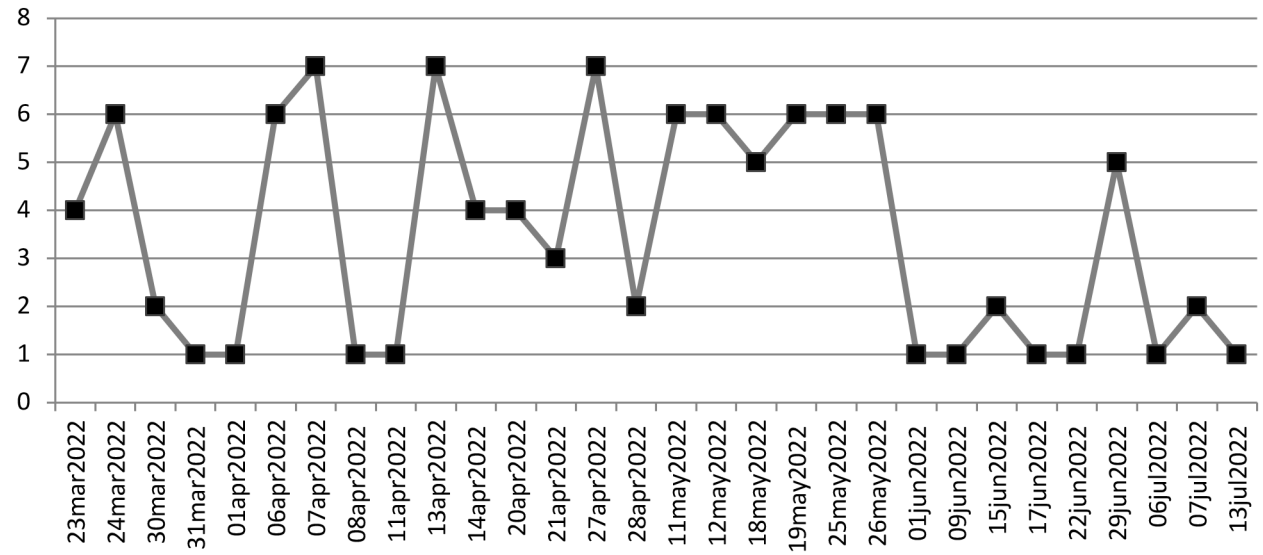
Inclusion and exclusion criteria

The study was conducted on all Ukrainian refugees under the age of 18 who accessed VC Rozzano during the study period. Minors had to be accompanied by a parent or guardian. The examined vaccinations were all those included in the Italian childhood vaccination schedule(obligatory or not). The anti COVID-19 vaccination was excluded from the study.

Results

From 23 March 2022 to 13 July 2022, 106 Ukrainian refugees received an appointment at VC Rozzano. Of these 27 (25.27%) missed the appointment.
The temporal trend of accesses to the Rozzano CV is summarized in Figure 1.
Females represented the 51.90% of patients (N = 41); the overall average age was 7.11 (sd ± 4.92, median 6.49 years). There was no statistically significant age difference between the two genders($p = 0.26$) as assessed by the Mann Whitney test (level of significance 95%).
Vaccinations that have been accepted or refused are resumed in Table I.

Fig. 1. Temporal trend of the accesses to the Rozzano vaccination center in the study period.



Tab. I. Accepted or refused vaccinations (anti-poliomyelitis, anti-diphtheria, anti-tetanus, anti-hepatitis B, anti-pertussis, anti-*Haemophilus influenzae* type b, anti-measles, anti-rubella, anti-mumps, anti-chickenpox are obligatory in Italy from 2017).

Vaccinations	Accepted (N)	%	Refused (N)	%
Hexavalent (DTaP-HepB-IPV-Hib i.e. diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B and inactivated poliovirus vaccine, *Haemophilus influenzae* type b conjugate and hepatitis B vaccine)	9	64.29	5	35.71
Men ACWY (Meningitis ACYW)	8	72.73	3	27.27
Men C	16	39.02	25	60.98
Men B	8	47.06	9	52.94
MMR (Measles, Mumps, and Rubella)	3	37.50	5	62.50
MMR + Chickenpox	15	83.33	3	16.67
PCV 13 (Pneumococcal Conjugate Vaccine)	12	54.55	10	45.45
Rotavirus	3	60.00	2	40.00
Chickenpox	8	57.14	6	42.86
Hepatitis B	3	75.00	1	25.00
dTp - Polio	6	66.67	3	33.33
HPV (Papillomavirus)	0	0	1	100.00
Polio	2	100.00	0	0

As evidenced from the percentages reported in Table I, the vaccines that parents (or guardians) decided mostly to refuse were: the vaccine against HPV 100% (N = 1), against measles-mumps-rubella 62.50% (N = 5), against meningococcus C 60.98% (N = 25).

Moreover, the anti-Men C vaccine was the most refused if we consider the total refusals (25 refusals).

There was no difference in the vaccine acceptance if the child was a male or a female(all $p > 0.05$).

Through the Mann Whitney's test we could observe a difference in vaccine acceptance related to child's age for the following vaccinations:

- men C ($p = 0.01$): average age of child if parent/guardian decided to refuse 6.25 (sd 3.46) years, average age of child if parent/guardian decided to accept 3.72 (sd 3.09) years;
- chickenpox ($p = 0.03$): average age of child if parent/guardian decided to refuse 7.73 (sd 4.30) years, average age of child if parent/guardian decided to accept 3.22 (sd 0.87) years.

Discussion

Our study tried to analyze the main characteristics of Ukrainian (minor) refugees who accessed the Rozzano Vaccination Center in a limited time span (almost three months), analyzing their socio-demographic data and the attitude of their parents / guardians towards the proposed vaccinations. War is, in fact, one of the most difficult emergencies [11], characterized by the interruption of basic social functions, including health care. In the health

system, treatment takes priority and less attention is paid to prevention and rehabilitation. The implementation of the mandatory immunization program is also overlooked as one of the most important achievements in medicine and one of the most important prevention programs, the introduction of which has saved millions of lives [12].

For example, during the war in Bosnia and Herzegovina (1992-1995), the immunization program in the Sarajevo canton was completely interrupted. There were several problems related to immunization implementation. The main ones were: vaccine shortages, problems with maintaining the cold chain, difficulties to take children to vaccination centers, a large number of orphaned children, a large number of injured children. Immunization has sometimes been overlooked by parents, but also by healthcare workers [12].

Surely the Ukraine case had further complications.

Between 2012 and 2013, vaccination coverage in Ukraine was maintained at 76% (DPT3 i.e. Diphtheria-tetanus-pertussis 3rd dose) (WHO UNICEF estimates), after which it dropped dramatically to 23% in 2014 following the onset of the conflict (the so called Donbass war) [13, 14].

Poor coverage has been amplified by the ongoing conflict and displacements in the east. In 2015, two circulating cases of vaccine-derived type 1 poliovirus were confirmed [14, 15], along with 3667 cases of rubella, 2937 cases of pertussis and 995 cases of mumps [16].

The ever-known vaccine hesitancy in Ukraine led to low childhood vaccination rates between 2008 and 2016. In 2016, only 19% of children received the third dose of the diphtheria-tetanus-pertussis vaccine, 31% the second dose of the measles, mumps and rubella vaccine and 56% received the third recommended dose of the oral polio vaccine. Vaccination rates increased dramatically thereafter, due to a major measles outbreak that resulted in numerous deaths [17].

Furthermore, the Ukrainian vaccination schedule does not include rotavirus and this infection accounts for a large percentage of childhood gastroenteritis [18].

Hepatitis B vaccinations were introduced in Ukraine in 2002. Initial coverage was high (92-98%) in 2004-2007, but then dropped to 21-48% in 2010-2016. Despite low vaccination rates, the prevalence of hepatitis B is low in Ukraine. Some areas of the country have reported a seroprevalence of the surface antigen of the hepatitis B virus (HbsAg) > 0.5% [19].

Fortunately the latest WHO data indicated that Ukraine had much higher childhood vaccination rates in 2019-2020 than in the decade before [18].

In our study, the highest rejection rates concerned the HPV vaccine 100% (N = 1), measles mumps rubella 62.50% (N = 5), and meningococcus C 60.98% (N = 25). The latter vaccination was the one most rejected in absolute numerical terms (25 refusals).

Beyond the historic vaccine hesitancy in Ukraine, a study conducted in Messina in 2017 partially tried to explain plausible reasons related to the vaccine hesitancy towards meningococcal and pneumococcal vaccinations. In this study 81.1% (95% CI: 78.3-84.0) of the parents agreed, while 18.9% (95% CI: 13.0-24.8) responded that these vaccinations are not necessary. The explanation given by the unfavorable parents was the fear of side effects for 44.4% (95% CI: 40.8-48.0), the lack of information received for 30.3% (95% CI: 23, 4-37.2) and doubts about the actual efficacy of these vaccines for 13.1% (95% CI: 8.4-17.8). Furthermore, 53.7% (95% CI: 49.5-57.9) stated that they had received information on these vaccinations and the main sources of information were doctors for 82% (95% CI: 77.8-86.2). Among the respondents, 46.3% (95% CI: 41.8-50.8) replied that they had not received information on these vaccinations. In particular, the misinformation involved vaccines for HPV, meningococcus C and pneumococcus. Compared to HPV vaccination, meningococcal C and pneumococcal vaccinations have received more attention from parents. In fact, on the basis of the parents' declaration, these vaccinations were carried out respectively in 52.2% and 46.4% of cases, compared to the percentage of 66.6% in favor of them. These data is probably due to the outbreaks of meningitis in some Italian regions. Furthermore, most of those who received pneumococcal vaccination did so because it was administered together with other mandatory vaccinations [20, 21].

This latter aspect could certainly also explain our results which highlight significant differences in age-related acceptance for vaccinations against MenC and against chickenpox: in fact the average age of children who do not undergo these vaccinations is significantly higher (Men c almost 6 years, Chickenpox almost 8 years).

In Italy, the so-called "Vaccines Decree" has increased the number of obligatory vaccinations in childhood and adolescence from four to ten. The goal is to counter the gradual decline in vaccinations, both mandatory and recommended, in place since 2013, which resulted in an average vaccination coverage in Italy < 95%.

The Law Decree 7 June 2017 n. 73 "*Urgent provisions on vaccine prevention*", amended by the conversion law 31 July 2017, n. 119, provides for the following compulsory vaccinations for minors between the ages of zero and sixteen and for unaccompanied foreign minors:

- anti-poliomyelitis;
- anti-diphtheria;
- anti-tetanus;
- anti-hepatitis B;
- anti-pertussis
- anti-Haemophilus influenzae type b;
- anti-measles;
- anti-rubella;
- anti-mumps
- anti-chickenpox.

The following vaccinations, instead, are actively offered (free of charge)by the Regions and Autonomous Provinces, but are not obligatory:

- anti-meningococcal B;
- anti-meningococcal C;
- anti-pneumococcal;
- anti-rotavirus.

Obligatory vaccinations are free of charge and must all be given to those born after 2017 [22].

In general, meningococcal C vaccination is offered in conjunction with measles-mumps-rubella-chickenpox vaccination [23].
So probably, even in our case, the parents/guardians of the youngest Ukrainian children have better accepted vaccinations because they are associated with other obligatory ones.
However, the problem of refusing vaccinations is a very important problem. In several studies, vaccine rejection has been associated with outbreaks of invasive Haemophilus influenzae type b disease, chickenpox, pneumococcal disease, measles, and whooping cough [24, 25].
In particular, a study conducted in Colorado in 1998-2008 found that children of parents who refuse chickenpox vaccinations are at higher risk of chickenpox infection than vaccinated children [1].
Chickenpox is a common vaccine-preventable disease that usually presents in children as a mild infection; however, serious complications also occur. The chickenpox burden is significant in terms of the incidence, complications and hospitalization rate related to chickenpox and obviously also in terms of the economic burden of the disease. Despite the evidence for the overall positive effects of chickenpox vaccination, there are large differences in the implementation of chickenpox vaccination and vaccine adoption from country to country. Improving the acceptance of chickenpox vaccination at the national and individual levels would reduce the burden of the disease on children's health and health resources.
The determinants of chickenpox vaccine acceptance have been examined in several studies and according to these, the most important factors associated with chickenpox vaccination were the doctor's recommendation of this vaccination and the perception of chickenpox as a sufficiently serious disease.
For most vaccine-preventable diseases, many parents may not be aware of the danger: since they have not personally seen the devastating effect of tetanus, measles, whooping cough or polio, some of them do not consider the vaccination enough important. This is not the case of chickenpox, as most parents had chickenpox as a child and / or saw the disease in others. However, this factor could backfire on accepting chickenpox vaccination. If parents remember chickenpox as a mild infection and if they have learned to accept chickenpox as a normal part of childhood, these elements can undermine their willingness to vaccinate their children [26].
The problem of whether or not to accept vaccinations is certainly much broader.
In research, individual and interpersonal approaches have long been used to examine and facilitate behavior change. More recently, the factors that facilitate and / or hinder the implementation of health behaviors are addressed using a new approach: the social determinants of health (Social Determinants of Health SDoH) [27].
SDOH include elements in an individual's neighborhood, community and environment determined by where the individual is born, resides, learns, works, worships, etc. As a result, the Healthy People 2030 SDoH Framework classifies SDoH indicators into five categories: social and community context, education, economic stability, neighborhood and built environment, health and healthcare [27].
SDoH includes access to education, affordable housing and health services, public safety, food safety [28].
SDoH are affected by the distribution of resources that improve quality of life and public health outcomes. For example, in the United States, people residing in certain metropolitan statistical areas (MSAs), non-MSAs (mostly rural), and without health insurance are disproportionately less likely to be vaccinated [29].
Also, parental education; living conditions and family income; access to health care; philosophical and cultural beliefs; religious affiliations; and urban *vs* rural residence are some of the SDoHs that influence childhood vaccination rates [30].
In 2019, a study conducted on American families showed that the prevalence of vaccine hesitancy was 6.1% for routine childhood vaccinations and 25.8% for influenza vaccines; 12% firmly and 27% somehow agreed to have concerns about the serious side effects of both routine childhood vaccines and influenza. A total of 70% firmly agreed that routine childhood vaccines are effective against 26% of the flu vaccine ($P < .001$). Also in this study, applying multivariable models, an education level below a college degree and a household income below 400% of the federal poverty level predicted hesitation on both routine childhood vaccines and influenza [31].

Study limits

Some limits should be certainly reported in our study: first, the limited number of patients (and their parents), that could not be representative of the entire population; second, although refugees received information in their language, the language barriers have represented a great problem for an efficient communication. Moreover, in case of vaccine refusal, the reasons have not been asked, so we are not able to have a complete overview of vaccine hesitancy phenomenon among Ukrainian refugees.

Conclusions

The war in Ukraine and the resulting migration crisis represent a major challenge for public health in Italy.
Years of organizational and vaccine procurement difficulties, as well as a long history of vaccine hesitancy in the country, widely spread both in the general population and among health workers, have resulted in low vaccination coverage in Ukraine and the occurrence of epidemic outbreaks. Low vaccination rates against major vaccine-preventable infectious diseases in Ukraine can certainly reduce the ability to effectively control probable outbreaks in the immediate and future.
The efforts made by the ASST Melegnano Martesana and the Rozzano Vaccination Center to ensure complete care and promote vaccination among refugees, offering them a complete evaluation of the vaccination status and the possibility of being vaccinated for free, seem

however to be insufficient to convince most refugees to get vaccinated.

Acknowledgments

No one.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Authors' contribution

GTr had the idea of the study, collected and analyzed data, AN and GTo supervised the work and helped to conceptualize the ideas

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Received on October 19, 2022. Accepted on December 26, 2022.

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How to cite this article: Troiano G, Torchia G, Nardi A. Vaccine hesitancy among Ukrainian refugees. J Prev Med Hyg 2022;63:E566-E572. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2774

Infectious diseases

Smear grading at initial treatment association with treatment outcomes among new smear positive pulmonary tuberculosis patients: A retrospective study

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Keywords

DOTS • *Mycobacterium* sputum smear • Treatment failure • Tuberculosis • Smear grading

Summary

Introduction. *Tuberculosis (TB) is one of the most challenging diseases in diagnosis, treatment and control. We aimed to assess the association of the initial grading of Mycobacterium Sputum Smear (MSS) on the outcomes of TB treatment.*
Materials and methods. *In a retrospective study, data of 418 positive pulmonary smear patients were retrieved from the TB registration system in Iran during 2014 to 2021. Patients' data included demographic, laboratory and clinical information and were recorded in our checklist. The grading of Mycobacterium Sputum Smear (MSS) at the initial treatment was assessed based on World Health Organization (WHO) guidelines. Chi-square test was used to assess the relationship between tuberculosis treatment outcomes and Mycobacterium grade at initial treatment in SPSS.*
Results. *The mean age of cases was 51.19 ± 22.29 years old and varied between 14 and 95 years. Laboratory results showed that the rate of 1-9, 1+,2+ and 3+ Mycobacterium tuberculosis was 17.7%, 44.3%, 19.4% and 18.7%, respectively. The rate of cure, death and treatment failure in patients was 87.1%, 6.9%, and 1.2%, respectively. The highest mortality rate (11.5%) occurred in patients with 3+ and the lower rate of cure was 79.5% in this group. Moreover, by increasing the Mycobacterium grade the rate of transferred out and lost to follow up from treatment increased (p = 0.024).*
Conclusion. *High smear grading of sputum is inversely associated with lower curing and on-time treatment. Moreover, by increasing the Mycobacterium grade at initial treatment, treatment failure and lost to follow up increased Therefore, improvement the health system and patient-diagnosis and screening programs is necessary to on-time diagnosis and facilitate the treatment process.*

Introduction

Tuberculosis (TB) is the major cause of death from infectious diseases that caused by *Mycobacterium* tuberculosis. Two main type of TB are pulmonary and external pulmonary TB that affected only the lugs and other organs of the body, respectively [1]. On the threshold of the 21th century, the world health organization (WHO) has declared tuberculosis as a global emergency, since it is not well controlled in some parts of the world and due to comorbidity and occurrence of resistant *Mycobacterium* and Acquired Immunodeficiency Syndrome (AIDS) [2]. The WHO estimates that one-third of the world's population is infected with TB and one person is added to their number per second [3]. In 2016, 10.4 million people were affected to tuberculosis, and 25% of them died due to this disease [4]. The overall incidence of tuberculosis in Iran was 14.4 per 100,000 populations and the incidence of positive pulmonary smear disease that year was 7.07 per 100,000 populations [5, 6].
Tuberculosis is one of the most challenging diseases in diagnosis, treatment and control. Despite the implementation of effective prevention and treatment programs, the expected success in reducing and controlling TB in Iran has not been achieved yet. Numerous factors are considered as related factors of failure of treatment, death and unsuccessful in TB control including drug resistance, delaying in diagnosis, immigration and the role of neighbor countries, poverty, ethnicity, gender, poor nutrition, smoking and drug use [7-9]. However, inappropriate patient management and using the wrong of medication dose and poor compliance of patients play significant role in the development of drug resistance [8, 10, 11]. The survival rate of untreated patients is 50% within the first 5 years of pulmonary tuberculosis, while 25% of TB patients will recover spontaneously due the desired immune system, and another 25% will remain chronic infectious tuberculosis [1]. Positive pulmonary smear patients with sneezing and coughing are the cause of microbial transmission in the community [12]. A positive sputum smear case can infect 10 to 15 people in a year [13]. Therefore, not only diagnosing TB cases is essential for successful control of the disease in the

community but also achieving appropriate treatment is important factor [14].

The WHO policy for TB control is a short-term treatment under direct supervision (DOTS) strategy that includes an effective structure for diagnosis (examination of sputum smears with a light microscope) and treatment (short-time drug therapy) [15]. The DOST strategy was launched by the WHO to control tuberculosis in 1995, and more than 180 countries are currently implementing the program [16]. Monitoring the outcome of TB treatment and understanding the reason for treatment failure important to assess the effectiveness of the TB control program[1, 16, 17]. Failure to treat patients create economic and health problems, including drug resistance and inability to perform daily activities in patients [12]. *Mycobacterium* Sputum Smear (MSS) at the beginning of treatment, known as an effective predictor of treatment [3, 14]. Studies have shown that there is a link between bacillus levels in MSS at the beginning of treatment and the outcome of treatment, so that the rate of recovery is higher in people with low levels of MSS [3, 7, 18]. Moreover, the rate of death and treatment failure among patients with more grade MSS is higher [19] and it is the cause a delay of negative smear conversion rate in patients [15, 20].

Despite the implementation of the national TB control and care program in the country, the TB disease remained as a public health problem [12, 17]. Therefore, knowing the factors affecting death rate and treatment failure from TB and preventive factors of smear conversion could helpful for health policy and providing medical education. This study aimed to determine the association of the grading of positive MSS at the beginning of treatment on the outcome of TB treatment in confirmed cases.

Method

This is a descriptive-analytical, a retrospective study on all 418 positive pulmonary smear patients during 2014 to 2021. All the patients were being treated free of charge based on Iranian national TB control and care protocol, and their treatment results were available and analyzed in SPSS software. The informed consent was taken from all patients and the study protocol approved in ethical committee of Qom University of Medical Sciences by IR.MUQ. Rec.1399.105 code.

The inclusion criterion was that patients had to be new cases suffering from positive pulmonary smear. The exclusion criteria were wrong diagnosis, a history of disease relapse and failed treatment. Patients' data included demographic, laboratory and clinical information retrieved from the TB registration system (TB Register) and other registration offices and were recorded in our checklist.

Based on standard definitions, a patient is assured to have contracted positive pulmonary smear in three situations. First, if he/she have undergone at least two sputum positive smear tests regarding fast-acid bacilli. Two, if he/she have undergone only one test but their chest's radiographic changes show pulmonary tuberculosis and Three, if he/she have undergone only one test but they have one sputum positive culture. Moreover, the bacillus level in the initial treatment is assessed based on the number of *Mycobacterium* tuberculosis in the microscopic field according to WHO guidelines [21]. Accordingly, if there are 1-9 bacilli in every 100 microscopic field, the exact number of observed bacillus is reported. If 10-99 bacilli are observed in every 100 microscopic fields, the grading is determined as +1, and if the ratio is 1-10 the grading is quantified as +2. Finally, if there are more than 10 bacilli in every microscopic field, the grading is specified as sputum smear 3+ [21, 22]. According to WHO's definitions, treatment outcome was classified to six different standard definitions including cured, treatment completed, treatment failed, died, lost to follow up and transferred out [21].

A patient is regarded as cured if the result of their positive pulmonary smear test is negative at the end of the treatment process or if the result of their previous sputum test, carried out for treatment piloting, is negative. On the other hand, failed treatment happens when the patient suffering from positive pulmonary smear has been still positive for five months or more since the initial treatment, they have been positive again after being tested negative in the same period or the patient suffering from negative pulmonary smear dies. Lost to follow up means that the patient has stopped their own treatment for two months or more. Transferred out means that the patient has been transferred to another treatment unit after their initial treatment with no information about the final result of their treatment [22].

Statistical Analysis

After data collection by reviewing the medical records of patients in TB register system, all data were entered in SPSS (V.22) software. The Chi-square test was used to assess the relationship between tuberculosis treatment outcomes and *Mycobacterium* grade at initial treatment. The significance level was assigned as 0.05 for the statistical tests.

Results

This study conducted on 418 tuberculosis cases with the mean age of cases was 51.19 ± 22.29 years old and varied between 14 and 95 years. According to Table I, from all patients 46.7% (195 cases) were male and 53.3% (223 cases) were female. Our laboratory results showed that the rate of 1-9, 1+,2+ and 3+ *Mycobacterium tuberculosis* in our patients was 17.7%, 44.3%, 19.4% and 18.7%, respectively. Therefore, 62% (259 cases) were affected to low grade of bacillus (1+ and lower bacillus) and 38% (159 cases) were affected to high grade of bacillus. The rate of cure, death and treatment failure in our patients was 87.1%, 6.9%, and 1.2%, respectively. Moreover, 4.8% (20 cases) were lost to followed or transferred out. Our results showed that gender, nationality, job and

Tab. I. Demographic characteristics of patients with tuberculosis.

Variables		Frequency (%)
Gender	Male	195 (46.7)
	Female	223 (53.3)
Nationality	Iranian	217 (51.9)
	Afghan	187 (44.7)
	Other	14 (3.3)
Job	Worker	71 (17.0)
	Without job	43 (10.3)
	Non-governmental	19 (4.5)
	Housekeeper	181 (43.3)
	Other	104 (24.9)
Education	Illiterate	228 (54.5)
	Elementary	67 (16.0)
	High school	36 (8.6)
	Advanced	54 (12.9)
	College	33 (7.9)
Residency are	Urban	359 (85.9)
	Rural	59 (14.1)
Year	2016	76 (18.2)
	2017	70 (16.7)
	2018	96 (23.0)
	2019	90 (21.5)
	2020	86 (20.6)
Basil count	1-9	74 (17.7)
	+	185 (44.3)
	++	81 (19.4)
	+++	78 (18.7)
Final Outcome	Cured	364 (87.1)
	Death	29 (6.9)
	Treatment failure	5 (1.2)
	Lost to follow up/ transferred out	20 (4.8)

education were significant variables that related to higher death, treatment failure and lost to followed or transferred out from treatment of tuberculosis (Tab. II). Based on our results, the mortality rate in male was 10.3% that was significantly higher from female patients ($p = 0.004$). The treatment failure was higher in patients from other countries (except Iranian and Afghan) who lived in Iran such as Pakistan and Iraq people. The mortality rate was 11.5% in Iranian patients, 2.1% in Afghan and 0% in Pakistan and Arab countries($P < 0.001$).

Chi square test showed that housekeeper have the highest rate of cured and the highest rate of treatment failure showed in patients with non-governmental ($p = 0.048$). The treatment failure rate increased among patients by decreasing the education and mortality rate was 8.8% in illiterate patients and 0% in patients with advanced education. However, the failure rate in college educated patients was highest as 9.1% ($p = 0.007$). Based on our results residency place was not significant variable on the outcome of tuberculosis ($p = 0.387$).

Table III showed that the highest mortality rate (11.5%) occurred in patients with 3+ and the lower rate of cure was 79.5% in this group. Moreover, by increasing the *Mycobacterium* grade the rate of transferred out and lost to follow up from treatment increased ($p = 0.024$). According to the Figure 1, treated rate was higher in patients with 1+ and lower *Mycobacterium* grade.

Discussion

Literature shows that there is a significant relationship between the high bacillus grading of smear in the initial treatment and negative smear and when the number of bacilli increases in the smear in the initial treatment, the

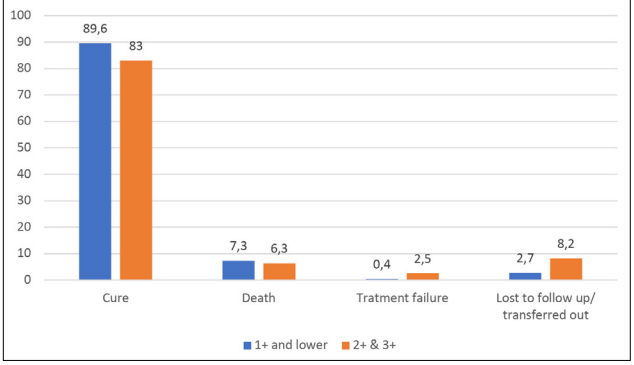
Tab. II. The association of demographic characteristics on the outcome of tuberculosis.

Variables		Cure n (%)	Death n (%)	Treatment failure n (%)	Lost to follow-up/ transferred out n (%)	P value
Gender	Male	162 (83.1)	20 (10.3)	0	13 (6.7)	0.004
	Female	202 (90.6)	9 (4)	5 (2.2)	7 (3.1)	
Nationality	Iranian	185 (85.3)	25 (11.5)	1 (0.5)	6 (2.8)	< 0.001
	Afghan	169 (90.4)	4 (2.1)	2 (1.1)	12 (6.4)	
	Other	10 (71.4)	0	2 (14.3)	2 (14.3)	
Job	Worker	63 (88.7)	2 (2.8)	0	6 (8.5)	0.048
	Without job	34 (79.1)	4 (9.3)	1 (2.3)	4 (9.3)	
	Non-governmental	14 (73.7)	3 (15.8)	1 (5.3)	1 (5.3)	
	Housekeeper	167 (92.3)	8 (4.4)	1 (0.6)	5 (2.8)	
	Other	86 (82.7)	29 (6.9)	5 (1.2)	20 (4.8)	
Education	Illiterate	197 (86.4)	20 (8.8)	2 (0.9)	9 (3.9)	0.007
	Elementary	58 (86.6)	5 (7.5)	0	4 (6)	
	High school	33 (91.7)	1 (2.8)	0	2 (5.6)	
	Advanced	50 (92.6)	0	0	4 (7.4)	
	College	26 (78.8)	3 (9.1)	3 (9.1)	1 (3)	
Residence	Urban	310 (86.4)	28 (7.8)	4 (1.1)	17 (4.7)	0.387
	Rural	54 (91.5)	1 (1.7)	1 (1.7)	3 (5.1)	

Tab. III. The association of ***Mycobacterium*** grade at initial treatment on the outcome of tuberculosis.

Bacillus count	Cure n (%)	Death n (%)	Treatment failure n (%)	Lost to follow-up/ transferred out n (%)	P value
1-9	66 (89.2)	6 (8.1)	0	2 (2.7)	0.024
+	166 (89.7)	13 (7)	1 (0.5)	5 (2.7)	
++	70 (86.4)	1 (1.2)	3 (3.7)	7 (8.6)	
+++	62 (79.5)	9 (11.5)	1 (1.3)	6 (7.7)	

Fig. 1. The effect of ***Mycobacterium*** grade on the treatment outcomes of tuberculosis.



smear becomes negative later [15, 23, 24]. Similarly, patients who have a huge number of bacillus in their smear remain infectious for a longer time and can easily transfer their disease to others [10, 15, 24]. In this study, a significant relationship was observed between the number of bacillus in the initial treatment and the cured rate. About 18.7% of the patients had high sputum smear grade *(3+)* whose rate of treatment was 79.5%. The rate of curing among these patients was lower than the rate of curing among all the patients (87.1%) and the cure expectation time among smear-positive patients (85%). Tiwari et al. [15] study showed similar results and they observed that there was a significant association between an initial positive smear and the treatment results so that those patients with a higher bacillus grading in their smears in the initial treatment had a weaker chance to be cured. Moreover, Buti et al. [25] found that high smear grading can negatively affect the process of smear conversion (changing from positive to negative). Qiao Liu et al. [26] reported the patients with high smear grade were less likely to respond to treatment.

Based on the results of this study, 6.9% of the patients died with a larger proportion (11.5%) belonging to those with high MSS grading (3+). Atif et al. [27] reported that high smear grading is a crucial factor in increasing the mortality of smear-positive patients. In addition, the higher rate of mortality among high smear grading patients was also reported by Hoa et al. [28]. We found that the rate of failed treatment in high smear grading patients (2+/3+) was higher than the rate in low smear grading patients. Similarly, Rajpal et al. [29] demonstrated that high smear grading patients experienced the highest rate of failed treatment. A study in Burkina Faso also showed that there was a significant relationship between the number of bacilli and failed treatment [8]. A significant association was observed between gender and treatment result in this study, which is in agreement with the findings of Izudi et al. [30] study wherein they observed that treatment success rate was lower among male compared to female patients. In another study in Ethiopia, it was found that men experienced lower rates of treatment success, meaning that they experienced more mortality, failed treatment and treatment absence [24]. Another finding of this study was that a significant relationship was observed between patients' nationality and their treatment result as Afghani patients (90.4%) were cured more successfully than Iranians (85.3%) and patients from Pakistan and Arab countries (71.4%). Although there was no significant difference between Iranian and Afghan patients regarding to curing TB, higher centralization on Afghan immigrants people due to high percent of them in Iran could be justify the better curing of tuberculosis. Tok et al. [31] revealed a significant correlation between nationality and treatment result. Additionally, Shahrezaei et al. [32] observed that the nationality had significant effect on outcome.

Our result showed, there was no significant relationship between patients' residence and their rate of treatment success. Similarly, Sengul et al. [33] found that no association between patients' Living area and treatment success. Gebrezgabiher et al. [34] also demonstrated that patients' residence was associated with failed treatment in a way that rural patients revealed a higher risk of failed treatment. A significant relationship was observed between education and treatment results in the current study. Patel et al. [35] observed that education can be regarded as one of the significant factors impacting treatment success as educated patients were 2.4 times more likely to be cured of pulmonary tuberculosis [35]. Moreover, a significant correlation was found between patients' job and the rate of treatment success in this study as the results showed that businesspeople had lower chances of success for their treatments.

One of the main limitations of the current study was that causal relationships could not be exactly established among the variables in this cross-sectional study. Besides, no questionnaires or interviews were conducted in this study; thus, it was not possible to tap into the role of other factors influencing treatment results. On the other hand, the main advantage of this study was that it included all smear-positive patients. Additionally, this study investigated detailed information regarding patients' demographic and clinical status to provide

a thorough analysis of the relationship between such factors and treatment success.

Conclusion

The findings of the study showed that death, treatment failure, lost to follow up and transferred out is more common in patients who have higher MSS. High smear grading of sputum is inversely associated with lower curing and on-time treatment. Moreover, by increasing the *Mycobacterium* grade at initial treatment, treatment failure and lost to follow up increased. Therefore, improvement the health system and patient-diagnosis and screening programs is necessary to on-time diagnosis, facilitate the treatment process and prevent the transference of the disease in suspicious cases. Moreover, the successful treatment in TB patients should be assured, and the TB patients with their families should receive necessary consultations and educations.

Source of Funding

Qom University of Medical Sciences.

Acknowledgement

The authors are very grateful for research deputy of Qom University of Medical Sciences that support financially this project.

Conflict of interest

None.

Contribution of authors

All authors have same contributions to the conception or design of the work, or interpretation of data for the work; and Final approval of the article.

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Received on January 5, 2022. Accepted on October 31, 2022.

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How to cite this article: Mohammadbeigi A, Hosseinali-Pour SA, Aligol M, Mohammadi M, Derakhshani M, Soleymani-Monfared M. Smear grading at initial treatment association with treatment outcomes among new smear positive pulmonary tuberculosis patients: A retrospective study. J Prev Med Hyg 2022;63:E573-E578. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2457

INFECTIOUS DISEASES

Determinants of public interest in emerging and re-emerging arboviral diseases in Europe: A spatio-temporal analysis of cross-sectional time series data

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Keywords

Arboviral diseases • Emerging diseases • Disease interest • Google Trends • Perceived susceptibility

Summary

Introduction. *Climate change, the resulting geographical expansion of arthropod disease vectors, and increasing international mobility are contributing to the emergence of arboviral diseases in Europe. Public interest in vector-borne diseases and a subsequent gain of awareness and knowledge are essential to control outbreaks but had not yet been systematically assessed prior to this analysis.*
Methods. *Trends, patterns, and determinants of public interest in six emerging and re-emerging arboviral diseases were assessed in a spatio-temporal analysis of Google Trends data from 30 European countries between 2008 and 2020 while controlling for potential confounders.*
Results. *Only public interest in endemic arboviral diseases in Europe displays seasonal patterns and has been increasing since 2008, while no significant patterns or trends could be determined for public interest in non-endemic diseases. The main drivers for public interest in all six analysed arboviral diseases are reported case rates, and public interest drops rapidly as soon as cases decline. For Germany, the correlation of public interest and the geographical distribution of locally-acquired reported cases of endemic arboviral infections could be shown on a sub-country level.*
Conclusions. *The results of the analysis indicate that public interest in arboviral diseases in Europe is heavily impacted by perceived susceptibility on a temporal as well as on a spatial level. This result may be crucial for the design of future public health interventions to alert the public to the increasing risk of infection with arboviral diseases.*

Introduction

Arthropod-borne viruses, often abbreviated as arboviruses, are a group of RNA viruses which are mainly transmitted via hematophagous arthropod vectors between vertebrate hosts [1]. Arboviruses pathogenic to humans include dengue virus (DENV), yellow fever virus (YFV), chikungunya virus (CHIKV), Japanese encephalitis virus (JEV), West Nile virus (WNV), Crimean-Congo haemorrhagic fever virus (CCHFV), tick-borne encephalitis virus (TBEV), Rift Valley fever virus (RVFV), and Zika virus (ZIKV). While infections in humans are often asymptomatic, symptomatic infection can range from a mild febrile illness to severe disease such as encephalitis or haemorrhagic fever, which may cause long-term impairment and death [2, 3].
Arbovirus transmitting vectors, which include mosquitoes, ticks, fleas, and sandflies, are primarily found in tropical and subtropical regions [4, 5]. However, the geographical distribution of arboviral vectors and the frequency and magnitude of epidemics caused by arboviruses have been increasing globally during the past decades [6]. In sub-Saharan Africa, arboviral infections are expected to replace Malaria as most urgent public health problem [7]. DENV, endemic in only nine countries during the 1960s, has become endemic in more than 100 countries all over the world, causing an estimated 390 million infections per year with an eightfold increase in the past two decades [6, 8, 9].
In Europe, climate change, urbanisation, and international mobility have led to the emergence of exotic arboviruses and to the geographical expansion of endemic arboviruses [10, 11]. In the past 40 years, five invasive mosquito species have established habitats on European territory [12], and locally-acquired, vector-borne cases of CHIKV, DENV, and ZIKV infection have been reported [13-15]. While infections with tick-borne CCHFV have remained at a low rate, its geographical range is expanding, with Spain reporting its first two CCHFV cases in 2016, and further cases in 2018 (two) and 2020 (three). WNV cases reached an unprecedent peak in 2018 with 1605 cases, a reported case rate eight times higher than the previous year [16, 17]. The European Centre for Disease Prevention and Control (ECDC) has called for immediate strengthening of surveillance and preparedness activities [18].
Awareness of arboviral diseases is not only considered important for clinicians in Europe [19-22]. Public awareness, interest, and knowledge of arboviral diseases are crucial to prevent and combat epidemics [23-25]. While public interest and its determinants have been analysed for select arboviral infections, disease vectors,

and regions [26-29], a comprehensive study of public interest in arboviral diseases in Europe had not been attempted to date.

In recent years, Google Trends data has emerged as a powerful tool in healthcare research to assess online seeking behaviour as a representation of public interest and disease awareness [30-33]. Google Trends data represents the popularity of key words used to query the internet search engine Google, reflecting relative public interest and awareness [30, 34]. The Google Trends platform (trends.google.com) provides quantitative data on a country- and sub-country level since 2004 [35]. Relative popularity of a search term is measured by using a sample of Google searches, normalizing it to the location and time of a query, and scaling it on a range from zero to 100 to generate an interest index. A Google Trends value of 100 represents peak popularity of a query during the time period of interest at a specified location, while a value of 50 indicates 50% of the maximum search volume [35-37].

Google Trends is frequently used as a data analysis tool in healthcare research for infodemiological and infoveillance studies, e.g., to assess geographical and temporal web interest in diseases, disease awareness, online health information seeking behaviour as well as for the prediction of outbreaks and epidemics [31, 36-43]. In this study, we will use Google Trends data for a comprehensive spatio-temporal analysis of public interest in three endemic and three non-endemic arboviral diseases in 30 European countries from 2008 to 2020.

Aim and objectives

This study aims to assess public interest in emerging and re-emerging arboviral infectious diseases in the European population and identify its determinants. To achieve this, the following objectives were set: First, to assess public interest in arboviral diseases in Europe using Google Trends data since 2008. Second, to identify determinants of public interest in arboviral diseases in European countries based on the acquired data. Third, to explore the spatial correlation of public interest and case rates on a sub-country level, using the example of Germany in 2020.

Methods

Study design

Using a cross-sectional study design with observational data, data collection included the extraction of the complete available epidemiological data from 30 European countries on arboviral diseases with an average of at least five cases per year as well as the extraction of the complete available Google Trends data representing public interest in arboviral diseases in 30 European countries since 2008. Trends and patterns of public interest were described and analysed via ordinary least squares (OLS) regression [44].

Potential determinants and confounders of public interest such as reported case rates, the proportion of the foreign-born population, latitude, gross domestic product (GDP), and preventive care expenditure were examined in a Prais-Winsten regression analysis, which considers the spatio-temporal nature of the data and is a proven method for the analysis of disease interest using Google Trends data [32]. The independent variables for this analysis were chosen based on prior studies on specific arboviral diseases in select countries, which showed a correlation of public disease interest, awareness, and knowledge with incidence rates [27, 45], immigration status [46, 47], socio-economic status [28] and exposure to public health campaigns [29, 48].

Germany, Europe's most populous country, was selected for an analysis on a sub-country level, correlating Google Trends data from German federal states in 2020 with geographical coordinates via OLS regression and comparing the results to the locations of reported cases.

Acquisition and processing of epidemiological data

For the six arboviral diseases with an average of at least five reported human cases per year since 2008 (CCHFV, CHIKV, DENV, TBEV, WNV, and ZIKV infection), the reported case numbers and notification rates (per 100,000 population) for all available countries were extracted from the ECDC Surveillance Atlas of Infectious Diseases (SAID) database on January 10, 2022.

For all diseases except CCHFV infection, a categorisation into locally-acquired and travel-associated cases was provided. Rates of locally-acquired cases per 100,000 population were extracted for TBEV and WNV infection. For CHIKV, DENV, and ZIKV infection, rates of locally-acquired cases per 100,000 population were calculated using the numbers of locally-acquired reported cases per year and the World Bank total population per country data for the respective years (indicator code: SP.POP.TOTL) [49]. The extracted SAID data on ZIKV infection further included information on the number of reported infected pregnant women, with case rates being calculated accordingly.

Acquisition and processing of Google Trends data (public interest)

Google Trends query data reflecting public interest in these arboviral diseases was obtained from the Google Trends platform using the first "Disease" topic suggestion as respective keyword for each disease, e.g., chikungunya virus infection (Disease), on January 21, 2022, with the time frame being set from 2008 to present. Disease topics include various terms from queries in any language that are related to a specific disease [30].

Using the "compare" feature of Google Trends, the search volume can be compared between up to five different terms or regions. After identifying the country with the highest peak for each disease term, it was kept in each of the groups of five as a "benchmark" region, while the other four slots were taken by the remaining 29 countries in eight iterations to generate equally scaled data for all 30 countries.

Acquisition and processing of data for further variables

The gross domestic product (GDP) per capita in purchasing power parity (PPP) for all 30 European countries of interest from 2008 to 2020 was extracted from the World Bank database (indicator code: NY.GDP.PCAP.PP.CD) and converted to the natural log [50]. Geographical coordinates in decimal degrees for the 30 countries were taken from a public dataset provided on the Google developers platform [51]. Geographical coordinates in decimal degrees for the capitals of the 16 German federal states were extracted from https://www.gps-coordinates.net.

The indicators "health care expenditure for preventive care" as well as the more specific subcategory "health care expenditure for preventive care information, education and counseling", both as percentage of GDP, were extracted from the Eurostat dataset "health care expenditure by function" (online data code: HLTH_SHA11_HC, indicator codes: [HC6] and [HC6.1], respectively) for all available countries and years [52]. The foreign-born population per 1000 inhabitants was calculated for each country and year using the Eurostat indicator "foreign-born population" (indicator code: TPS00178) and the World Bank total population per country data (indicator code: SP.POP.TOTL) [49, 53].

Assessment of trends and patterns of online interest

For the assessment of trends and patterns of public interest in each disease, monthly Google Trends data points were averaged between all 30 countries. Data points reported as "< 1" were counted as 0.5. The Google Trends "compare "feature was used to compare the six benchmark countries for each disease term with each other. The maximum peak for each disease term and benchmark country was then used to scale the data for the other 29 countries in each disease category accordingly. After plotting the resulting values for each disease over time, trends and patterns were described. To analyse potential seasonal patterns further, Cochrane-Orcutt regression analyses with first-order serial correlation and iterated estimates were performed for each disease using the statistical software package Stata 17.0 and the 'prais' command [54, 55], with public interest in the respective disease averaged over 30 European countries as the dependent variable and the months of the year as (categorical, binary) independent variables (syntax: prais *depvar* [*indepvars*], corc). The analysis includes both original and transformed Durbin-Watson statistics. Autocorrelation plots were generated using the 'ac' command on the dependent variable (Supplementary Fig. 1). Two-tailed t tests were performed to determine the significance of coefficients of single variables, F statistics and Wald Chi-Squared tests to determine significance of Cochrane-Orcutt, OLS and Prais-Winsten regression models, respectively [56]. Significant p-values are indicated as follows: *** $p \leq 0.001$; ** $p \leq 0.01$; * $p \leq 0.05$.

Spatio-temporal analysis of determinants of public interest

For the linear analysis of a variety of potential determinants of public interest, the monthly relative Google search volume indices reflecting public interest (not scaled between diseases) were summed up for each country, disease term, and year, to generate a value for yearly public interest, since all relevant co-variates are available as yearly values. The resulting data was used to compare public interest between countries for each disease separately.

To explore the correlation of public interest in each disease with multiple variables across all available countries and years, a linear cross-sectional time-series model with Prais-Winsten regression parameter estimation was used [57]. The Stata command 'xtpcse' computes panel corrected standard error estimates, assuming heteroskedastic and contemporaneously correlated disturbances across panels with a first-order autoregression (AR1) model autocorrelation structure [56, 58]. To compute the covariance, a pairwise selection was used to include all available observations with non-missing pairs (syntax: xtpcse *depvar* [*indepvars*], corr(ar1) pairwise). To assess the temporary nature of the influence of reported case rates on public interest, this independent variable was lagged by one year in an additional analysis using the command L1.*indepvar*. Further, the correlation of public interest and reported case rates was analysed for each country and each disease separately in bivariate OLS regression analyses using the Stata "reg" command.

Analysis of public interest on sub-country level

To analyse subregional public interest in TBEV and WNV in Germany in 2020, the Google Trends feature "interest by subregion" was used. It assigns the German federal state in which the disease term was most popular in 2020 a value of 100 and scales interest values for the remaining 15 states accordingly. States with insufficient data for the disease term are given a value of 0. The feature also includes a map of the country divided into its 16 federal states, indicating the relative popularity of a search term by colour shading. In multiple linear regression analyses using the Stata command reg, public interest values for each arboviral disease in the 16 German federal states were correlated with the geographical coordinates of the state capitals. The results were then compared to the locations of reported cases on maps marking districts with reported cases were generated on the SAID platform for the most recent available year (2020).

Results

Trends and patterns of public interest in arboviral diseases in Europe

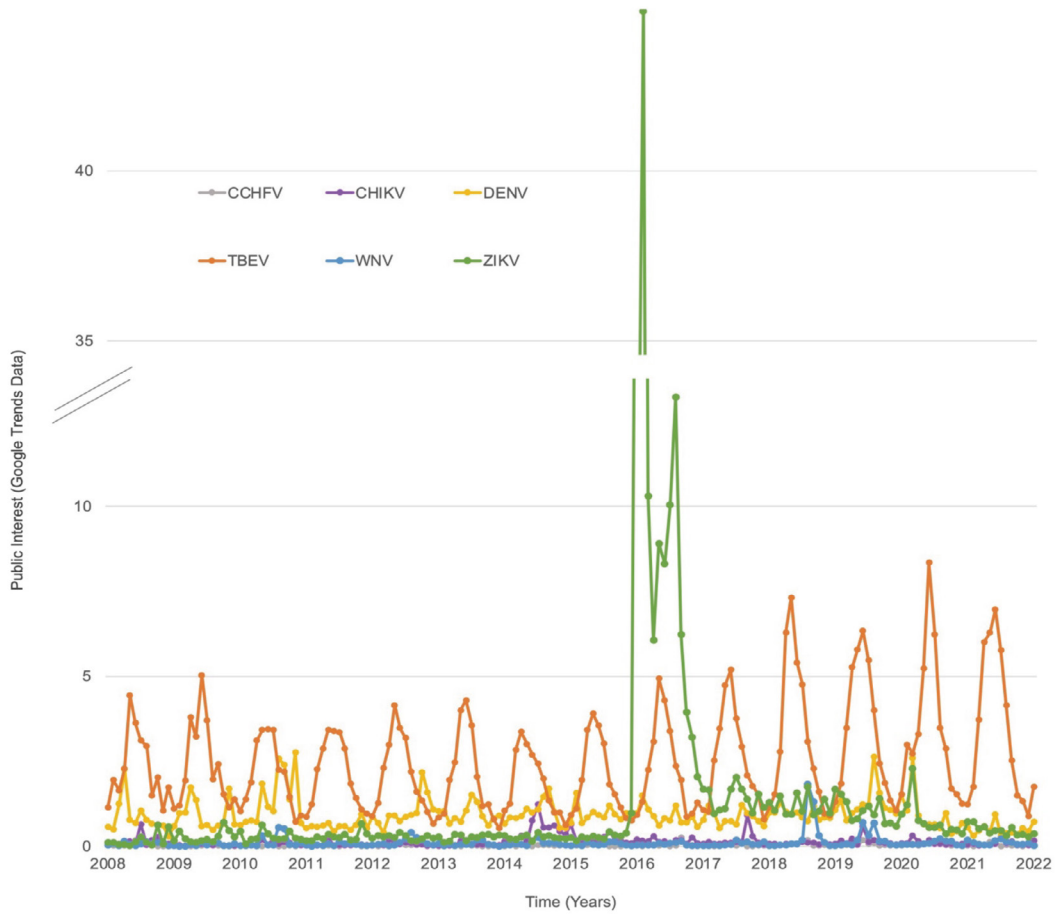
Six arboviral diseases with an average of at least five reported cases in Europe per year are recorded in the ECDC Surveillance Atlas of Infectious Diseases

(SAID). Of those, CCHFV, TBEV, and WNV infections are classified as endemic diseases in Europe, while CHIKV, DENV, and ZIKV infections are classified as non-endemic diseases [19, 59].

Public interest in the six arboviral infectious diseases in Europe was analysed using relative search volume indices generated from Google Trends data from January 2008 to January 2022. For each disease, the single highest interest peak in any of the 30 European countries served as a benchmark to scale the data points in any of the 29 remaining countries (see Methods). Using the Google Trends compare feature on the six benchmark countries and the respective disease, reveals how public interest values for the six different diseases relate to each other: Interest in ZIKV infection has by far the highest peak and keeps its value of 100, while data points for the other five diseases are scaled down accordingly, with peak interest in TBEV at 68%, DENV at 29%, WNV at 16%, CHIKV at 14%, and CCHFV at 6% of ZIKV peak interest. Transferring this scaling to the monthly data points averaged over all 30 countries for each disease, gives rise to Figure 1, with a ZIKV interest peak in 2016 being more than five times higher than the maximum TBEV interest peak in 2020, and values for interest in the other four diseases trailing far behind. After the abrupt initial spike in public interest in 2016 and 2017, ZIKV interest declined rapidly in subsequent years, even falling behind the interest values for TBEV and DENV infection.

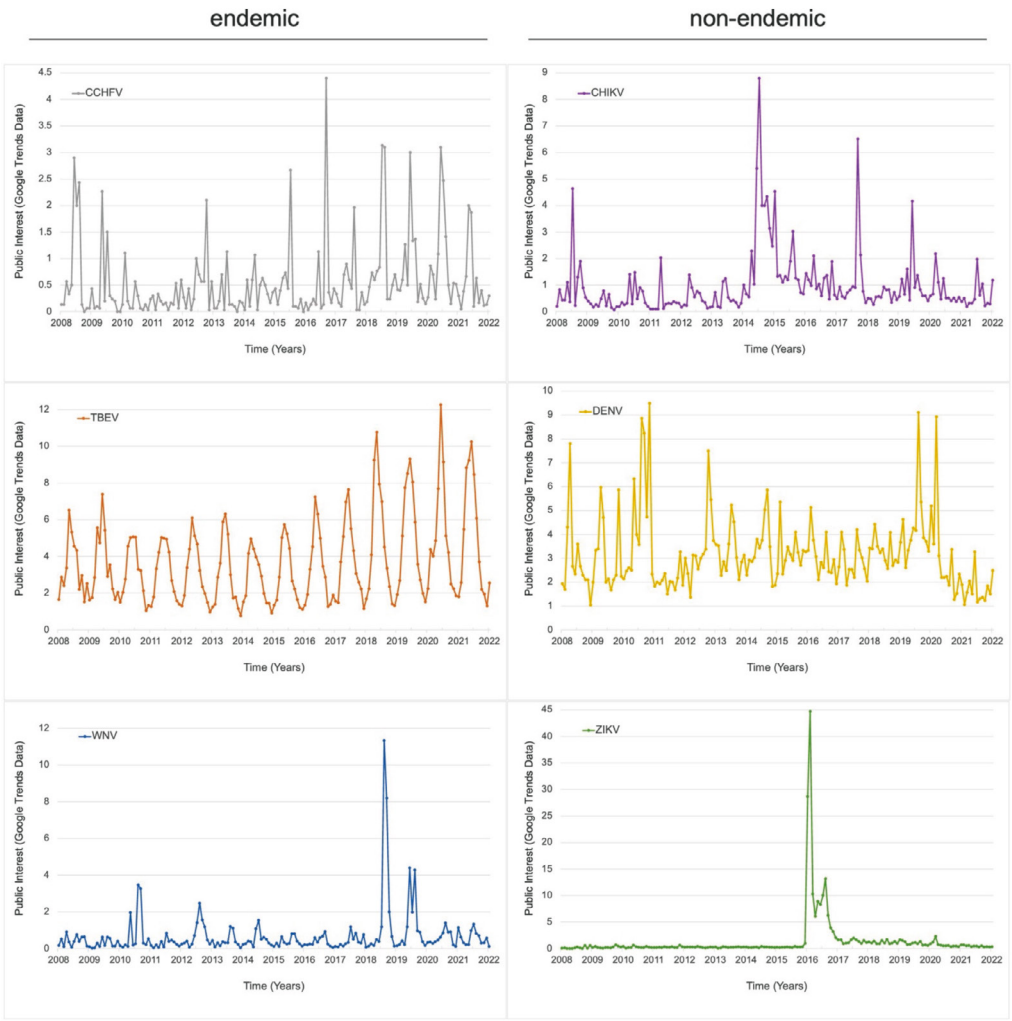
Visual inspection of the temporal distribution of public interest in arboviral diseases from January of 2008 to January of 2022 shown in Figure 1 indicates a distinct seasonal pattern for interest in TBEV infection, with a mid-year peak and a low point around the turn of the year. To investigate this phenomenon further, the average monthly public interest values for all six arboviral infectious diseases were plotted separately and unscaled between diseases (Fig. 2), revealing a more regular distribution for the three endemic diseases CCHFV, TBEV, and WNF infection, and an irregular course for the three non-endemic diseases CHIKV, DENV, and ZIKV infection.

Fig. 1. Comparison of public interest in six arboviral infectious diseases in 30 European countries.



Public interest is represented by Google Trends data from January of 2008 to January of 2022. For each disease, monthly data points were averaged over all 30 countries, then scaled according to the values of the respective benchmark countries (see Methods) to represent differences of public interest between diseases. To enhance legibility of data points with lower values of public interest compared, the y axis is broken between the values of 10 and 35.

Fig. 2. Seasonal trends of public interest in six arboviral infectious diseases in Europe.



Public interest is represented by Google Trends data from January of 2008 to January of 2022. For each of the diseases, monthly data points were averaged over all 30 countries. While the three endemic diseases CCHFV, TBEV, and WNV infection (left panel) show significant seasonal patterns, the three non-endemic diseases CHIKV, DENV, and ZIKV infection (right panel) do not (Tab. I). Public interest data is not scaled between diseases.

A Cochrane-Orcutt analysis, correlating the months of the year with public interest values for each disease, confirms this result (Tab. I): Models with public interest in the three endemic diseases are highly significant (F stats: p-value < 0.001), with maximum coefficients for the month of June for both CCHFV and TBEV, and for the month of August for WNV. Of the three models for endemic diseases, the model for TBEV shows the most distinct seasonal pattern with an adjusted R^2 of 0.65. While the coefficient for July has a slightly significant positive correlation with public interest in CHIKV infection and a negative correlation for the month of December for interest in ZIKV infection, the overall models for these two diseases are not significant, nor are the models for interest in DENV, the third non-endemic infectious disease.

As an additional independent variable, the overall order of observations was included in the respective models (Tab. I), with the first observation being January 2008 and the last (observation 168) being December 2021. Interestingly, the order of observations has a significant positive correlation for interest CCHFV and TBEV, indicating that only public interest in tick-borne endemic arboviral diseases has been increasing from 2008 to 2021. The increase of interest has the highest coefficient for TBEV (0.014), the arboviral disease with the highest and fastest increasing rate of locally-acquired cases in Europe, and lowest for CCHFV (0.003), the disease with the lowest case rate of the six. For WNV, the third endemic arboviral disease, public interest over time also has a slight positive coefficient (0.004), however it is not significant. No significant trend in public interest over time could be detected for any of the three non-endemic diseases.

While monthly public interest values seem to reveal seasonal patterns, plotting yearly values for each of the 30 European countries separately (Fig. 3) shows diverse

Tab. I. Seasonal patterns and trends of public interest in arboviral diseases in Europe from January 2008 to January 2022.

	Endemic in Europe			Non-endemic in Europe		
	Model	Model	Model	Model	Model	Model
	CCHFV	TBEV	WNV	CHIKV	DENV	ZIKV
Independent variables	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)
January	Omitted	Omitted	Omitted	Omitted	Omitted	Omitted
February	0.058 (0.249)	**0.646* (0.260)**	-0.028 (0.303)	-0.096 (0.321)	0.419 (0.449)	1.075 (1.000)
March	0.113 (0.261)	**2.084*** (0.329)**	-0.003 (0.370)	-0.207 (0.394)	0.414 (0.538)	-1.381 (1.284)
April	0.207 (0.262)	**3.923*** (0.363)**	0.023 (0.399)	0.081 (0.426)	0.514 (0.572)	-1.870 (1.435)
May	0.496 (0.263)	**5.197*** (0.381)**	0.246 (0.412)	0.100 (0.440)	0.304 (0.586)	-1.659 (1.520)
June	**0.961*** (0.263)**	**5.421*** (0.390)**	0.477 (0.418)	0.484 (0.446)	0.078 (0.591)	-1.647 (1.563)
July	**0.844** (0.263)**	**4.265*** (0.393)**	0.615 (0.420)	0.994* (0.448)	0.111 (0.593)	-1.519 (1.577)
August	**0.674* (0.263)**	**2.461*** (0.391)**	**1.822*** (0.418)**	0.263 (0.447)	1.091 (0.592)	-1.323 (1.565)
September	0.264 (0.263)	**1.365*** (0.382)**	**1.247** (0.413)**	0.649 (0.441)	0.771 (0.586)	-1.882 (1.524)
October	0.100 (0.262)	0.582 (0.365)	0.333 (0.400)	0.178 (0.427)	0.127 (0.573)	-2.052 (1.443)
November	-0.069 (0.261)	0.025 (0.332)	0.0361 (0.373)	-0.056 (0.397)	0.713 (0.541)	-2.079 (1.299)
December	0.024 (0.249)	-0.150 (0.267)	-0.028 (0.309)	-0.269 (0.328)	-0.450 (0.457)	-2.210* (1.027)
Overall order of observations	**0.003* (0.001)**	**0.014*** (0.003)**	0.004 (0.003)	0.001 (0.003)	-0.003 (0.004)	-0.010 (0.015)
Constant	0.026 (0.216)	0.365 (0.421)	-0.048 (0.405)	0.683 (0.436)	3.134*** (0.550)	1.906 (1.833)
Rho	0.101	0.591	0.487	0.495	0.427	0.646
Adjusted r^2	0.142	0.647	0.131	0.021	0.023	-0.002
F stats (p)	**< 0.001*** **	**< 0.001*** **	**< 0.001*** **	0.223	0.206	0.473
D-statistic (original)	1.796	0.814	1.025	1.010	1.143	0.706
D-statistic (transformed)	2.000	1.932	1.838	2.24	2.081	1.701
N	167	167	167	167	167	167

Dependent variable: public interest in respective disease averaged over 30 European countries (Google Trends data). Models are estimated by an Cochrane-Orcutt AR(1) regression with iterated estimates including transformed Durbin-Watson (d) statistics. *** $p \leq 0.001$; ** $p \leq 0.01$; * $p \leq 0.05$ (two-tailed tests). Coefficients with significant p-values are shown in light blue, with darker shades representing higher significance. Standard errors (se) are shown in parentheses below the coefficients. The month of January was omitted due to collinearity.

distributions across countries for all diseases except ZIKV infection, which has a characteristic, simultaneous course for all countries: Virtually no public interest until 2015, a rapid increase in 2015 and 2016, and a sharp decline in subsequent years.

Determinants of public interest in arboviral diseases in Europe

To examine the correlation of public interest in arboviral diseases in Europe with potential determinants and to control for possible confounders, five independent variables were included in a spatio-temporal analysis using data from 30 European countries from 2008 to 2020: reported case rates, geographical latitude of the country, percentage of foreign-born population, GDP per capita, and expenditure for preventive health care measures (Tab. II).

Reported case rates are the only variable that consistently correlates significantly with public interest in all six arboviral infectious diseases [p-values: 0.016 (CCHFV), 0.003 (DENV), < 0.001 (CHIKV, TBEV, WNV, ZIKV)]. All coefficients are positive, with the highest values for CCHFV, ZIKV, and CHIKV infection. However, this effect is only temporary: If reported case rates are lagged by just one year, the significant correlation disappears for all six diseases.

Geographical latitude has a negative correlation with public interest in all diseases but TBEV infection, meaning that interest is higher in Northern countries for TBEV, but higher in Southern countries for all others (significant results for CCHFV (p-value < 0.001), CHIKV (p-value = 0.015), and TBEV (p-value = 0.018)) (Tab. II). The foreign-born population per 1000 inhabitants has a significant positive correlation only with public interest

Fig. 3. Diverse patterns of yearly public interest in arboviral infectious diseases in 30 European countries.

Monthly Google Trends data points from 2008 to 2020 were summed up over 12 months for each country and disease.

in ZIKV infection (p-value = 0.006). Correlation with GDP per capita (in PPP) has positive coefficients for public interest in all six diseases [significant for CCHFV (p-value = 0.043) and DENV (p-value = 0.001)], indicating a higher interest in countries with higher GDPs.

Only interest in DENV and ZIKV infection have a significant positive correlation with expenditure for preventive health care measures (p-values = 0.023 and 0.029, respectively; Tab. II). Using the more specific indicator "expenditure for preventive care information, education, and counselling programmes", however, does not result in a significant correlation with public interest in any of the diseases. Replacing the reported case rate variable with rates for only locally-acquired cases, however, leads to highly significant positive correlations for public interest in CHIKV, TBEV, and WNV (p-values < 0.001; Tab. IIIA). For the DENV model, results are not significant. For CCHFV case data, no distinction was made between locally-acquired and travel-associated cases. For the ZIKV model, the number of observations is insufficient for an analysis using locally-acquired cases. However, public interest in ZIKV is highly correlated with the case rates of ZIKV infected pregnant women (p-value = 0.004; Tab. IIIB).

Analysing public interest each of the 30 European countries separately, using reported case rates as the sole determinant in a simple linear regression is sufficient to explain variation in public interest in more than 40% of countries (p-values ≤ 0.05). For each of the six arboviral

Tab. II. Determinants of public interest in emerging arboviral diseases in Europe.

	Model	Model	Model	Model	Model	Model
	CCHFV	TBEV	WNV	CHIKV	DENV	ZIKV
Independent variables	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)
Reported case rate	228.696* (94.925)	8.038*** (1.374)	21.807*** (2.995)	124.913*** (12.907)	12.056** (4.081)	141.976*** (31.696)
Latitude	-0.365*** (0.085)	2.346* (0.989)	-0.184 (0.182)	-0.710* (0.292)	-0.622 (0.360)	-0.059 (0.225)
Foreign-born population (per 1,000 inhabitants)	-0.007 (0.008)	-0.026 (0.018)	-0.008 (0.008)	0.019 (0.016)	-0.030 (0.020)	0.148** (0.054)
Gdp per capita (ln PPP)	8.817* (4.262)	7.351 (8.691)	4.453 (4.133)	13.373 (12.059)	28.127*** (8.345)	11.252 (21.206)
Preventive care expenditure (% of GDP)	12.045 (9.901)	46.821 (38.586)	18.582 (20.276)	-34.587 (28.619)	46.801* (20.578)	34.280* (15.705)
Constant	-70.009 (45.424)	-169.262* (70.394)	-34.050 (42.773)	-92.794 (116.036)	-236.919** (86.324)	-111.641 (207.521)
R^2	0.077	0.306	0.262	0.447	0.214	0.350
N observations	228	159	223	202	220	97
N countries	28	26	28	25	27	26
Wald Chi^2	43.29***	73.30***	72.91***	115.52***	133.78***	142.13***
Rho	0.311	0.691	0.477	0.397	0.361	-0.110

Models are estimated by a Prais-Winsten regression with correlated panel-corrected standard errors and a first-order auto-regressive error process. *** $p \leq 0.001$; ** $p \leq 0.01$; * $p \leq 0.05$ (two-tailed tests). Coefficients with significant p-values are shown in light blue, with darker shades representing higher significance. Standard errors (se) are shown in parentheses below the coefficients.

Tab. III. Models using case rates for locally-acquired cases and infections in pregnant women.

A				B	
	Model	Model	Model		Model
	CHIKV	TBEV	WNV		ZIKV
Independent variables	Coefficient (se)	Coefficient (se)	Coefficient (se)	Independent variables	Coefficient (se)
Reported locally acquired case rate	248.742*** (12.670)	8.064*** (1.436)	21.595*** (3.023)	Reported case rate in pregnant women	1183.424** (411.709)
Latitude	-0.685** (0.260)	2.798** (1.024)	-0.95 (0.180)	Latitude	-0.229 (0.379)
Foreign-born population (per 1,000 inhabitants)	0.0253226 (0.030)	-0.028 (0.018)	-0.008 (0.008)	Foreign-born population (per 1,000 inhabitants)	0.233*** (0.071)
GDP per capita (ln PPP)	20.738 (13.824)	3.574 (8.929)	4.466 (4.118)	GDP per capita (ln PPP)	22.971 (26.918)
Preventive care expenditure (% of GDP)	-8.622 (20.686)	46.163 (39.202)	19.043 (20.558)	Preventive care expenditure (% of GDP)	-3.550 (19.252)
Constant	-171.760 (128.903)	-149.653* (67.699)	-33.575 (42.823)	Constant	-222.967 (251.492)
R^2	0.171	0.311	0.247	R^2	0.249
N observations	194	149	223	N observations	97
N groups	25	26	28	N groups	26
Wald Chi^2	139.66***	89.77***	72.21***	Wald Chi^2	56.94***

(A) Replacing the independent variable "reported case rate" with "reported locally-acquired case rate". **(B)** A model using reported case rates of ZIKV infection in pregnant women. Dependent variable: public interest in respective disease in 30 European countries (Google Trends data). Models are estimated by a Prais-Winsten regression with correlated panel-corrected standard errors and a first-order auto-regressive error process. *** $p \leq 0.001$; ** $p \leq 0.01$; * $p \leq 0.05$ (two-tailed tests). Coefficients with significant p-values are shown in light blue, with darker shades representing higher significance. Standard errors (se) are shown in parentheses below the coefficients.

infections, the countries with the most significant coefficients for the correlation of public interest with case rates are shown in Figure 4. The plots show public interest based on Google Trends data closely following reported case rates. For interest in CCHFV infection, however, Spain is the only country with a significant correlation (p-value < 0.001) due to a low number of cases. Interest in ZIKV infections yields the highest

Fig. 4. Reported cases and public interest in arboviral diseases in individual European countries over time.

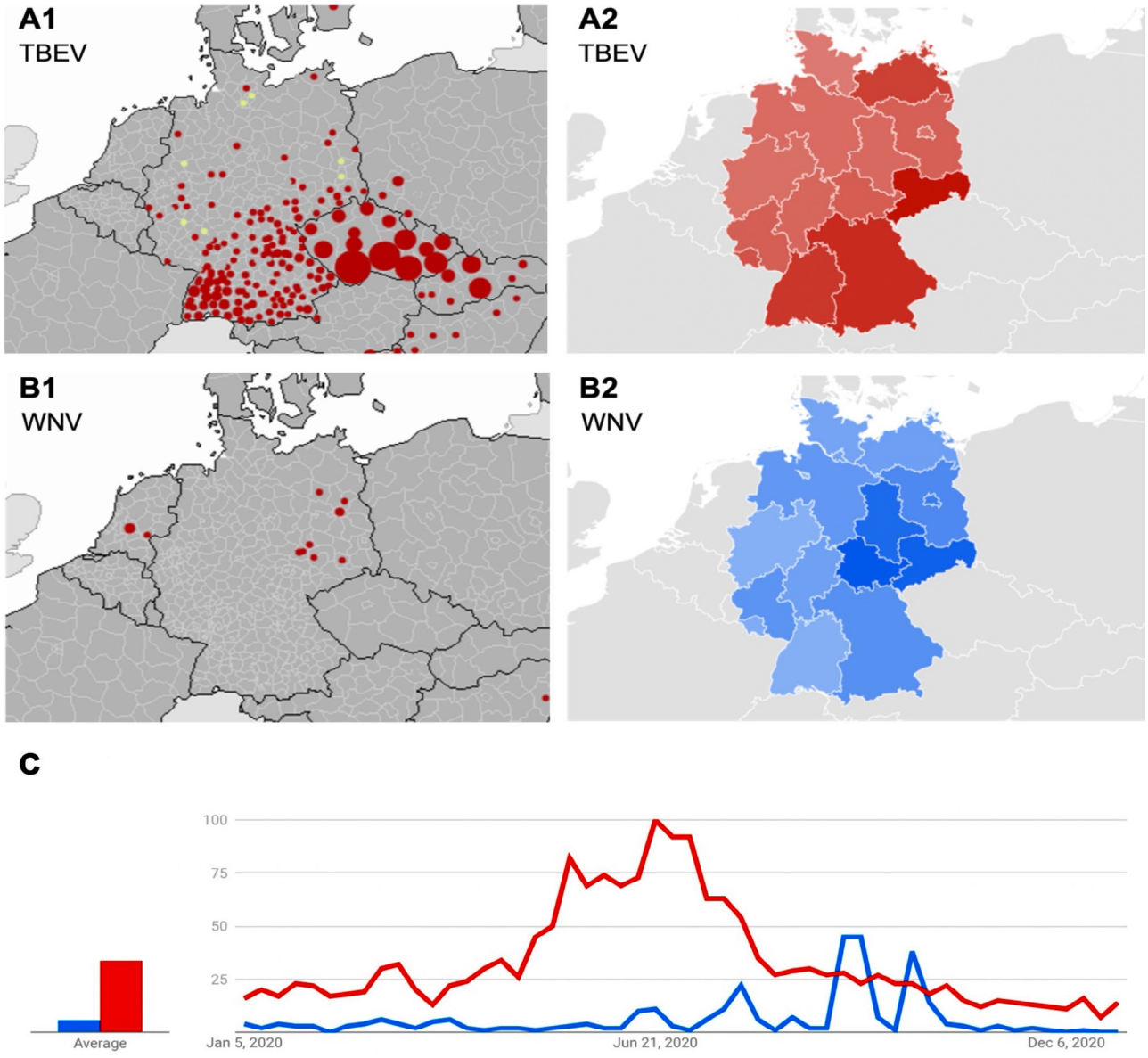
For each of the six arboviral infections, plots are shown for the countries with the most significant coefficients ($p \leq 0.05$) from a bivariate analysis using reported case rates as only independent variable. For CCHFV, Spain is the only country with a significant correlation due to a low number of data points.

percentage of countries with a significant bivariate model (68 % out of all countries with sufficient data), followed by 53 % for WNV, 38 % for CHIKV, 28 % for TBEV, 27 % for DENV, and 25 % for CCHFV infection (p-values ≤ 0.05).

Public interest in arboviral diseases on sub-country level (case study: Germany)

In the ECDC Surveillance Atlas of Infectious Disease, reported case data on a sub-country level is only available for the endemic arboviral infections with TBEV and WNV

Fig. 5. Subregional analysis of TBEV and WNV in Germany in 2020.



Red dots mark regions that report one or more locally acquired confirmed cases of TBEV **(A1)** and WNV **(B1)**, with larger dot sizes representing a higher number of cases. Green dots mark regions that report zero cases. Public interest in TBEV infections is higher in federal German states located in the South-East of the country **(A2)**, while public interest in WNV infections is higher in Eastern German states **(B2, Tab. IV)**. **(C)** Comparison of weekly public interest in TBEV (red) and WNV (blue) infections over the course of 2020. Maps and plots were created using the ECDC Surveillance Atlas of Infectious Diseases database **(A1, B1)** and the Google Trends platform **(A2, B2, C)**.

(ECDC, 2022f). In 2020, TBEV cases were clustered in the South-Eastern part of Germany, while WNV cases were exclusively reported in the Eastern region, as can be seen in Figures 5A1 and 5B1, respectively.

For Germany, public interest data is available on a federal state level on the Google Trends platform. A visual inspection of the Google Trends "interest by subregion" visualisation of TBEV and WNV interest in Germany in 2020 shows increased interest in TBEV infection in the South-Eastern region of the country and increased interest in WNV infection in the Central-Eastern part (Figs. 5A2 and 5B2, respectively), congruent with the areas of reported infections.

To confirm this observation, a multiple linear regression analysis was performed, correlating public interest values for each of the six arboviral diseases on a federal state level with the geographical coordinates (latitude and longitude in decimal degrees) of each state's capital (Tab. IV).

Only the models for the two diseases endemic in Germany, TBEV and WNV, had significant results (F stats: p-values = 0.004 and 0.007, respectively), with a significant negative correlation of latitude and a positive correlation of longitude for TBEV interest (p-values = 0.003 and 0.013, respectively) and a positive correlation of longitude for WNV interest

Tab. IV. Correlation of TBEV and WNV public interest in Germany in 2020 with geographical coordinates.

	Model	Model	Model	Model	Model	Model
	CCHFV	TBEV	WNV	CHIKV	DENV	ZIKV
Independent variables	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)	Coefficient (se)
Latitude	1.122 (4.571)	**-7.024** ** **(1.941)**	-3.086 (2.651)	-9.962* (4.616)	-4.377 (3.026)	-6.475 (4.975)
Longitude	3.802 (3.903)	**4.756*** **(1.657)**	**8.793** ** **(2.264)**	1.803 (3.942)	-3.029 (2.5849)	6.855 (4.249)
Constant	-62.990 (130.614)	371.352 (96.741)	118.005 (132.127)	526.204 (230.083)	309.716 (150.842)	297.677 (247.992)
Adjusted R^2	-0.054	0.499	0.466	0.151	0.154	0.086
F stats (p)	0.556	0.004**	0.007**	0.136	0.133	0.220
N (regions)	16	16	16	16	16	16

Dependent variable: public interest in respective disease in 16 German federal states (Google Trends data). Models are estimated by OLS regression. *** $p \leq 0.001$; ** $p \leq 0.01$; * $p \leq 0.05$ (two-tailed tests). Standard errors (se) are shown in parentheses below the coefficients. The independent variables latitude and longitude constitute the geographical coordinates for the respective German state capitals.

(p-value = 0.002), confirming that interest in TBEV is highest in the South-East and interest in WNV is highest in the East of Germany. While the coefficient for latitude shows a slightly significant negative correlation with CHIKV interest (p-value = 0.050), the overall CHIKV model is not significant (F stats: p-value = 0.136), nor are any of the other models for interest in non-endemic diseases.

Overall, public interest in TBEV infection in 2020 was more than six-fold higher than public interest in WNV infection (Fig. 5C), with a broad peak for TBEV interest in the summer months and narrower peaks for WNV later in the year.

Discussion

Only public interest in endemic arboviral diseases increases and shows seasonal patterns

An analysis of trends and patterns of public interest in arboviral diseases across 30 European countries from 2008 to 2020 showed that significant seasonal patterns of public interest are only present in the endemic viral diseases, CCHFV, TBEV, and WNV infection, with (F statistic) p-values for each of the models below 0.001. For WNV, the two months of August and September show a significant seasonal increase of public interest, for CCHFV the three months from June to August. For TBEV, however, public interest increases most significantly during the seven months from March to September. These months closely match the seasons during which the underlying disease vectors – ticks for TBEV and CCHFV as well as *Culex* mosquitoes for WNV– are most active [60, 61].

While this analysis is the first to include a comprehensive set of arboviral diseases and countries, a seasonal pattern of public interest has previously been shown for select countries and arboviral disease-associated terms. Jensen et al. (2022) use Google Trends data of search terms synonymous with "tick(s)" in nine European countries and identify seasonal patterns that represent changes in precipitation and temperature [62], in accordance with the findings in this analysis.

Interestingly, the analysis of patterns and trends also showed that public interest in the two tick-borne endemic arboviral diseases, CCHFV and TBEV infections, was increasing significantly, while public interest in the three non-endemic arboviral diseases, *Aedes* mosquito-borne CHIKV, DENV, and ZIKV infections, showed no significant trends.

Both the existence of seasonal patterns and the increasing trends of public interest in only endemic arboviral diseases may be explained by the Health Belief Model, which maintains that health-related behaviours are more likely to occur when the perceived susceptibility to developing a health problem is high [63-65]. A population's perceived susceptibility to a disease which is already endemic would naturally be higher than to one that has not yet reached endemic status. The likelihood of catching an arboviral infection also increases temporarily during the seasons in which the respective disease vectors, i.e., ticks and mosquitoes, are most active, resulting in health-related behaviours, which in this case manifests itself in the online search for information on the disease.

Other key constructs of the Health Belief Model include perceived severity of the disease as well as perceived barriers and perceived benefits of the health action, the last of which may be a decreased risk of an arboviral infection due to preventive measures or the timely identification of symptoms of an arboviral infection, enabling the infected to seek appropriate medical treatment [66]. The concepts "cue to action" and "self-efficacy" were added to the Health Belief Model in more recent adaptions and refer to a stimulus to undertake the health action and to the self-confidence in the ability to perform the health action, respectively [65].

Among the three analysed endemic arboviral diseases, TBEV has both the highest coefficient for the increase of public interest and the fastest increasing rate of locally-acquired cases, while CCHFV, the arboviral disease with the lowest case rate, has the lowest – yet significant – positive coefficient for public interest, showing that interest in CCHFV is growing comparatively slowly.

This result indicates a correlation of public interest and case rates, which was investigated in more detail in the subsequent analysis and will be discussed in the following section.

Case rates drive public interest in arboviral diseases - but only temporarily

In a spatio-temporal Prais-Winsten regression analysis using Google Trends data from 2008 to 2020 across 30 European countries, reported case rates was the only one of five independent variables (see study design) to correlate significantly with public interest in all six analysed arboviral diseases, confirming the previous indication that case rates are an important driver of public interest ($p < 0.001$ for TBEV, WNV, CHIKV, and ZIKV; $p < 0.01$ for DENV, $p < 0.05$ for CCHFV).

The identified correlation of public interest in arboviral diseases and incidence rates in Europe is in accordance with results from studies in select countries for arboviral infections like WNV in Italy [27], DENV in Mexico [67] as well as for other viral infections such as Ebola in West Africa [68] and influenza in the United States [69].

Due to this correlation, Google Trends data was shown to be a valuable source of information for surveillance and dynamic prognostic tools to predict outbreaks and epidemics, using Google queries of disease terms such as "Zika" and "chikungunya" in Venezuela [43], of disease vectors like "ticks" in Sweden [42] or of common disease symptoms such as "bone pain" and "fever" in Singapore [70]. While surveillance via Google Trends data is considerably less expensive than conventional surveillance methods, the novel technique has also raised concerns that search queries could be more influenced by the media than by the actual disease burden, and may not be suitable for either widespread diseases with low media coverage or for rare diseases with high media coverage [71, 72].

Our analysis also revealed the temporary nature of the correlation of public interest and reported case rates. The significant correlation of yearly public interest values and reported case rates is lost for all six arboviral infections when values of reported case rates are lagged by one year. This transiency of public interest based on yearly Google Trends values confirms the previous result showing the seasonality of monthly values, indicating that public interest in arboviral diseases immediately declines when the risk of infection – or the perceived susceptibility, as stated in the Health Belief model – decreases again.

The impermanence of public interest in arboviral infections becomes immediately obvious when looking at the example of interest in Zika. For decades ZIKV had been endemic in Africa and Asia, before the Asian lineage started spreading to naïve areas, causing massive outbreaks in Micronesia in 2007, French Polynesia and other Pacific islands from 2013 on [73]. The ECDC only started recording cases after the large outbreak in South America in 2015/16, when the WHO declared ZIKV infections a "Public Health Emergency of International Concern" and clusters of foetal malformations and neurological disorder emerged [74]. After a sharp increase from 2015 to 2016, ZIKV cases have declined rapidly – and so has public interest in all European countries. At the time of writing, ECDC data for ZIKV infection is only available until 2019, which is the year the first three European cases of vector-borne ZIKV transmission were reported in France [75, 76]. Future analyses will need to determine whether vector-borne acquisition via local *Aedes albopictus* mosquitoes becomes a major transmission mode for ZIKV infections in Europe, and what effect this development may have on public interest in the disease.

The finding that public interest in diseases – represented by online health information-seeking behaviour – may be short-lived, matches results from Google Trends analyses in other contexts: The analysis of Google Trends data from six countries on the Arabian Peninsula before and after four different public health interventions, i.e., "Global Public Health Days", which were supposed to raise awareness for specific health topics such as diabetes and hypertension, showed that the search volume declined by up to 80 % within a week of peak interest [77].

Public health interventions like these awareness campaigns have also been considered in our analysis, by including the annual preventive care expenditure per country as an independent variable. However, the results show that preventive care expenditure (as percentage of the GDP) had a significant positive correlation only with public interest in DENV and ZIKV infection ($p = 0.023$ and 0.029, respectively), two closely related viruses that are primarily transmitted by *Aedes aegypti* mosquitoes [78] and have the lowest yearly average number of locally-acquired cases in Europe (5.4 and 5.8, respectively). It may be speculated that prior to public health campaigns, public awareness and knowledge is lowest for the infections with the lowest number of local transmissions, and interventions may therefore have the greatest effect.

Analysing only locally-acquired cases also shows a high positive correlation with public interest in the respective arboviral diseases, with significant results for CHIKV, WNV, and TBEV ($p < 0.001$ for all) and larger coefficients compared to the analysis using the total case rates. For ZIKV, public interest is correlated positively with the case rates of infected pregnant women ($p = 0.004$), with a coefficient more than eight times higher than for total case rates. This effect may be explained by the phenomenon that risk is perceived as being higher when future generations are potentially impacted [79-81]. Lozano et al. (2021) propose that an overestimation of the perceived risk of ZIKV transmission compared to other arboviruses is mainly caused by the fact that ZIKV is known to cause malformations in foetuses of pregnant infected women [81].

A difference in perceived risk or susceptibility may also be the reason why – even when controlling for the countries' case rates – public interest in arboviral infections with viruses that are widespread in tropical and subtropical regions such as CCHFV and CHIKV

is significantly higher in European countries at a lower geographical latitude ($p < 0.001$ and $p = 0.015$, respectively), while public interest in TBEV, which is more prevalent in regions with cooler climates, is positively correlated with countries at a higher latitude ($p = 0.018$).

Spatial correlation of public interest in arboviral diseases can be shown on sub-country level

The identified correlation of public interest and geographical location could also be shown on a sub-country level in a case study using Google Trends data from the 16 German federal states in 2020. In an OLS regression, geographical coordinates of the state capitals were correlated with public interest in TBEV and WNV infection, the two arboviral diseases that are endemic in Germany. The results of this analysis showed that public interest in TBEV correlates significantly with South-Eastern coordinates, while public interest in WNV correlates significantly with Eastern coordinates. These geographical distributions closely match the locations of locally-acquired infections of the respective diseases in Germany in 2020, according to maps extracted from the ECDC Surveillance Atlas of Infectious diseases.

For WNV in Europe, the main geographical distribution are countries is in the South-East. However, an Eastern-German cluster has formed in recent years, with a distinct group of WNV strains termed the "Eastern German WNV clade" [82]. Even though TBEV infection is generally more widespread in Northern-European regions, in Germany, the main TBEV risk areas are located in the woodland habitats of the Southern States of Bavaria and Baden-Württemberg as well as the Eastern States of Thuringia and Saxony [83]. Interestingly, a significant correlation of geographical coordinates of public interest and geographical coordinates does not exist for any of the other four arboviral diseases, all of which are non-endemic in Germany.

The findings of this analysis indicate that perceived susceptibility, an important element in the Health Belief Model [63] as discussed above, also influences public interest in arboviral diseases on a sub-country level. The use of subregional Google Trends data has already proven to be useful in other contexts: In the United States, influenza-related Google queries have been used to improve flu surveillance on a state level [84]. For TBEV, a precise knowledge of the location of infections is particularly crucial, since TBEV infested ticks are known to cluster in specific focus areas [85-87].

The results of our spatio-temporal analysis point to perceived susceptibility as the main driver of public interest in arboviral diseases in Europe on all levels. This finding is in accordance with a qualitative study of vector control strategies following the ZIKV epidemic of 2015/16 in Brazil, which revealed susceptibility to infection to be a key influence on the engagement in health protection measures [88]. In Indonesia, a cross-sectional study on behaviour to prevent DENV infection found that participants with a higher perceived susceptibility showed better prevention behaviour [89]. However, an evaluation of public health messages on *Aedes aegypti* mosquito-transmitted arboviruses in Brazil discovered that less than a third of messages were aiming to convey perceived susceptibility, while "cue to action" was the most frequently featured concept of the Health Belief Model [90].

Limitations of analysis

This study is subject to several limitations. In our analysis, only arboviral diseases in the ECDC SAID with an average of at least five reported human cases per year since 2008 were considered. This excludes other arboviruses that are considered potential threats to humans in Europe [59, 91, 92], but had either an insufficient reported case count such as infections with RVFV, YFV, and the SAID category "other viral haemorrhagic fevers", or are not at all covered in the SAID, such as JEV, Usutu virus, Toscana virus, and louping ill virus infections.

A valid Google Trends analysis depends on the correct selection of key words. This may be complicated by the comparison of trends across countries with different languages as well as by queries with alternative spellings and nomenclatures [30]. Since suggested "disease topics" such as "Zika fever (Disease)" instead of individual search terms were selected for the analysis in this dissertation, queries cover a group of terms related to the disease topic that share "the same concept in any language" [35]. While this approach solves the problems regarding language, nomenclature, and spelling, the exact key words included in each disease topic are not public and can therefore not be evaluated. However, the "related queries" section on the platform includes queries searched for by users who also searched for the topic in question and may give an indication of the contents aggregated within disease topics (*the most popular related queries for the six disease topics for 30 European countries are available as Supplemental Data*). While related queries for tick-borne encephalitis (TBE) include apparent misspellings of the video platform YouTube ("you tbe"), the very distinct seasonal pattern of the TBE disease topic makes it seem unlikely that this related query, which has no apparent seasonal trends, has been included. In some countries, related queries refer to more specific encephalitis subtypes caused by TBEV, such as the abbreviation FSME for early summer meningoencephalitis in Germany, Austria, and Luxemburg. However, some queries also refer to unrelated tick-borne infections such as borreliosis. In other cases, a lack of searches may not reflect a lack of interest but a lack of inclusion of proper search terms in the disease topic. While a distortion of results cannot be ruled out, it has likely been at least partially mitigated by the simultaneous analysis of queries across 30 countries and the separate analyses for each disease, levelling out potential biases arising from the tool's inclusion of key words for disease topics.

A further limitation of Google Trends analyses may arise through the fact that only a sample of the billions

of Google searches per data is used to generate Google Trends data [35]. For regions of interest that are small, sampling noise may be extensive [93] and results should be evaluated with caution. To keep sampling noise as low as possible for the analysis on sub-country level, the most populous European country, Germany, was selected for the case study.

In some cases, public interest in arboviral diseases may have been substantially influenced by variables not included in this analysis. Hantavirus haemorrhagic fever and hantavirus pulmonary syndrome are emerging diseases in Europe that are not caused by an arbovirus but by a rodent-borne virus (robovirus), orthohantavirus or hantavirus [93, 94]. In late March 2020, shortly after the onset of the COVID-19 pandemic, Google searches for keywords related to orthohantavirus spiked more than 10 times higher than the previous maximum peak in the Google Trends data, which dates back to 2004 [95]. This sudden increase of interest does not seem to have been caused by rising incidence rates. On the contrary, the number of reported hantavirus infections in 2020 had dropped to its lowest point since the start of ECDC reporting in 2008 [96]. However, a "viral" post claiming that hantavirus had emerged as a new fatal virus in China and could potentially cause a COVID-19 like pandemic, had started spreading rapidly across social media after one fatal case of hantavirus infection had been reported in the Chinese Shandong province on March 24, 2020 [97-99]. This example shows that random and seemingly minor occurrences like a single fatality may have a major and hardly predictable impact on public interest in diseases. Triggers for these phenomena may not always be identifiable in retrospect.

Less surprisingly, a major world event such as the COVID-19 pandemic may have influenced public interest in other viral diseases as well, either by drawing attention to or deflecting attention from other potential viral threats. However, the data collected for this analysis does not seem to show outliers for public disease interest in 2020 compared to other years.

The COVID-19 pandemic also may have had an impact on reported case rates of arboviral diseases through travel restrictions, rising outdoor activities, and underdiagnoses due to overburdened healthcare systems. Underdiagnoses, however, do not only occur during a global pandemic. Especially emerging diseases are frequently underdiagnosed due to a lack of knowledge among clinicians as well as due to insufficient standardised diagnostic testing methods when unexplained and non-specific febrile illnesses occur [19, 22].

Conclusion

This work marks the first comprehensive spatio-temporal analysis of Google Trends data from 30 European countries to assess trends, patterns, and determinants of public interest in emerging and re-emerging arboviral diseases.

The results of this analysis indicate that public interest in arboviral diseases in Europe is heavily impacted by perceived susceptibility on a temporal as well as on a spatial level. Only public interest in the three endemic arboviral diseases, CCHFV, TBEV, and WNV, displayed significant seasonal patterns, with a significant increase of public interest since 2008 for the tick-borne infections with CCHFV and TBEV. While controlling for potential confounders, a Prais-Winsten regression showed that public interest in all six analysed arboviral diseases, including non-endemic CHIKV, DENV, and ZIKV infections, is driven by reported case rates. This effect is temporary, and public interest drops rapidly when cases decline. A correlation of public interest in arboviral infections and the geographical distribution of locally-acquired reported cases could be shown both on a country level in Europe as well as on a sub-country level in a case study using Google Trends data from German federal states.

In future studies, the presented results could be validated and supplemented by further quantitative analyses that include other novel data streams such as Twitter data and Wikipedia edits as well as traditional data collection methods such as surveys. The latter would enable both the acquisition of demographic metadata and an evaluation of the impact of specific public health interventions and awareness campaigns on public interest arboviral diseases. Future public health interventions should focus on perceived susceptibility being the main driver of public interest and attempt to alert the public to the increasing risk of infection with currently non-endemic arboviral diseases.

Ethical approval

Ethical approval for this study was obtained from the Ethics Committee at the Health Department of the University of Essex Online prior to data acquisition

Acknowledgements

The author thanks Debbi Marais for her helpful feedback and comments.

Funding sources: this research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The author declares no conflict of interest.

Authors' contributions

The author developed the research concept and design, collected and analysed the data, interpreted the results and wrote the manuscript.

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Received on October 11, 2022. Accepted on December 29, 2022.

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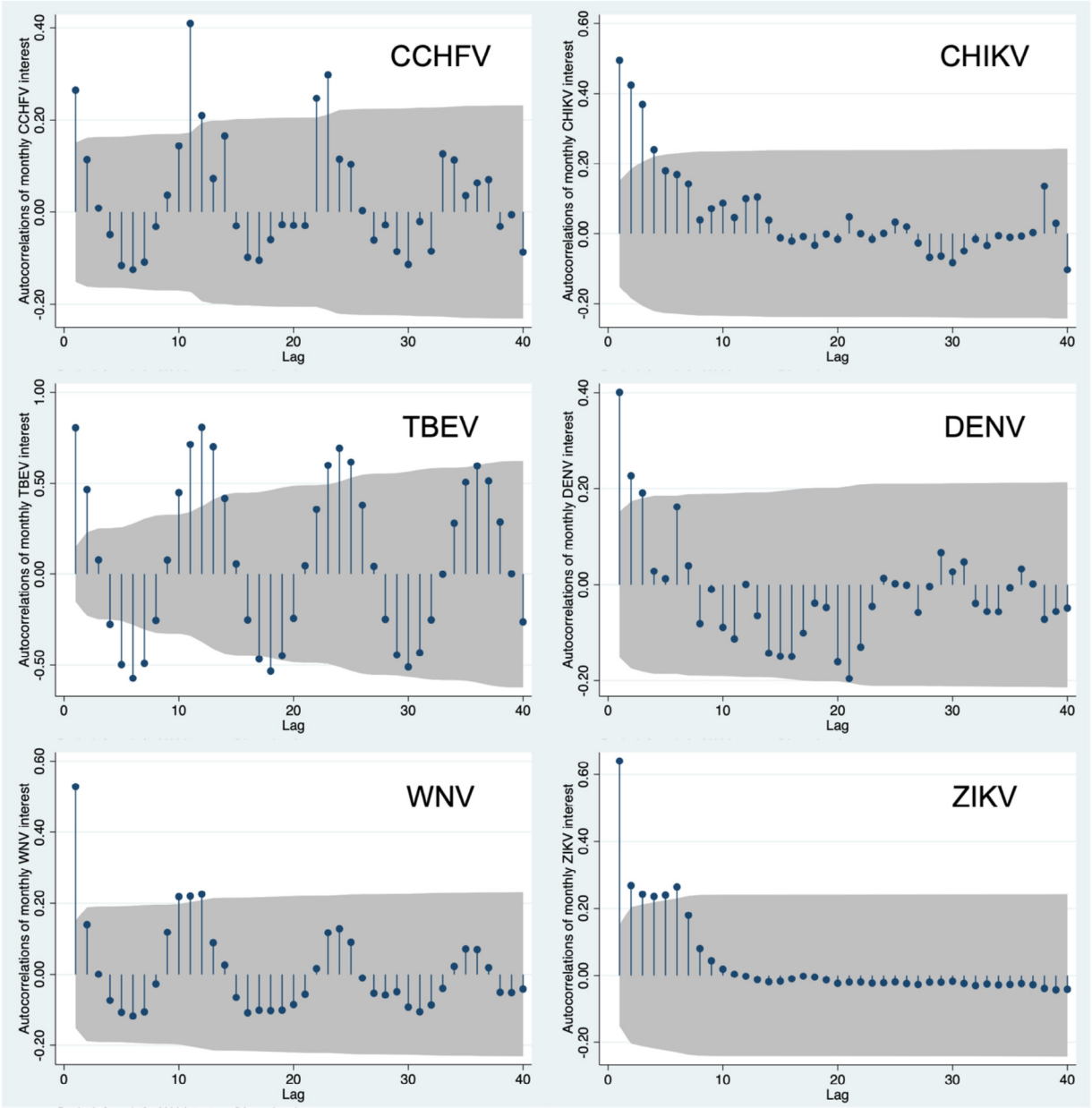
How to cite this article: Allgoewer K. Determinants of public interest in emerging and re-emerging arboviral diseases in Europe: A spatio-temporal analysis of cross-sectional time series data. J Prev Med Hyg 2022;63:E579-E597. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2736

Supplementary Fig. 1. Autocorrelation plots of monthly disease interest averaged over 30 European countries from January 2008 to January 2022.



The autocorrelation visible in the plots is corrected by using an Cochrane-Orcutt AR(1) regression with iterated estimate for the analysis of trends and patterns of public interest.

Non Communicable Diseases

Inadequate management of cardiovascular risk factors prior to admission for an acute coronary event

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Keywords

Cardiovascular risk factors • Primary prevention • Secondary prevention • Acute coronary syndrome • Diabetes mellitus

Summary

Objectives. *Optimal regulation of modifiable risk factors has been proposed as the standard of care both for primary and secondary prevention of cardiovascular disease (CVD). The aim of this study was to assess primary and secondary cardiovascular risk management received before admission for an acute coronary event.*

Methods. *Data were analyzed for 185 consecutive hospitalized patients with a diagnosis of acute coronary syndrome (ACS) in the Cardiology department of a University hospital during an annual period (1/7/2019 until 30/6/2020). The study population was divided into two groups, the primary and secondary prevention subgroups, according to previous medical history of cardiovascular disease (CVD).*

Results. *The mean age of the participants was 65.5 ±12.2 years and most patients were male (81.6%). Previous CVD was present in 51 patients (27.9%). Fifty-seven patients (30.8%) had a history of diabetes mellitus (DM) and 97 (52.4%) had a history of dyslipidemia. Hypertension was present in 101 (54.6%) patients. In the secondary prevention group, the LDL-C was on target in only 33.3% of the patients, while 20% patients did not use statins. The use of antiplatelet/anticoagulant agents was 94.5%. Among patients with diabetes, only 20% had been using a GLP-1 receptor agonist or/and an SGLT-2 inhibitor, while the HbA_{1c} was on target in 47.8%. Twenty-five percent of the patients were active smokers. In the primary prevention group, the use of statins was overall low (25.8%) but more frequent in patients with diabetes and those without diabetes at very high-risk for CVD (47.1% and 32.1% respectively). The LDL-C was on target in less than 23.1% of the patients. The use of antiplatelet/anticoagulant agents was low (20.1%), but higher in those with diabetes (52.9%). In the diabetic group, HbA_{1c} was on target in 61.8%. Active smoking was practiced by 46.3% of the patients.*

Conclusions. *Our data show that in a substantial proportion of patients presenting with ACS, previous CVD prevention, both primary and secondary, fails to meet the current recommendations provided by scientific societies.*

Introduction

Acute coronary syndrome (ACS) is associated with significant morbidity and mortality, despite advances in pharmacological and non-pharmacological management [1]. The prevalence of coronary artery disease (CAD) worldwide remains high due to aging of the population, improved survival after an initial cardiovascular (CV) event and increasing prevalence of certain CV risk factors such as diabetes and obesity [2]. Primary and secondary prevention of CV disease (CVD) through aggressive modification of classical risk factors has been proposed as the most effective way to reduce the incidence and severity of ACS and its long-term complications [3, 4]. In order to implement aggressive primary and secondary prevention of CVD, several risk stratification scores have been developed[5]. The European Society of Cardiology and the European Atherosclerosis Society (ESC/EAS) have adopted the SCORE (Systematic Coronary Risk Estimation) system for risk stratification in individuals without known CVD, while they have further proposed a global risk stratification to encompass the entire spectrum of the population at risk [6].

Aim of the present study was to investigate if individuals who suffered an ACS had previously been receiving adequate preventive care against risk factors for CVD.

Methods

The Institutional Review Board of Laiko General Hospital, a University tertiary hospital in Athens, Greece, approved the study protocol, which conforms to the principles outlined in the 1975 Declaration of Helsinki [7]. An informed consent was obtained from all participants prior to their involvement in the study.

We prospectively enrolled all patients with a diagnosis of ACS who were hospitalized at the Cardiology department during a one-year period (between 1/7/2019 and 30/6/2020) and analyzed their clinical characteristics. ACS was defined as unstable angina, non-ST elevated myocardial infraction or ST elevated myocardial infraction, as indicated by the admission ICD-10 code and further adjudicated by the investigators on the basis of clinical features, electrocardiogram and cardiac enzymes on admission and during hospitalization.

Data regarding the patients' previous medical history, use of medications, demographics, somatometric

 https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2684

features and laboratory parameters on admission were recorded. Body weight was measured on admission only in ambulatory patients. The presence of diabetes mellitus (DM), hypertension and dyslipidemia were ascertained by self-reporting and/or previous intake of relevant medications. The use of medications preceding the ACS was also self-reported and ascertained on the basis of a dispensed prescription (from the national prescription electronic database) up to three months before admission.

In order to assess the adequacy of the antecedent risk factor management, individuals were classified, as being "at very high risk" (VHR), "at high risk" (HR), "at moderate risk" (MR) or "at low risk" (LR), according to the 2016 ESC/EAS guidelines [8], which rely on factors such as history of established CVD, presence duration and possible end-organ damage of diabetes, presence of chronic kidney disease, SCORE levels etc.

The study participants were initially divided into two groups, according to the absence or presence of established CVD prior to the indexed ACS, comprising the primary and secondary prevention group, respectively. Patients with established CVD were identified as those with a medical history of previous coronary artery disease or/and previous cerebrovascular accident or/and previous peripheral artery disease as reported and ascertained on the basis of their medical files/documents. All individuals in the secondary prevention group were considered as VHR. In the primary prevention group, the risk stratification of individuals without DM was based on the SCORE for European populations at low cardiovascular disease risk, ranging from LR to VHR. The risk stratification of individuals with DM in the primary prevention group, depended on specific parameters indicated by the ESC/EAS guidelines, such as the presence of target organ damage (such as proteinuria or retinopathy) or the co-existence of a major risk factor such as smoking, hypertension or dyslipidemia [8]. An LDL-C target of < 70 mg/dl and < 100 mg/dl was considered as appropriate for the VHR and HR categories respectively, while an LDL-C target of < 115 mg/dl was considered for both the MR and LR categories [8]. For patients with diabetes, an HbA_{1c} of < 7% was considered as appropriate, according to the 2018 American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD) guidelines (Fig. 1) [9].

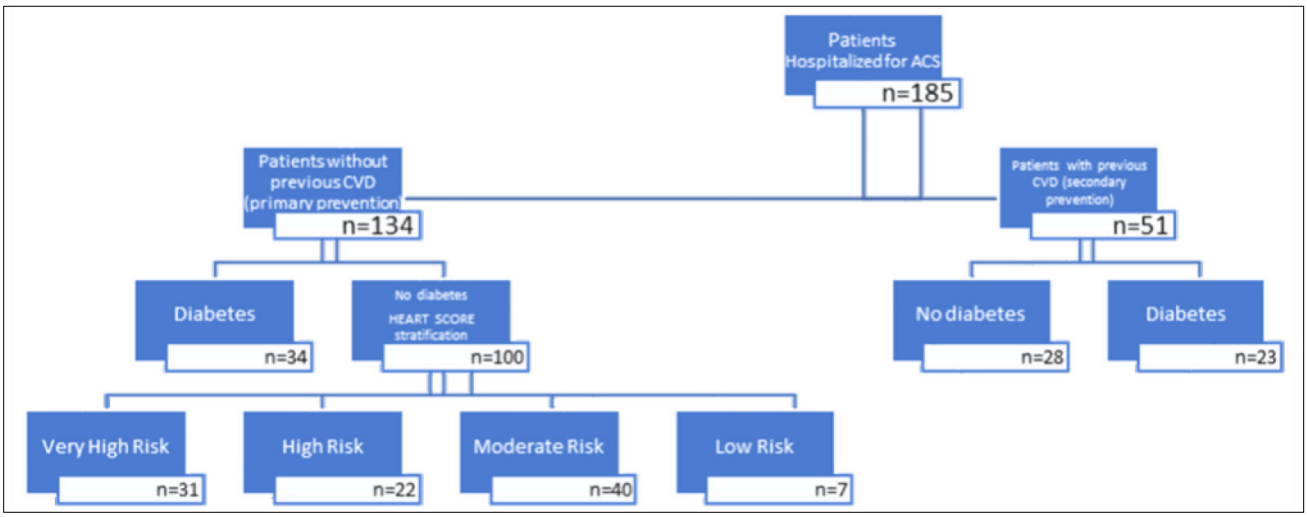
Statistical analysis was performed using IBM SPSS Version 28.0 (IBM Corporation, Armonk, NY, USA). Baseline characteristics were presented as means ± SD, median (25th-75th percentile) or counts (percentage). Between-group comparisons were performed using the chi-square test. In all instances, statistical significance was evaluated at the 0.05 level ($p < 0.05$).

Results

A total of 185 patients with ACS were hospitalized during the indicated period and were included in the present analysis. The mean age ± SD was 65.5 ± 12.2 years, and 81.6% were men. The main demographic and clinical characteristics of the study population are shown in Table I. A history of CVD was pre-existing in 51 (27.6%) patients (secondary prevention group) and, within this group, 23 patients (45.1%) had a history of DM (Tab. II). Out of the remaining 134 patients without previous CVD (primary prevention group), 34 (25.4%) had a history of DM (Tab. III). All the patients with DM were classified as VHR. Out of the non-DM patients of the primary prevention group, 53 were classified as VHR or HR and 47 as MR or LR (Tab. III). Out of the total study population, a history of hypertension was reported by 101 (54.6%) patients. This proportion was higher in patients with diabetes (61.4%) as compared to the patients without DM (51.6%).

Among the secondary prevention group (Tab. II), although 42/51 patients (82.4%) were previously treated with a statin and 22/51 (43.1%) with a high-intensity statin or a statin plus ezetimibe, LDL-C was on target in only

Fig. 1. Flowchart of the study.



Tab. I. Main demographic and clinical characteristics of the study population.

ACS	n = 185
Age (years)	65.5 (± 12.2)
Male sex n (%)	151 (81.6)
Height (cm)	171.6 (± 8.4)
Weight (kg)	84.4 (± 15)
BMI (kg/m2)	28.6 (± 4.6)
Hypertension n (%)	101 (54.6)
Diabetes n (%)	57 (30.8)
Lipid disorders n (%)	97 (52.4)
Coronary artery disease n (%)	51 (27.6)
Smoking n (%)	
Never	86 (46.5)
Active smokers	74 (40.0)
Ex-smokers	25 (13.5)
Family history of CVD n (%)	22 (11.9)
Chronic kidney disease n (%)	46 (24.9)
Prior PCI or CABG n (%)	47 (25.4)

17/51 (33.3%). The proportion of patients with LDL-C on target was higher in those receiving a statin (20/42 patients, 47.6%) than in those not on statin therapy (1/9, 11.1%, $p < 0.001$). The highest proportion of LDL-C target achievement was observed among patients under a high-intensity statin or a statin plus ezetimibe (59.1%, $p < 0.01$ *vs* those on low-intensity statin treatment). An antiplatelet agent had been received by 48 patients (94.1%), while active smoking had been practiced by 13 patients (25.5%). Among the patients with diabetes, 5/23 (21.7%) were previously being treated with a glucagon-like receptor agonist (GLP-1RA) or a sodium-glucose transporter-2 inhibitor (SGLT-2i) and 11/23 (43.7%) had an HbA_{1c} on target. The use of statins and/or antiplatelet agents, active smoking and LDL-C target achievement did not differ between patients with and without diabetes (Tab. II).

Among the primary prevention group (Tab. II), the use of a statin prior to the ACS event was overall low (25.8%) but more frequent in patients with diabetes and those without diabetes at VHR (47.1 and 32.1% respectively) than in those at HR (27.3%), MR (10%) and LR (14.3%), with all p values < 0.01. Accordingly, less than one quarter of patients achieved the appropriate LDL-C target across all the risk categories (Tab. II). The proportion of patients with LDL-C on target was higher in those receiving a statin (14/36, 38.8%) than in those not on statin therapy (17/98, 17.3%, $p < 0.001$). Among patients with diabetes, 21 (61.8%) had an HbA_{1c} on target. Antiplatelet/anticoagulant agents had been previously received by 52.9% of patients with diabetes, but, within the non-diabetic population, their use was, as expected, infrequent (Tab. II). More than one third of patients were active smokers, the proportion being lowest in those with diabetes (35.3%) and highest in those at HR (59.1%).

Hypertension was present in 102/185 (55.1%) of the total study population and its prevalence was highest among those with established CVD (80.4%) and diabetes (67.7%), while it was lowest in the primary prevention cohort among those at LR (14.3%) and at MR (17.5%) (Tabb. II, III). Among patients with hypertension, anti-hypertensive medications were used by 90.2% in the secondary cohort and by 72.1% in the primary cohort.

Discussion

Despite the progress being achieved in the pharmacological and supportive management of patients hospitalized for ACS over the last decades, coronary artery disease still remains the number one cause of morbidity and mortality worldwide [10]. Primary and secondary prevention of CVD, by aggressively modifying risk factors, is mandatory in order to prevent CV events and their complications. Nevertheless, according to the present study's findings, the majority of patients suffering from an ACS had been receiving insufficient prevention management of modifiable CVD risk factors prior to the event.

Among patients in the secondary prevention group requiring very aggressive management of risk factors, although the majority was receiving lipid-lowering medications, a notable proportion (15.7%) was no

Tab. II. Prevention measures, active smoking and target achievement in key metabolic parameters in patients with previous CVD (secondary prevention group).

Patients with previous CVD (secondary prevention group), n = 51			
	Diabetes n = 23	No diabetes n=28	p
Statin, n (%)	18 (78.2)	24 (86)	NS
Antiplatelet/anticoagulant, n (%)	20 (87)	28 (100)	NS
SGLT-2-i/GLP-1, n (%)	5 (21.7)	-	NA
Smoking, n(%)	6 (26)	7 (25)	NS
LDL-C on target, n (%)*	10 (43.5)	11 (39.3)	NS
LDL-C on target among those on statin n (%)*	9 (50%)	11 (45.8)	NS
HbA_{1c} on target n (%)**	11 (47.8)	-	NS
Hypertension	17 (73.9)	24 (85.7)	NS
Anti-hypertensive drugs	20 (86.9)	20 (71.4)	NS

NS: Not Significant at the level 0f 0.05; NA: Not Applicable.
* The LDL-C target for patients both with and without diabetes was considered as < 70 mg/dl. ** The HbA_{1c} target for patients with diabetes was considered as < 7.0%.

Tab. III. Prevention measures, active smoking and target achievement of key metabolic parameters in patients without previous CVD (primary prevention group).

Patients without previous CVD (primary prevention group), n = 134					
	Diabetes n = 34	No diabetes n = 100			
HEART Score		VHR n = 31	HR n = 22	MR n = 40	LR n = 7
Statin n (%)	16 (47.1)	10 (32.3)	6 (27.3)	4 (10)	0 (0)
Antiplatelet/anticoagulant	18 (52.9)	5 (16.1)	3 (13.6)	1 (2.5)	0 (0)
Hypertension	18 (52.9)	19 (61.2)	16 (72.7)	7 (17.5)	1 (14.3)
Anti-hypertensive drugs	16 (47)	14 (45.2)	10 (45.4)	4 (10)	0 (0)
SGLT-2-i/GLP-1, n (%)	7 (20.6)	-	-	-	-
Smoking	12 (35.3)	12 (38.7)	13 (59.1)	22 (55)	3 (42.7)
LDL-C on target n (%)*	8 (23.5)	8 (25.8)	2 (9,1)	12 (30)	1 (14.3)
LDL-C on target among those on statin n (%)*	4 (25)	4 (40)	2 (33,3)	4 (100)	-
HbA_{1c} on target n (%)**	21 (61.8)	-	-	-	-

* The LDL-C target for VHR and HR patients was considered as < 70 mg/dl, for MR as < 100 mg/dl and for LR as < 115 mg/dl. ** The HbA_{1c} target for patients with diabetes was set at < 7.0%

under such treatment at all, while a remarkable fraction (43.1%) should have required treatment intensification. Disappointingly, active smoking was practiced by one quarter of the patients. In the diabetic subgroup, 52.2% of the patients seemed to need intensification of glucose-lowering treatment, while a substantial underuse of GLP-1RA and/or SGLT-2i was also noticed (21.7%), despite the latest ADA/EASD guidelines strongly recommending their use in patients with diabetes and established CVD [11]. Antiplatelet/anticoagulant treatment seemed to be the most well-established preventive treatment in this group, as it was followed by 94.2% of the patients.

In primary prevention, considerable heterogeneity regarding the previous CV risk status was noticed among. Almost two thirds of the patients in this group had been at HR or VHR to suffer an ACS (87/134, 64.9%), either because they had diabetes (and additional risk factors) or because of their calculated SCORE. Among them (at VHR/HR), 60% were not treated with any kind of lipid-lowering medications and only 25% had their LDL-C on target. Additionally, about one third of these patients were active smokers and about 40% of those with diabetes needed glucose-lowering treatment intensification. The proportion of patients with diabetes under GLP-1RA and/or SGLT-i was 20%, similar to that in the secondary prevention group. About one third were treated with an antiplatelet/anticoagulant, a proportion that was significantly higher in those with diabetes (52.6%) than in those without (16.1%). One third of the patients comprising the primary prevention group (and hence one quarter of the total study population) had been at MR or LR, previously to the indexed acute coronary event. Among these patients, only one quarter had their LDL-C on target, and, strikingly, more than 50% were active smokers.

Overall, the present study shows that the vast majority of patients suffering an ACS had been receiving insufficient preventive management of classical CV risk factors, while some individuals had not been receiving such management at all. A significant underuse/underdose of lipid-lowering medications, especially statins, in both primary and secondary prevention, was shown. An even greater underuse was noticed regarding the novel glucose-lowering medications (GLP-1Ras and SGLT-2i), which have been recently shown to reduce CV events in patients with DM at high CV risk. The use of antiplatelet/anticoagulant agents was sufficiently high in secondary prevention but relatively low in high and very high-risk patients of the primary prevention group, with the exception of patients with diabetes, in whom it slightly surpassed 50%. Last but not least, an alarming finding of the present study is the high proportion of active smokers in all groups. Vigorous counselling for smoking cessation and offering of structured smoking cessation programs are urgently needed.

In line with the results of the present study, previous studies have also shown concerning gaps in managing CV risk factors in patients with a history of CVD [12], diabetes [13] and acute myocardial infarction [14]. To our knowledge, however, no previous studies have considered the adequacy of CVD prevention management in the context of risk stratification according to the ESC/EAS guidelines in patients presenting with ACS. This approach offered the opportunity to eschew some limitations of larger registry-based studies, such as missing information and misclassification of CVD risk. The present analysis included a broad range of risk factor management, including lipid-lowering, glucose-lowering and antiplatelet medications. Importantly, very few studies have yet reported on the use of the newer glucose-lowering medications in this population. Additionally, the prospective inclusion of patients offered more accurate data collection and ascertainment of actual ACS events. Finally, the study population came from Greece, a medium-to-high income country under austerity measures, in which such an analysis has not been previously performed. On the other hand, the present study has some important limitations: first, this is a single-center study, a fact limiting representativeness of the sample population and generalizability of the results; second, the number of ACS events is relatively

small and third, some important factors related to CVD prevention such as diet habits and physical activity were not recorded. Importantly, however, the study population included patients admitted during the shift schedule of the single participating Cardiology clinic, which, being part of the Greek National Health System, allows access to virtually all inhabitants of the broader Athens area who need emergency care.

Physician's lack of awareness, clinical inertia, patients' non-adherence to follow up, the lack of a national program for systematic outpatient CVD prevention and high cost of newer hypolipidemic and glucose-lowering agents, are all probable contributing factors, explaining our results [15-17].

In conclusion, data from a single cardiology clinic of a tertiary hospital in Greece show that in a substantial proportion of patients presenting with ACS, previous CVD prevention, both primary and secondary, fails to meet the current recommendations. Establishing stricter local prescription protocols, implementing adequate follow up, enhancing physicians' awareness and addressing clinical inertia might serve as measures to improve management and achieve proper care.

Acknowledgements

The project was partially supported by an unrestricted grant from Boehringer Ingelheim Hellas. Boehringer Ingelheim Hellas was not involved in the study design, roll-out, data collection, and data analysis.

Authors' contribution

S.L., M.B. and J.B. conceived of the presented idea. C.S, C.K. and M.S processed the data and performed the analysis. C.S. and S.L. wrote the manuscript with input from all authors. All authors provided critical feedback and helped shape the research, analysis and manuscript.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. Written informed consent has been obtained from the patients to publish this paper.

Conflict of interest statement

The authors declare no conflict of interest.

Ethical approval

The study was approved by the Ethics Committee of our institution and was carried out in accordance with the Declaration of Helsinki.

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Received on August 16, 2022. Accepted on October 12, 2022.

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How to cite this article: Siafarikas C, Liatis S, Kapelios C, Skouloudi M, Bonou M, Barbetseas J. Inadequate management of cardiovascular risk factors prior to admission for an acute coronary event. J Prev Med Hyg 2022;63:E598-E603. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2684

Non Communicable Diseases

Predicting role of illness perception in treatment self-regulation among patients with type 2 diabetes

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Keywords

Treatment self-regulation • Illness perception • Chronic disease • Type 2 diabetes

Summary

Background and Objective. *Impaired self-regulation negatively impacts self-efficacy, self-management, blood sugar control, and quality of life among patients with diabetes. Hence, identifying the predictors of self-regulation is a necessity for healthcare providers. The current study aimed to determine the predictive role of illness perception in treatment self-regulation in patients with type 2 diabetes.*

Methods. *The current study is a descriptive cross-sectional study. A total of 200 patients with type 2 diabetes, who were referred to the only specialized clinic for endocrinology and diabetes affiliated with Qazvin University of Medical Sciences in 2019-2020, were recruited through a convenience sampling method. For data collection, the brief Illness Perception Questionnaire and the Treatment Self-Regulation Questionnaire were used. Collected data were analyzed by SPSS v21 using a multivariable regression model.*

Results. *Mean and standard deviation scores of self-regulation and illness perception were 69.11 ± 17.61 and 36.21 ± 7.05, respectively. Results of the multivariate regression model revealed the significant correlations of self-regulation with illness perception, age, cardiovascular complications, diabetic retinopathy, and diabetic foot ulcers.*

Conclusions. *In this study, participants presented a moderate level of self-regulation. The results also revealed that illness perception could be a predictor of improving patients' self-regulation. Therefore, providing infrastructure programs such as continuous education and appropriate care programs for diabetic patients to improve their illness perception can effectively improve their self-regulation behaviors.*

Introduction

Diabetes is one of the most common chronic diseases in the world [1, 2]. According to the International Diabetes Federation announcement in 2019, the total number of people living with diabetes is projected to rise to 700 million by 2045 [3]. In Iran, the number of people suffering from diabetes mellitus is projected to rise to 9.2 million by the year 2030 [4]. The condition can lead to many problems, such as cardiovascular, renal and brain dysfunction, and imposes a large economic burden on patients as well as their societies [5]. Diabetes is the seventh leading cause of death in the United States and has been one of the ten most common causes of death in Iran [6]. In 2010, the mortality rate was estimated at 10.6 deaths per 100,000 population in Iran that was higher than Greece (7.9 per 100,000 people) and lower than Italy (32.2 per 100,000 people) [7]. The mortality rate among diabetic patients is mostly related to an unhealthy diet and a sedentary lifestyle [8]. Self-regulation assists as a guide for diabetic patients to attain their goals and continue self-care behaviors [9].

Self-regulation is defined as one's common values or motivations to execute certain behaviors in order to improve health when suffering from diseases [10]. It is classified as controlled and independent motivations. Controlled motivation is comprised of external regulation, and internal motivations are controlled by internal feelings, leading to certain beliefs in a person to execute a behavior [11]. Basic structures of self-regulation learning abilities include the following processes: goal-setting, planning to achieve them, monitoring them, comparing them with standards, and changing behaviors to improve performance [12]. Self-regulation leads to adaptive behaviors which are effective in dealing with disease [13], improving one's physical health, quality of life, and self-care behaviors [14], and reducing disease complications and its psychological burden [15]. Impaired self-regulation negatively impacts health outcomes [10], self-efficacy [13], disease complications, self-management, blood sugar control and quality of life [15, 16]. Diabetic patients are responsible for executing certain behaviors, such as having a healthy lifestyle, controlling blood sugar, and taking medications on time, in order to improve their own health [17, 18], and self-regulation strategies strengthen their efforts to meet such ends [19]. However, poor treatment self-regulation leads to poor adherence to medication as well as poor

 https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2727

blood sugar control, and long-term hyperglycemia increases the risk of microvascular and macrovascular complications [20].

Recent studies conducted in different settings showed that the prevalence of adherence to diabetes medication varied between 36 and 93%. Motivation plays a predictive role in diabetes self-management through consuming more vegetables/fruits and fewer fats, eating healthier foods, changing diet, doing regular exercise, regularly taking medication, and self-monitoring blood sugar levels resulting in better diabetes control. Cultural, religious, personal and social factors can also affect patients' beliefs and motivation in this regard. Taking several oral drugs and insulin, being concerned about their side effects, lack of confidence in their efficacy and lack of knowledge about them can all negatively impact individuals' adherence to medication [21, 22]. Illness perception and knowledge about diabetes significantly predict self-care behaviors in diabetic patients [23]. Hence, identifying such predictors is of great importance in these patients.

When dealing with a disease, patients usually create an image of the disease and its treatment process in their mind, which is defined as "illness perception" [24]. Factors such as poor blood sugar control, duration of treatment, presence or absence of complications lead to emotional reactions, and impaired self-management can affect individuals' illness perception [25]. In other words, patients living with diabetes consider their disease as a threat, and this belief leads to poor illness perception, and eventually depression [26]. The way people perceive an illness (illness perceptions) plays a role in how they adapt to their illness [27]. Therefore, assessing illness perception in such patients should be considered as a part of the healthcare services [28].

Regardless of the physiological factors, illness perception significantly affects the consequences of the disease [27]. Paying attention to the physical and mental problems of patients living with diabetes and assessing the consequences of their disease, including illness perception, are highly important. As a member of the treatment team, nurses play a key role in this regard by promoting self-regulation and assessing illness perception [10]. Due to the fact that the role of illness perception, as an effective factor in self-regulation, is not clearly evident, the current study aimed to determine the predictive role of illness perception in treatment self-regulation in patients with type 2 diabetes.

Methods

The current study is a descriptive cross-sectional study. The study population included patients with type 2 diabetes, who were referred to the only specialized clinic for endocrinology and diabetes in Qazvin, Iran, from 2019 to 2020. This clinic is located in Velayat teaching hospital affiliated with Qazvin University of Medical Sciences.

Considering $\alpha = 0.05$ (a 95% confidence interval), $\beta = 0.05$ (95% power), results of a previous study (r = -0.33) [23], and the possibility of a 30% not responding, the final sample size was calculated to be 200.

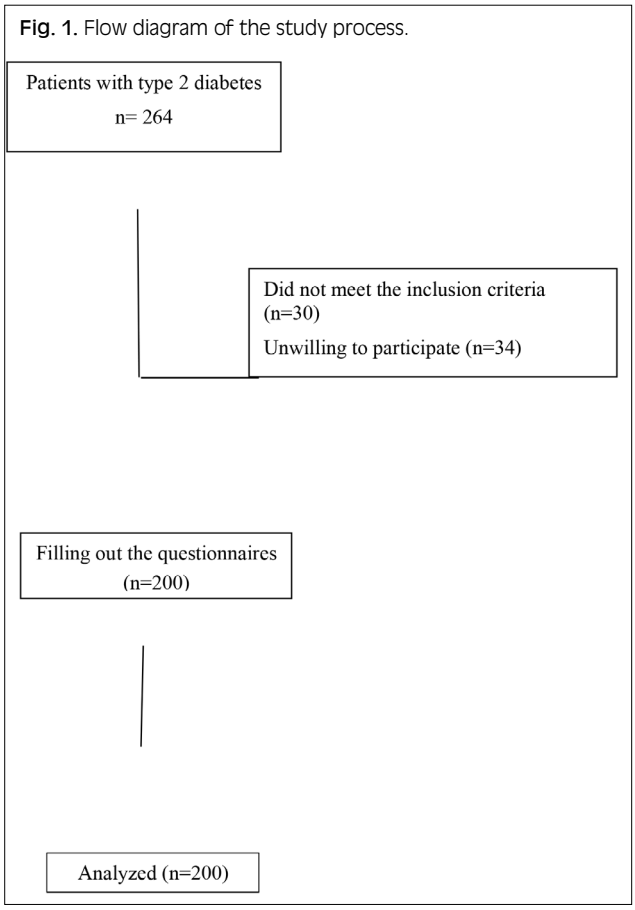

Fig. 1. Flow diagram of the study process.

A convenience sampling method was applied for sampling. Patients met the inclusion criteria if they were diagnosed with type 2 diabetes by a specialist, were able to read and write, and consented to participate in the study. Those patients who were diagnosed with type 1 or gestational diabetes and suffered from acute mental problems were excluded from the study. For data collection, each patient completed the demographic characteristics and disease information forms, the brief Illness Perception Questionnaire (Brief IPQ), and the Treatment Self-Regulation Questionnaire (TSRQ). Figure 1, shows the flow diagram of the study.

The demographic characteristics and clinical characteristics associated with diabetes mellitus forms included age, gender, educational level, marital status, employment status, medications prescribed, and duration of the disease.

The brief IPQ is a 9-item questionnaire designed to assess one's emotional and cognitive perception of his/her illness. The 9 items, respectively, assess consequences, timeline, personal control, treatment control, identity, concern, illness comprehensibility, emotional impact, and cause of the disease. Items 1-8 are scored on a 10-point Likert scale, ranging from 1-10. Item 9, which is an open-ended question,

involves patients identifying the three most important perceived causes of their disease. In the final analysis, it is recommended that each of the subscales be analyzed separately. In items 3, 4, and 7, a higher score indicates a more negative perception, and in the other items, a lower score indicates a more positive perception. The Cronbach's alpha for this questionnaire is 0.80, and the test-retest reliability coefficients for a 6-week interval were reported between 0.42 and 0.75. To assess the concurrent validity of the questionnaire, the revised IPQ was applied to a sample of patients with asthma, diabetes, and renal problems, indicating a correlation of the subscales from 0.32 to 0.63. The discriminant validity of the brief IPQ was calculated and confirmed by comparing the scores of patients with diabetes, asthma, chest pain, and colds [29].

The TSRQ is a 19-item questionnaire developed by Ryan and Cannell to assess self-regulation in patients with diabetes [30-31]. It utilizes a general approach to autonomously assessing self-regulation using the following subscales: autonomous regulatory style, controlled regulatory style, and motivation. The autonomous regulatory style represents the most self-determined form of motivation and has consistently been associated with maintained behavior change and positive healthcare outcomes [32, 33]. Based on the 19-item version, there are a variety of reasons why diabetic patients take their medications, check their blood sugar levels, follow a diet, or do regular exercises. The questionnaire is comprised of 2 subscales, autonomous self-regulation, and controlled self-regulation, which are assessed with 2 headings: 1. I take or would take my medications or control my glucose because … (8 items), and 2. I follow or would follow the recommended diet and exercise or would regularly because … (11 items). Items 2, 3, 7, 10, 13, 16, 18, and 19 assess the first subscale, and items 1, 4, 5, 6, 8, 9, 11, 12, 14, 15, and 17 assess the second subscale. Responding to each item is based on a 7-point Likert scale, ranging from 1-7. A relative autonomous index is also calculated [34, 35].

Data Analysis

Collected data were analyzed by IBM SPSS Statistics for Windows, version 21.0, using descriptive statistics (mean, standard deviation and frequency distribution), and a multiple linear regression model. Kolmogorov–Smirnov test was used to assess the normality of data, and Levene's test was used to assess the equality of variance for the groups. A p-value of < 0.05 was considered significant.

Results

In this study, 200 patients were enrolled. Of them, 103 patients (51.5%) were female and 97 patients (48.5%) were male. Their mean age was 59 years. Table I shows patients' demographic characteristics in more detail.

Tab. I. Patients' demographic characteristic.

Variables		Freq.	%
Gender	female	103	51.5
	male	97	48.5
Marital status	single	17	8.5
	married	165	82.5
	widowed	15	7.5
	divorced	3	1.5
Educational level	illiterate	60	30.0
	under diploma	94	47.0
	diploma and higher	46	23.0
Employment status	unemployed	102	51.0
	employed	54	27.0
	retired	44	22.0
Diabetes duration (year)	< 1	19	9.5
	1-5	59	29.5
	6-10	59	29.5
	> 10	63	31.5
Type of treatment	tablet	113	56.5
	insulin	44	22.0
	tablet + insulin	31	15.5
	no medication	12	6.0
Insulin (unit)	0	122	61.0
	1-10	27	13.5
	11-20	38	19.0
	21-30	13	6.5
Tablet	0	63	31.5
	1-2	42	21.0
	3 and more	95	47.5
Underlying disease	yes	115	57.5
	no	85	42.5
MI	yes	6	3.0
	no	194	97.0
ACS	yes	41	20.5
	no	159	79.5
CKD	yes	3	1.5
	no	197	98.5
Diabetic complications	yes	116	58.0
	no	84	42.0
Diabetic nephropathy	yes	18	9.0
	no	182	91.0
Diabetic retinopathy	yes	61	69.5
	no	139	30.5
Cardiovascular complications	yes	50	25.0
	no	150	75.0
Diabetic neuropathy	yes	75	37.5
	no	125	62.5
Diabetic foot ulcers	yes	23	11.5
	no	177	88.5

N: Number; %: Percent; MI: Myocardial Infraction, ACS: Acute Coronary Syndrome; CKD: Chronic Kidney Disease.

Patients' mean and standard deviation scores of self-regulation and illness perception were 69.11 ± 17.61 and 36.21 ± 7.05, respectively.

The multivariate regression model showed that diabetic patients' self-regulation decreases as their age increases.

Tab. II. Predictors for self-regulation among diabetic patients.

Variables		M (SD)	Adjusted β	p-value	95% CI
Marital status	Married	70.79 (17.78)	-		-
	Single	88.76 (21.35)	-0.019	0.806	-11.70-9.11
	Divorced	85.33 (7.77)	0.039	0.536	-12.94-24.79
	Widowed	59.33 (12.40)	-0.033	0.621	-11.59-6.94
Educational level	Illiterate	66.78 (16.72)	-		-
	Under diploma	70.64 (17.77)	-0.113	0.159	-10.10-1.67
	Diploma and higher	80.20 (20.33)	-0.134	0.179	-14.51-2.68
Type treatment	Tablet	66.14 (14.89)	-0.032	0.857	-14.42-12.00
	Insulin	73.48 (22.04)	-0.144	0.248	-17.52-4.55
	Tablet+ insulin	68.39 (17.38)	0.046	0.751	-12.26-16.96
	No medicine	83.00 (15.99)	-		-
Diabetes duration (year)	< 1	76.58 (16.23)	0.037	0.474	-7.43-12.13
	1-5	72.86 (18.25)	0.056	0.503	-4.46-9.05
	6-10	67.73 (16.46)	0.017	0.820	-5.42-6.84
	> 10	64.65 (17.38)1	-		-
Underlying disease	Yes	65.11 (15.71)	0.074	0.302	-0.71- -0.037
	No	74.53 (18.68)	-		-
Diabetic retinopathy	Yes	62.10 (15.24)	-0.152	0.04	-12.27- -0.49
	No	72.19 (17.76)	-		-
Cardiovascular complications	Yes	58.44 (10.93)	-0.170	0.022	-13.59- -1.07
	No	72.67 (18.01)	-		-
Diabetic neuropathy	Yes	63.67 (15.51)	-0.018	0.801	-6.15-4.76
	No	72.38 (18.05)	-		-
Diabetic foot ulcers	Yes	79.61 (15.74)	0.255	0.000	7.03-22.75
	No	67.75 (17.43)	-		-
Tablet	0	74.51 (20.70)	-		-
	1-2	71.19 (15.61)	-0.148	0.218	-17.61-4.04
	3 and more	64.62 (15.05)	-0.271	0.056	-20.42-0.25
Variables	**M (SD)**	**Range**	**Adjusted β**	**p-value**	**95% CI**
Age	59.91 (14.09)	15-84	-0.329	0.001	-0.70- -0.17
Perceived illness	43.89 (7.05)	5-70	-0.141	0.030	-0.71- -0.04

M: Mean; SD: Standard deviation; CI: Confidence Interval.

The results also showed that as illness perception increases, patients' self-regulation improves (p = 0.03). Compared to other patients, self-regulation was significantly lower in patients with diabetic retinopathy (p = 0.048) or cardiovascular complication (p = 0.022). Also, compared to other patients, self-regulation was significantly lower in patients with diabetic foot ulcers (p < 0.0001) (Tab. II).

Discussion

The current study aimed to determine the role of illness perception in treatment self-regulation among patients with type 2 diabetes.

In this study, participants presented a moderate level of self-regulation. This finding is supported by Shahbazi et al. (2018) and Salehi et al. (2014) studies, in which self-regulation was reported to be at a moderate level among diabetic patients [36, 37]. However, Mahdilouy et al. (2019) and Lin et al. (2016) concluded that self-regulation is low in diabetic patients [38, 39]. Fuladvandi et al. (2017) also reported that self-regulation is low in patients with high blood pressure [40]. Based on these results, it seems that the current educational programs are not enough to improve and promote self-care behaviors among patients with diabetes. Hence, the treatment team, especially nurses, should consider other measures to better and more effectively educate this group of patients in order to improve their awareness about the potential and hazardous complications of improper diabetes control.

Based on the results of the current study, diabetic patients with greater illness perception used more self-regulation. This is consistent with national [41] and international [42, 43] studies which reported similar results. For instance, Kugbey et al. (2017) reported that illness perception and diabetes knowledge significantly predict overall diabetes self-care practices [23]. Abubakari et al. (2018) also found that illness perceptions are important determinants of self-management among diabetic patients [42]. Furthermore, illness perception was correlated with

medication adherence in patients with type II diabetes [41]. A possible explanation for this finding might be that illness perception is the patient's organized cognitive beliefs about his/her disease. These beliefs in turn affect coping strategies and health-related behaviors that he/she uses to manage the disease.

The results of the current study also showed a significant decrease in self-regulation among diabetic patients with cardiovascular complications, diabetic retinopathy, and diabetic foot ulcers. In line with this finding, Gholamaliei et al. (2016) reported that patients with type 2 diabetes who develop diabetes complications and have elevated HbA1C levels show lower levels of self-regulation [43]. Gabr et al. (2015) also concluded that self-care and self-regulation are low in epilepsy patients suffering from complications [44]. Poor treatment self-regulation leads to poor medication adherence as well as poor blood sugar control, and long-term hyperglycemia increases the risk of microvascular and macrovascular complications [45].

Based on the results of the current study, self-regulation significantly decreased with advancing age. Fuladvandi et al. (2017) concluded that patients' self-regulation decreases as their age increases [40]. However, on the contrary, Mahdilouy et al. (2019) showed that self-regulation has no statistically significant relationship with age [38]. Also, Gholamaliei et al. (2016) reported that older patients have higher levels of self-regulation and better medication adherence [43]. It seems that age-related conditions, such as hearing loss, vision problems, and cognitive/physical disorders, cause older adults to become dependent and reduce their self-efficacy in adopting self-regulation behaviors.

Conclusions

In this study, diabetic patients presented a moderate level of self-regulation. Predictive factors of self-regulation including illness perception, age, cardiovascular complications, diabetic retinopathy, and diabetic foot ulcers should be taken into consideration by healthcare providers. Therefore, providing infrastructure programs such as continuous education and appropriate care programs for diabetic patients to improve their illness perception can effectively improve their self-regulation behaviors.

Ethical consideration

The current study was approved by the ethics committee of Qazvin University of Medical Sciences (IR.QUMS.REC.1398.313). Patients were reassured about the confidentiality of data, and necessary explanations on how to complete the questionnaire were provided to them. Prior to data collection, informed consent was also obtained from them.

Acknowledgments

We would like to appreciate the Vice-Chancellor for Research of Qazvin University of Medical Sciences as well as all the patients participated in the current study.

Funding

This research was funded by Research Council of Qazvin University of Medical Sciences (Grant ID: 14003851).

Conflict of interest statement

The author declares no conflict of interest.

Authors' contributions

Conceptualization: FA, HB, RK, SAM.
Methodology: FA, HB, RK, SAM.
Investigation, Writing – original draft, and Writing – review & editing: All authors.
Data collection: HB and RK.
Data analysis: SAM.
Supervision: FA and SAM.

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Received on October 3, 2022. Accepted on December 12, 2022.

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How to cite this article: Abdollahi F, Bikdeli H, Zeabadi SM, Sepasi RR, Kalhor R, Motalebi SA. Predicting role of illness perception in treatment self-regulation among patients with type 2 diabetes. J Prev Med Hyg 2022;63:E604-E610. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2727

Nursing

Validation of the Italian version of the SexContraKnow instrument

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Keywords

Validation study • Contraception • Sex education • Adolescent • Health literacy

Summary

Introduction. *A large proportion of all pregnancies worldwide occur in young adolescent women, and almost all these pregnancies are unintentional. To address effective educational interventions, it is necessary to assess adolescents' literacy on this topic. The aim of this study was to translate and validate the Italian version of the SexContraKnow instrument.*

Methods. *This was a methodological study. The validation of the instrument was performed following the EORTC Quality of Life Group translation procedure. The process consisted of four phases: translation, content validation, face validation, and pilot test. Data were collected between May and September 2021. The STROBE guidelines were followed for this study.*

Results. *After performing forward and backward translations, we evaluated content validity (Scale-Content Validity Index = 0.91) and face validity. We then conducted a pilot test, test re-test, with 10 students (Cronbach* α *= 0.928; Pearson's R = 0.991).*

Conclusion. *The Italian Version of the SexContraKnow instrument has a good level of validation and reliability and can be effectively used by nurses to assess adolescents' literacy about the use of contraceptives and to develop targeted educational interventions. This instrument will help to evaluate the effectiveness of education programmes about health literacy about safe sex and contraception. The attention of nurses should be actively directed towards the process of health literacy among adolescents, in the perspective of a society focused on the empowerment of the population.*

Introduction

Health literacy is a set of skills that improve people's ability to process information that enables to live in a healthier way. Such skills include reading, writing, listening, talking, calculating, and critical analysis, as well as communication and interaction [1]. Health literacy is an important social benefit [2] because it reduces improper access to hospital and emergency services, drug utilization, and increases health autonomy, individuals' usage of preventive services and the development of correct health care behaviours [3]. To achieve a good level of health literacy, people should have the ability to find, select and understand healthcare information from the Internet, brochures about health, verbal or written healthcare instructions, and healthcare journals [3]. Although the process of health literacy is of undoubted relevance, today half of the adult population still have inadequate levels of health literacy and is unable to understand information about their health [4] and require more support when having to manage their health problems [5].

Similarly, in the adolescent population – meaning people of any gender aged between 10 and 19 years [6] – the situation is no better, as less than one-fifth of all European students have a high level of health literacy [7]. This deficiency affects the broader concept of health, defined as a "state of physical, psychological and social well-being […]" [8], but is even more true in sexual and reproductive health, defined as "…a state of physical, emotional, mental and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination, and violence. For sexual health to be attained and maintained, the sexual rights of all persons must be respected, protected and fulfilled" [9]. Adolescents face numerous physical, cognitive, emotional, and behavioural changes that they know very little about, as they acquire increasing autonomy and experience in many areas [10, 11]. These experiences may include alcohol use, drugs, smoking, and sexual activities, each of which may be associated with sexual and reproductive risks, such as sexually transmitted diseases and/or unintentional pregnancies [7].

In fact, 11% of all pregnancies worldwide involve young adolescent women, and almost all these pregnancies are unintentional [12]. Health literacy is especially important in adolescents because it impacts not only on the individual but also on the whole family. Education

enables individuals to change behaviours about their health habits [5]. In literature, it is widely recognised that adolescence is a critical period due to frequent incorrect health behaviours [5, 10, 12-14]. Moreover, health behaviours are acquired during adolescence, and therefore receiving correct health education at this age is an important determinant for health promotion [10]. The Health 2020 Strategy of the World Health Organization Regional Office for Europe [15] highlighted the importance of health literacy for the population and has become a key point on the European health agenda [13]. This context suggests that there is a need to increase educational interventions aimed at providing health literacy and skills regarding sexual and reproductive health, especially in adolescents. To properly design such interventions, it is necessary to understand what this population knows about this topic. Adequate literacy about sexuality and contraception is defined as the possession of training about sexuality and contraception that allows one to make informed decisions and pursue one's sexuality safely [10, 16]. Several studies have been conducted internationally and in the Italian context focusing on adolescents' literacy of safe sex and contraception, but most of them used non-validated ad-hoc tools [14, 17-20]. It is essential to use valid and reliable tools. Sebastian Sanz-Martos and his Spanish nursing research group of the University of Jean in 2019 developed an instrument to evaluate health literacy about sexuality and contraceptive methods in young university students. The *SexContraKnow* instrument proved to have sufficient validity and reliability and could be used in future research also to evaluate the effect of educational interventions or develop future educational programmes [5].

Methods

Aim

The purpose of this study is to provide a valid and reliable Italian instrument to assess adolescents' health literacy about contraception and develop an effective educational program. We selected the *SexContraKnow* instrument [5], translated it (Appendix 1) in Italian, adapted it to the adolescent population (aged between 14 and 19 years) and validated it.

Methodology

For the validation of the *SexContraKnow* instrument, we followed the EORTC *Quality of Life Group* guidelines [21]. The validation process consisted of four phases: translation, content validation, face validation, pilot test.

To translate the instrument, we used the *forward-backward translation* method. We asked two different Italian mother-tongue translators with a good knowledge of the Spanish language to independently translate the questionnaire. They had not been previously informed of the study or the content of the questionnaire. The two translations were reconciled into one through an online meeting with the two translators and the researchers. This final version was translated back into Spanish by a native Spanish translator with a good knowledge of the Italian language.

To validate the content of the instrument, we submitted it to a group of experts and asked them to rate the relevance of the 15 items of the questionnaire. These were scored using a four-point *Likert* scale, from 1 (not-relevant at all) to 4 (very relevant). Then we calculated the Content Validity Index (CVI) for each item and for the whole instrument. Following the recommendation on an acceptable indicator of content validity [22] we determined that each item-CVI (I-CVI) had to be at least ≥ 0.78 to be considered item relevant. The scale-CVI (S-CVI) had to be at least ≥ 0.90 for the entire instrument to be valid.

To test the face validity, we asked a group of volunteer high school students (between 14 and 19 years) to evaluate the questionnaire and then we performed a qualitative analysis of their answers. We asked them whether the 15 items were difficult to understand, confusing, contained difficult words, contained offensive words, or needed to be rephrased. At the end of this phase, we considered all the changes proposed by the students and performed the cultural adaptation.

To test the internal consistency, we performed a pilot *test re-test* and calculated *Cronbach's alpha* and the *Pearson correlation coefficient (Pearson's r)*. We asked a convenience sample of high school students to complete the questionnaire (T0) and then to repeat this after one week (T1). During the week, the students did not receive any further information or education.

Participants

Sample sizes were consistent with the EORTC *Quality of Life Group* guidelines [21]. Throughout the phases, we used a convenience sample. The content of the questionnaire was validated by a group of 9 experts of adolescent sexual health. For face validity, we invited 12 volunteer high school students (between 14 and 19 years) whose mean age was 16.5 years (SD = 1.78) to evaluate the questionnaire. For the pilot test, the sample included 10 volunteer high school students (between 14 and 19 years) with a mean age of 18.1 years (SD = 1.6).

Data collection

The data across all the phases were collected using a Google Forms® link. The link was sent to the participants via email. For content validity, the data were collected in May 2021. We gave the participants two weeks' time to answer the questionnaire. For face validity, the data were collected in July 2021 and the students had two weeks to answer. For internal consistency, instead, the data were collected in September 2021. The first administration of the questionnaire took place on the 21st of September 2021 and the second on the 28th of September 2021. The high school students had to complete the questionnaire within the day after it was emailed to them on both occasions.

Data analysis

For content and face validity the data we collected were codified and analysed using a Microsoft Excel® spreadsheet. I-CVI was obtained using the mean relevance score of each item. S-CVI was obtained using the computed mean of all the I-CVIs. Face validity was qualitatively analysed. The data relating to the pilot test were entered in a Microsoft Excel sheet and analysed using the Jamovi® software version 2.2.2. We calculated Cronbach's alpha to assess internal consistency and Pearson's r value to assess internal reliability.

The instrument

The purpose of the *SexContraKnow* instrument is to verify the level of health literacy about safe sex and contraception in university students [5]. It was validated on a population of university students aged 19-24 years, attending the faculty of nursing and the faculty of law. The instrument contains 15 items about sex and contraception. The possible answers for each question are: "true", "false", "I don't know". The third possible answer is useful to identify the least known subjects and therefore develop an educational intervention. The highest possible score is 15 and the average completion time was about 10 minutes.

Ethical considerations

The questionnaire was translated only after obtaining the approval of the authors for use. This pilot study was part of a larger study about health literacy approved by the Ethical Regional Committee of Liguria (156/2019). Participation was voluntary. The students aged over 18 signed a consent form, whereas, for students who were still minors, the consent form was signed also by their parents. The collected data were stored in a password-protected computer. Only the researchers of the study could access the data.

Results

Content and face validity

We invited a group of experts to evaluate the instrument. The experts were all females (mean age 43.7; SD = 14.7): 5 high school teachers, 2 midwives, 1 gynaecologist, and 1 healthcare assistant. All the healthcare professionals involved were employed in a counselling centre. We calculated the Content Validity Index (CVI) for each item (I-CVI) and for the entire questionnaire (S-CVI). The S-CVI score was 0.91, meaning that the Italian experts found the instrument to be relevant to evaluate adolescents' health literacy. All the I-CVI scores are reported in Table I. Only one item had an I-CVI score < 0.78 but, since the S-CVI score was ≥ 0.90, it was not excluded from the instrument. At the end of this phase, the questions were transformed into sentences, as suggested by the group of experts.

For the face validation, a convenience sample of 12 high school students was invited to evaluate the instrument. The sample consisted of 6 males and 6 females, and the mean age was 16.5 years (SD = 1.78). None of the items was considered offensive. The questions that were considered confusing or containing difficult words were modified and reformulated based on the students' suggestions.

Internal consistency

To verify the internal consistency of the instrument we performed a pilot test re-test on 10 volunteer students.

Tab. I. Item-Content Validity Index values.

SexContraKnow items	I-CVI[§]
N. 1 - There is a risk of pregnancy when you have unprotected sex in the 2 days before or after ovulation	1.00
N. 2 - The male condom is safe if placed just before ejaculation, even if penetration has occurred previously	0.89
N. 3 - The "calendar method" (calculating the fertile period to not have sexual intercourse within this period) is effective in preventing pregnancy	1.00
N. 4 - When you start taking the birth control pill, it is effective from day one	1.00
N. 5 - Hormonal contraceptive methods of birth control (for example, the birth control pill or vaginal ring) are recommended for adolescents	1.00
N. 6 - When the contraceptive pill is not taken at the correct time due to forgetfulness, the pill can be taken without loss of effectiveness as long as no more than 12 hours have passed since the correct time	1.00
N. 7 - The "dual contraceptive method" consists of the simultaneous use of a barrier contraceptive method (e.g., male condom) and a hormonal contraceptive method (e.g., contraceptive pill)	1.00
N. 8 - If the contraceptive pill is started after the 5th day of the menstruation cycle, the use of another contraceptive method for one week is recommended	1.00
N. 9 - The regimen for taking the contraceptive pill is one pill per day for 21 days starting from the 1st day of the cycle, followed by a week of rest or use of 7 placebo pills during this rest period	0.78
N. 10 - The contraceptive skin patch must be applied on the first day of the menstruation cycle	0.78
N. 11 - The birth control skin patch should be replaced only when the patch detaches itself	0.78
N. 12 - The contraceptive skin patch should be placed on the buttocks, lower abdomen, upper back, or outer arms	0.67
N. 13 - It is necessary to see a specialist for the placement of the vaginal ring	0.78
N. 14 - The vaginal ring can be removed for 2 hours during sexual intercourse without risk of pregnancy	1.00
N. 15 - The vaginal ring should be left in place for 21 days, followed by a week of rest	1.00

[§] Item-content validity index.

Tab. II. Characteristics of the test-retest sample (N = 10).

Characteristics	High school students	
	N (%)	Mean (SD)
Gender		
Males	2 (20)	
Females	8 (80)	
Age		18.1 (1.66)
High school classes		
First year	1 (10)	
Fourth year	2 (20)	
Fifth year	7 (70)	
Parents' relationship		
Married/cohabiting	7 (70)	
Separated/divorced	3 (30)	
Parents working in healthcare		
Yes	3 (30)	
No	7 (70)	
Older siblings		
Yes	5 (50)	
No	5 (50)	

Tab. III. Descriptive analysis of the items (N = 10).

SexContraKnow items	Percentage of success		Percentage of mistakes		Percentage of "don't know/ no answer" responses	
	T0	T1	T0	T1	T0	T1
1	90%	90%	0	0	10%	10%
2	60%	60%	20%	20%	20%	20%
3	90%	90%	10%	0	0	10%
4	70%	60%	10%	20%	20%	20%
5	70%	80%	0	0	30%	20%
6	70%	70%	10%	10%	20%	20%
7	80%	80%	0	0	20%	20%
8	40%	40%	0	0	60%	60%
9	70%	60%	10%	10%	20%	30%
10	30%	30%	10%	0	60%	70%
11	30%	30%	10%	10%	60%	60%
12	40%	30%	0	0	60%	70%
13	40%	40%	40%	50%	20%	10%
14	20%	20%	30%	20%	50%	60%
15	60%	60%	10%	10%	30%	30%

The majority were females (80%) with a mean age of 18.1 years (SD = 1.6) (Tab. II).
After the second administration of the instrument, we analysed the data and calculated Cronbach's alpha ($\alpha = 0.928$) and Pearson's r ($r = 0.991$).

Descriptive data

We performed a descriptive analysis on the answers of the students at T0 and T1. After calculating the mean score between T0 and T1, the items with the highest score were Item 1, "There is a risk of pregnancy when you have sex without any protection in the two days before or after ovulation.", and Item 3, The "calendar method (calculating the fertile period for not having sex during this period) is effective to avoid a pregnancy". The item with the lowest score was Item 13: "For the placement of the vaginal ring it is necessary to consult a medical specialist". The items the students were least knowledgeable about were: Item 10, "The contraceptive skin patch must be applied on the first day of menstrual cycle", and Item 12, "The contraceptive skin patch should preferably be applied on the buttock, to the lower abdomen, on the upper back or the outer arms". All the answers are summarized in Table III.

Discussion

The results we obtained, following the EORTC *Quality of Life Group* guidelines [21], showed that the reliability and validity of the Italian version of the *SexContraKnow* instrument were acceptable. Therefore, this instrument could be reliably used to explore adolescents' literacy about safe sex and contraception. The original instrument also showed good fit and reliability [5]. The invariability of the 15 items of the scale was assessed for differences across gender (male/female), previously training in using the questionnaire (yes/no) and academic degree discipline (nursing/law). The Bonferroni-adjusted α value ($0.05/15 = 0.0033$) showed no significance. The reliability of the scale was 0.99 for items and 0.74 for people. Both values indicate the fitness of the items to adequately rank people on the latent trait. The temporal stability of the scale was calculated using test-retest, obtaining a value of 0.81 (CI 0.692-0.888).
A descriptive analysis of the answers given to the instrument was also performed by the Spanish research group. Considering that the maximum score is 15 points, the mean score of all the answers was 7.47 (SD = 3.16). The item that obtained the highest percentage (93%) of correct answers was Item 2, "The male condom is safe if placed just before ejaculation, even if penetration has occurred previously", while the lowest (15.8%) was Item 14, "During sexual intercourse, the vaginal ring can be removed for 2 hours without risk of pregnancy". The most unknown item (73.9%) was Item 10, "The contraceptive skin patch must be applied on the first day of menstrual cycle" [5]. Although we validated the Italian version of the SexContraKnow Instrument on a high school population, the results were comparable to those obtained from the Spanish nursing research group of the University of Jean. We found that teenagers had more health literacy about the contraceptive methods they used most, in accordance with the National Survey on Contraception carried out by the Spanish Society of Contraception in 2018 [23].
For the Italian context, we found that it was essential to have this instrument for the adolescent population. The Ministry of Health in Italy performed several surveys on adolescents' health, including sexual health, but the instruments used were old [19] or non-specific for contraceptive methods and safe sex [20, 24]. Thanks to the validation of this instrument, Italian researchers

now have a new validated and reliable tool that could be used also in combination with the surveys that will be conducted by the Italian Ministry of Health in the future. It is important to improve health literacy through formal health education provided in schools. Health literacy provided through formal health education, improves people's self-efficacy, knowledge, and correct health behaviours [3, 12, 25]. People with a high level of health literacy can educate their children and help them adopt correct health behaviours, and adolescents would be more conscious about safe sex and contraception [2]. Nurses are the healthcare professionals who mostly interact with people and are the key to improving health literacy in the society [10]. Nurses play an active role because they can understand how to address appropriate educational interventions and how to transfer correct health information to adolescents [2, 12]. In particular, public health nurses and school nurses have the responsibility to promote health programs for adolescents [10].

Limitations

This study has some limits. First, the sample size for the pilot test-retest was limited to 10 participants because the validated instrument was intended to be used for a secondary larger study. Second, all the participants were from the same city. Third, we selected a sample aged between 14-19 years (high school population) so that more parents would accept their children's participation in our study. It would have been interesting to evaluate contraceptive health literacy in an even younger population.

Conclusions

The Italian version of the *SexContraKnow* instrument showed evidence of acceptable reliability and validity. It can be reliably used in Italy to assess adolescents' (high school students) health literacy about safe sex and contraception. It could be useful to test the instrument with younger or older populations than high school students. To further confirm its validity and reliability, it would be useful to conduct a multicentre nationwide study. This instrument could also be used to evaluate the effectiveness of educational programs currently available in Italy and promote the implementation of the most effective ones.

Acknowledgements

None.

Funding sources

This research did not receive any spe-cific grant from funding agencies in the public, commer-cial, or not-for-profit sectors.

Conflict of interest statement

The author declares no conflict of interest.

Authors' contributions

All authors contributed to the study conception and design. Material preparation and data collection were performed by VR, FN, and GC. Data analyses were performed by VR, FN, and MC. The first draft of the manuscript was written by VR, FN, MC, MH, RW, and GA. All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Received on August 5, 2022. Accepted on January 16, 2023.

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How to cite this article: Rossi V, Napolitano F, Hayter M, Watson R, Calzolari M, Aleo G, Zanini M, Catania G, Sasso L, Bagnasco A. Validation of the Italian version of the SexContraKnow instrument. J Prev Med Hyg 2022;63:E611-E617. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2676

Appendix 1

Di seguito, troverai una serie di affermazioni sulla sessualità, sulla gravidanza e sui metodi anticoncezionali. Alcune affermazioni sono vere e altre sono false, indica in ogni caso l'opzione che ritieni più corretta. Indichiamo una terza opzione di risposta, non sa/ non risponde. Nel caso non si conosca se l'affermazione è vera o falsa, per favore indicacelo tramite l'opzione NS/NC e non rispondere a caso.

1 - C'è rischio di gravidanza quando si hanno rapporti sessuali senza alcuna protezione nei due giorni precedenti o posteriori all'ovulazione	V	F	NS/NC
2 - Il preservativo maschile è sicuro se si mette giusto prima di eiaculare, anche se precedentemente ci sia stata una penetrazione	V	F	NS/NC
3 - Il "metodo del calendario" (calcolare il periodo fertile per non avere rapporti sessuali durante questo periodo) è efficace per evitare una gravidanza	V	F	NS/NC
4 - La pillola anticoncezionale è efficace sin dal primo giorno	V	F	NS/NC
5 - I metodi anticoncezionali ormonali (per esempio, la pillola anticoncezionale o l'anello vaginale) sono raccomandabili per gli adolescenti	V	F	NS/NC
6 - Quando ci si dimentica di assumere la pillola anticoncezionale all'ora corretta, si può prendere entro 12 ore senza perdita di efficacia	V	F	NS/NC
7 - Il "doppio metodo anticoncezionale" consiste nell'utilizzo simultaneo di un anticoncezionale di barriera (per esempio, preservativo) e uno ormonale (per esempio, pillola anticoncezionale)	V	F	NS/NC
8 - Se l'inizio dell'assunzione della pillola anticoncezionale è dopo il 5° giorno del ciclo, è raccomandabile usare un altro metodo anticoncezionale per una settimana	V	F	NS/NC
9 - Lo schema di assunzione della pillola anticoncezionale è giornaliero partendo dal 1° giorno del ciclo, per 21 giorni con una settimana di riposo. Per mantenere l'abitudine alcune aziende hanno inserito la possibilità di assumere una pastiglia placebo in tale settimana	V	F	NS/NC
10 - Il cerotto cutaneo anticoncezionale si deve applicare sin dal primo giorno di ciclo	V	F	NS/NC
11 - La sostituzione del cerotto cutaneo anticoncezionale si deve fare solo quando questo si stacca in autonomia	V	F	NS/NC
12 - Il cerotto cutaneo anticoncezionale si deve applicare preferibilmente sul gluteo, sulla zona del basso ventre, sulla parte superiore della schiena o esterna delle braccia	V	F	NS/NC
13 - Per la collocazione dell'anello vaginale è necessario rivolgersi a un medico specialista	V	F	NS/NC
14 - Durante un rapporto sessuale, l'anello vaginale si può rimuovere per 2 ore senza che ci sia il rischio di gravidanza	V	F	NS/NC
15 - L'anello vaginale si deve lasciare inserito per 21 giorni, lasciando successivamente una settimana di pausa	V	F	NS/NC

Health Promotion/History of Medicine and Ethics

Hepatitis B vaccination in Iran: Historical policies and programs

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Keywords

Health policy • Hepatitis B • Vaccine • Iran • Sustainable Development Goals

Summary

Hepatitis B virus (HBV) infection is a main challenge of the health system worldwide. Health policymakers in most countries attempt to help HBV patients by implementing support programs in addition to controlling HBV in their community so that the economic burden caused by HBV do not deprive the patients of accessing health services and reducing their quality of life. There are several health interventions for the prevention and control of HBV. Providing the first dose of the HBV vaccine within 24 hours after the infant is born is the most cost-effective way to prevent and control HBV. The purpose of this study is to review the nature of HBV, its epidemiology in Iran and worldwide, and to review the various policies and programs in Iran regarding the prevention and control of HBV, especially the use of vaccination. One of the goals of Sustainable Development Goals (SDGs) is to consider hepatitis as a threat to human health. In this regard, one of the top priorities of WHO is the prevention and control of HBV. In connection with the prevention of HBV, it is claimed that vaccination is the most effective and best intervention. Thus, vaccination in the safe's program of countries is highly recommended. According to the Ministry of Health and Medical Education (MOHME) reports, Iran has the lowest prevalence of HBV among the countries in Eastern Mediterranean Region Organization (EMRO). There is a hepatitis unit in MOHME whose responsibility is to coordinate and implement the hepatitis prevention and control programs. The HBV vaccine has been officially included in the vaccination program for children in Iran since 1993, and three doses of the vaccine are given to all infants. In 2007, during a large-scale program in Iran, 17-year-olds received the HBV vaccine, followed by adolescents born in 1990 and 1991. In recent years, the health system in Iran has made significant progress in preventing and controlling HBV. Over 95% coverage of the HBV vaccination is one of the achievements that have had a great impact on reducing the trend of HBV infection. In order to achieve the 2030 goals, the Iranian government, in addition to paying more attention to HBV elimination programs, should encourage other organizations to cooperate more effectively with MOHME.

Introduction

Hepatitis B virus (HBV) is a liver disease that can occur in both acute and chronic forms. Acute hepatitis refers to cases in which the virus takes less than 6 months from onset to recovery, during which time the infection is completely removed and the virus clears from the blood [1]. In this case, the structure and function of the liver remains normal, and usually the patient does not need any treatment except in special cases. On the other hand, in chronic hepatitis the virus stays in the body for more than 6 months, and the body's immune system is unable to kill the virus. Using contaminated syringes, unsafe sex, mother-to-child transmission, contacting with contaminated needles or equipment in hospital settings, and organ transplants are methods of disease transmission [2].

The World Health Organization (WHO) 2021 Report states that approximately 296 (Uncertainly interval (UI) 95%: 228 to 423) million people worldwide have already been infected with HBV; however, this report underscores the very important point that health policymakers should pay special attention to this serious challenge [3]. According to the 2021 Report, the highest rate of HBV infection based on the WHO region is in the Western Pacific, African, and South-East Asia (Fig. 1) [3].

Compared with WHO 2017 Report [approximately 257 (UI 95%: 199 to 368) million people worldwide were infected with HBV], the number of people infected with HBV has increased. This increase is worrying, warning countries to adopt more coherent policies and programs in order to combat HBV. HBV and hepatitis C virus (HCV) can cause chronic diseases in infected people, and if these people do not receive appropriate health services, it can lead to liver cirrhosis, a malignant disease that is likely to cause death [4].

https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2731

Fig. 1. Prevalence of HBV infection in general population by WHO region (Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021).

Mother-to-child transmission of hepatitis B continues to be a major mode of transmission [5]. Other reasons for the increase of HBV worldwide are: Increasing costs of care and medical services, lack of proper political interactions, lack of information and strategic surveys, lack of a meticulous action plan, and shortage and cost of diagnosis [6].

Meanwhile, HBV and HCV are among the most common causes of cancer and mortality worldwide [7]. Due to the nature of HBV and the highly likelihood of causing severe complications in infected patients, HBV can place a great economic burden on patients and their family. Alongside, health systems pay large sums for HBV annually [8].

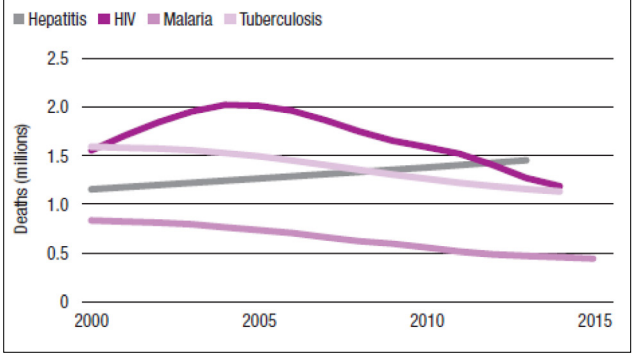
There are several health interventions for the prevention and control of HBV. Vaccination is one of the most important interventions that can provide the 98-100% protection. Implementing blood safety strategies is another valuable intervention, which means that all donated blood and blood components used to transfuse blood to patients need to be carefully screened [9]. Another important intervention in the prevention and control of HBV is to educate and raise the level of awareness of all people in the community about the transmission and prevention of HBV. In this regard, syringes and condoms should also be readily available to anyone in the community, especially those with high-risk behaviors. Screening mothers before pregnancy, and creating a safe environment for tattoos and piercings are other health interventions in preventing and controlling HBV [10].

Hepatitis B virus (HBV) infection is one of the main challenges of the health system worldwide, where a large number of people die every year due to the complications of this disease [11]. Health policymakers in most countries attempt to help HBV patients by implementing support programs in addition to controlling HBV in their community so that the economic burden caused by HBV do not deprive the patients of accessing health services and reducing their quality of life [12]. Reducing prices and making services available to patients, increasing insurance support, and reducing out-of-pocket (OOP) payments are some of the main patient support policies [13]. The purpose of this study is to review the nature of HBV, its epidemiology in Iran and worldwide, and to review the various policies and programs in Iran regarding the prevention and control of HBV, especially the use of vaccination.

Hepatitis and Sustainable Development Goals

The Millennium Development Goals (MDGs) were to focus on HIV, malaria, and tuberculosis; and with the efforts of many countries, the incidence and mortality of these diseases were reduced [14]. However, the mortality of HBV has been on the rise since 2000 [15]. Figure 2 compares the mortality rates of HBV, HIV, malaria, and tuberculosis [16].

Fig. 2. Mortality rate between 2000 and 2015.



In September 2015, world leaders agreed to set on a path toward Sustainable Development Goals (SDGs) by approving the 2030 Agenda [17]. The agenda, which contains 17 goals and 169 targets, envisages quantitative operational goals in the social, economic, and environmental domains of sustainable development that must be achieved by 2030 [18]. One of the goals of SDGs is to consider hepatitis as a threat to human health. In this regard, the following two targets should be achieved by 2030 [10]:

- *90% reduction in new cases of chronic HBV and HCV infections by 2030;*
- *65% reduction in HBV and HCV deaths by 2030;*
- Therefore, in order to achieve the 2030 goals, the coverage of some HBV- and HCV-related services should also be change, some of which are as below:
- *90% coverage of HBV vaccination by 2030;*
- *90% coverage of prevention of mother-to-child transmission of HBV by 2030;*
- *100% of blood donations screened in a quality-assured manner by 2030;*
- *90% of injections administered with safety-engineered devices in and out of the health system by 2030;*
- *300 sterile needles and syringes provided annually per person who injects drugs by 2030;*
- *90% of chronic viral hepatitis B and C infections diagnosed by 2030.*

The purpose of determining HBV controlling programs is to plan for reducing the incidence, mortality rate, complications, and transmission of HBV and HCV [19]. The implementation of these policies requires high political commitment, resource mobilization, and the advocacy of policymakers [20].

The Center for Disease Analysis (CDA) and the Center for Disease Analysis Foundation (CDAF) evaluate countries' performance on hepatitis B and C in their programs. According to these organizations, Australia, Austria, Egypt, and Georgia were successful in achieving the 2030 goals [21].

Despite ubiquitous efforts to achieve the 2030 goals, it seems that some countries are not yet on the track toward achieving these goals [22]. In order to achieve the 2030 goals regarding viral hepatitis, awareness of these infections should first be increased. In terms of the political commitment to achieving the 2030 goals, governments need to use all their resources, especially for diagnostic, screening, and treatment services, which require extensive financial resources to be provided to the health system. Having an action plan based on demographic, cultural, social, political, and economic characteristics that are based on valid data will be also effective [17].

The Iraninan healthcare system

The Ministry of Health and Medical Education (MOHME), as the main custodian of health in Iran, has the responsibility for taking care of public health [23]. At the macro level, the ministry prioritizes some services by adopting policies and programs based on the country's health problems. Also, the centers for disease control (CDC) in Iran is responsible for planning and controlling diseases [20]. In all provinces of the country, medical universities also play the main role in implementing health policies and programs at the regional level [23].

Epidemiology of HBV infection in Iran

According to MOHME reports, Iran has the lowest prevalence of HBV among the countries in Eastern Mediterranean Region Organization (EMRO). The MOHME estimates the prevalence of HBV in Iran at less than 1%. Also, it is estimated that about 1.4 million people are infected with HBV in Iran, many of whom are not aware of their infection with this disease [24]. In this regard, Rezaei et al. (2020) conducted a small-scale meta-analysis study in order to assess the HBV prevalence in Iran between 2000 and 2016. The findings of their study showed that the prevalence of HBV decreased from 3.02% in 2000 to 1.09% in 2016 [25]. To the best of our knowledge, however, no large-scale study in the general population of Iran has ever been conducted in order to assess the status of HBV in the country.

HBV surveillance system in Iran

There is a hepatitis unit in MOHME whose responsibility is to coordinate and implement the hepatitis prevention and control programs. Screening is provided to diagnose patients in public and private health-care centers. Also, all insurance companies in Iran cover these services; thus, OOP payments have declined in recent years [12]. Due to the limited financial resources of the MOHME, free and universal diagnostic tests are not available to everyone in the community [20]. Meanwhile, the National Committee for Hepatitis in the MOHME is responsible for all hepatitis programs, their annual evaluation, preparation of guidelines, and coordination with other health-related departments in the fight against hepatitis [26].

Also, there is a monitoring and reporting system throughout the country. All public and private laboratories are required to report the latest patient cases to CDCs in the cities, which is eventually is reported to MOHME [26]. One of the most important and valuable parts of the health system in Iran is the primary health-care (PHC) network that exists even in small villages [27]. This network has played a significant role in improving health indicators in recent decades; some of its achievements are: reducing infant and maternal mortality, increasing access to health services, and increasing life expectancy [27]. In connection with hepatitis programs, the network runs training programs annually in order to raise awareness about HBV; in parallel, the network is undoubtedly the most important player in the field of immunization through the HBV vaccination [28].

HBV vaccination

One of the top priorities of WHO is the prevention and control of HBV; in this regard, various programs and policies are introduced by this organization to be on the agenda of policymakers worldwide [29]. Along the same line, various hepatitis B training programs have been set up around the world in order to raise public awareness [30].

There is no treatment for acute hepatitis B. Thus, a safe and effective vaccine can play a very important role in preventing HBV, which is also a cost-effective prevention policy. Meanwhile, the implementation of this policy might motivate policymakers to continue to support HBV vaccination [22].

Providing the first dose of HBV vaccine within the 24 hours after the infant is born is the most cost-effective way to prevent and control HBV. By adopting this policy, protection is thus created for other groups in the general population that also reduces the incidence of chronic HBV [31].

HBV vaccination in Iran

The HBV vaccine has been officially included in the vaccination program for children in Iran since 1993, and three doses of the vaccine are given to all infants. In 2007, during a large-scale program in Iran, 17-year-olds received the HBV vaccine, followed by adolescents born in 1990 and 1991 [28]. Since 1993, with the inclusion of the HBV vaccine into the immunization program in Iran, various groups have received the vaccine.

The data shows that various countries have made great strides in preventing HBV through vaccine immunization. Figure 3 compares the coverage of the third dose of HBV vaccine between the geographical region of WHO and Iran.

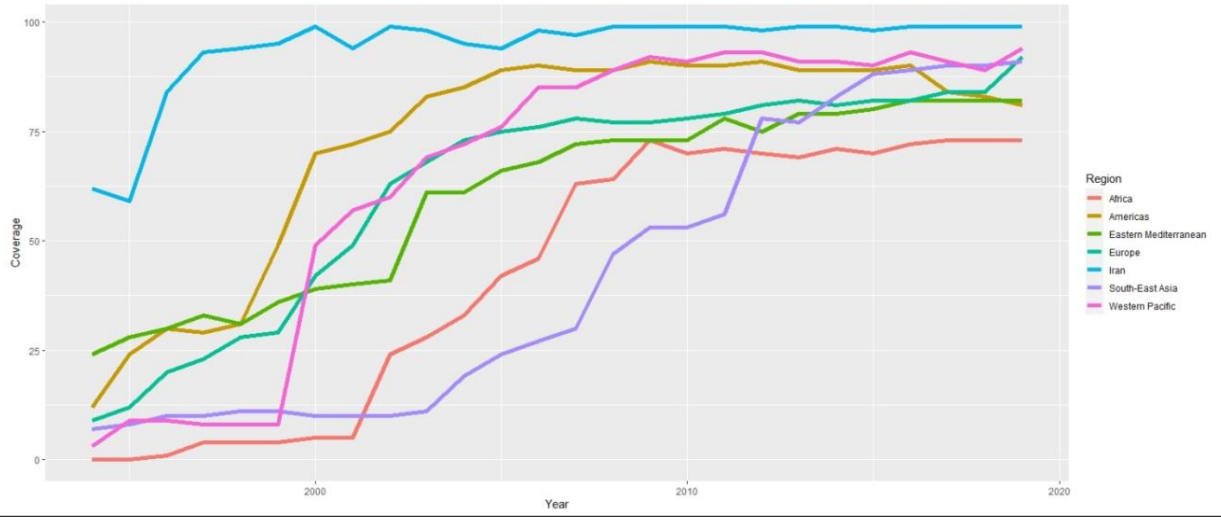
The trend in Figure 2 demonstrates that HBV vaccination coverage has been very high in Iran. According to MOHME reports, with the implementation of various policies and, most importantly, the high percentage of vaccination coverage, a decrease is observed in the cases of HBV infection in Iran.

Challenges of HBV immunization program in Iran

Although health policymakers in Iran hope to make the HBV immunization program as effective as possible, there are still some issues that need to be addressed. After the COVID-19 pandemic, most health-related programs in Iran, like other countries, have been suspended. Alongside, care and screening programs in connection with the HBV prevention and control programs have been decreased. Also, some families were reluctant to visit health centers for HBV vaccination because they were afraid of being infected with COVID-19. Due to the pandemic and a higher number of patients visiting health centers, the routine activities that health professionals were to take care have unprecedentedly increased in these centers; therefore, the quality of services related to HBV programs has been reduced.

Meanwhile, Iran's being under crippling sanctions in recent years caused MOHME to face serious problems in importing laboratory equipment, drugs, and WHO-approved rapid hepatitis virus kits. Also, sanctions reduce Iran's economic revenues, affecting negatively the financial resources allocated to the health sector. Another issue influencing the HBV programs is the population dispersion in Iran; the health sector due to lack of sufficient health professionals could not provide services to all residents appropriately. In this regard, the refugee population in Iran, mainly from Afghanistan and Iraq, has also increased marginalization. Due to insufficient financial resources available from international organizations, the refugees face serious problems accessing all services, including the HBV vaccine.

Fig. 3. Third dose HBV vaccine coverage in WHO region.



Tab. I. List of all the groups that received HBV vaccine in Iran.

No	Group
1	All infants
2	People who are exposed to have occupational exposure to blood
3	People who have been hospitalized and cared for a long time in certain institutions due to their disability and special medical problems
4	Patients with chronic liver disease and people infected with HCV
5	Hemodialysis patients
6	Frequent recipients of blood or blood products
7	Users of injecting drugs
8	People with high-risk sexual behaviors, especially those with a history of sexually transmitted diseases
9	Prisoners with a history of high-risk behaviors and a stay of more than 6 months in jail
10	Municipal sweepers, firefighters, emergency workers, prison guards, forensic experts, and crime scene experts
11	People who are candidates for organ transplants
12	Health-care workers
13	People with HIV infection
14	Families of patients with HBV
15	Residents of homeless shelters
16	Patients with hemophilia and thalassemia

Many of these refugees may be unaware of their infection with HBV. Due to the financial problems of the health system in Iran, the diagnostic, prevention, and control services are not provided for all patients, which can lead to a failure in achieving the 2030 goals. Accessing to health services for the vulnerable refugee population is important, and in line with the international community's call for the elimination of viral hepatitis, countries need political and health strategies in order to combat this infection.

Iran has implemented extensive programs to prevent and control HBV that seems to have made good progress, given its priority in widespread vaccination, especially at birth. The use of skilled professionals, the provision of vaccines, improving the safety of blood and blood products, as well as the establishment of harm reduction centers in all provinces are other successes that can be a good example for other countries. However, serious issues in the nuclear Iran deal have affected Iran's economic activities that have led to a devastating effect on plans to eliminate viral hepatitis by 2030 due to financial issues. Also, to produce the vaccine inside the country, companies need raw materials, and the Blood Transfusion Organization of Iran uses imported kits for hepatitis screening. In addition, due to Iran sanction and the refusal of foreign companies to have financial transactions, Iran has suffered from hepatitis B immunoglobulin. We believe that these restrictions can affect the goals of eliminating viral hepatitis in Iran, as well as international programs.

Meanwhile, the weak hepatitis registration and reporting systems have deprived MOHME away from receiving comprehensive information. Another issue is the fact that several small urban areas in Iran cannot afford to have a diagnostic laboratory; and thus, the residents of such areas can not have access to the HBV services. In addition, many organizations that are involved with high-risk groups in the community do not have proper cooperation with MOHME in implementing the HBV prevention and control program; thus, MOHME alone is not able to cover all the services. Although MOHME has been working with insurance companies to reduce the cost of diagnosing HBV, its costs are still high for many, making them unable to use diagnostic services. The final issue we want to mention here is that achieving the goals of SDGs has been only acknowledged as a political commitment, and because of insufficient financial resources it has never been top on the agenda of policymakers in Iran.

Conclusion

In recent years, the health system in Iran has made significant progress in preventing and controlling HBV. Over 95% coverage of the HBV vaccination is one of such achievements that have had a great impact on reducing the trend of HBV infection. In parallel with efforts to provide a high coverage of vaccination in Iran, and paying attention to at-risk groups, lack of financial resources, lack of sufficient health professionals, international sanctions, and lack of sufficient attention from top policymakers are the major challenges in implementing HBV-related programs. In order to achieve the 2030 goals, the Iranian government, in addition to paying more attention to HBV elimination programs, should encourage other organizations to cooperate more effectively with MOHME.

Acknowledgements

This study was part of a PhD thesis supported by the School of Health Management, Iran University of Medical Sciences, Iran (IUMS/SHMIS_1396/9423557001).

Ethics approval

The study was reviewed and approved by the Ethics Committee of the School of Health Management and Information Sciences, Iran University of Medical Sciences.

Conflict of interest statement

The authors declare no conflict of interest.

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Received on September 28, 2022. Accepted on November 29, 2022.

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How to cite this article: Behzadifar M, Azari S, Shirkhani S, Gholamrezaei S, Shahabi S, Doshmangir L, Ehsanzadeh SJ, Martini M, Bragazzi NL, Behzadifar M. Hepatitis B vaccination in Iran: Historical policies and programs. J Prev Med Hyg 2022;63:E618-E624. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2731

History of Medicine and

The Story of the plague in the Maritime Republic of Genoa (Italy) (1656-1657): An innovative public health system and an efficacious method of territorial health organization

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Keywords

History of pandemics, Plague • Maritime Republic of Genoa • History of public health • Hygiene regulations

Summary

Introduction. *With the recent COVID-19 pandemic, the terms quarantine, contagion and infection have again become part of our everyday speech, prompting historians to reflect on the settings in which they were originally used and to make comparisons with the present time. How did people cope with epidemics in the past? What measures were taken?*
Objectives. *Here, we analyse the institutional response of the Republic of Genoa to a calamity that shook the city – the plague of 1656-1657. In doing so, we focus particularly on the public health measures implemented, as recorded also in unpublished and archival documents.*
Discussion. *In order to tighten control over the population, Genoa was divided into 20 zones, each of which was placed under the authority of a Commissioner endowed with criminal jurisdiction. The Commissioners' duties concerned the spheres of public health, public order and those tasks which today we would assign to "civil protection". Through the official documentation and the trial records kept by the Chancellor of one of these zones, we can shed light on the Commissioners' everyday activities and assess the impact of the public health measures on the population.*
Conclusions. *The 17th century plague in Genoa provides us with an important testimony of a well-organised and structured public health policy – an institutional response involving the adoption of efficacious measures of safety and prevention in the field of hygiene and public health. From the historical-social, normative and public health perspectives, this meaningful experience highlights the organisation of a large port city, which was at the time a flourishing commercial and financial hub.*

Introduction

The epidemic of bubonic plague that struck Genoa and its domain between May 1656 and August 1657 has gone down in history as the most fierce and devastating calamity to strike the territory of the Republic of Genoa during the modern age.
"To preserve and to rid the city of the plague" (Fig. 1)
Its severity is revealed by copious historiography, which, right from the beginning of the epidemic, dealt with the characteristics of the disease and the means utilised to curb its spread. In addition to the testimony of those who played an active role in the fight against the plague, such as the Augustinian friar Antero da San Bonaventura [1], Chaplain of the Consolazione plague hospital, and the Capuchin friar Maurizio da Tolone (a so-called "perfumer") [2], we have the accounts collected by the notary Giovanni Bartolomeo Campasso, Chancellor to the Health Magistrate in 1669 [3].

The plague in Genoa: a "Mediterranean plague"

The Republic of Genoa, which had been spared (and therefore not immunised) by the 1630-1633 series of epidemics recalled by Manzoni, was one of the four Italian theatres, together with Sardinia, the Papal State and the Kingdom of Naples, of what Bruno Anatra described as "a Mediterranean plague" [4]. The epidemic broke out in 1647 on the African coast, from where it spread first to Andalusia and then to Catalonia. It was subsequently carried by an infected ship from the port of Barcelona, reaching Sardinia in 1652. In Sardinia, the disease struck in two waves:

- the first wave (1652-1653) involved the northern part of the island and carried a mortality rate of over 55%;
- the second wave (1654-1657) involved the central and southern parts, from where it spread to mainland Italy.

Between April and May 1656, the plague reached Naples, followed by Rome and finally Genoa. The pattern of its spread was always the same; the disease first appeared in the vicinity of a port (in Rome, the cities of Civitavecchia and Nettuno) and then spread like wildfire throughout the rest of the territory, following trade routes and the pathways of flight from the cities to the countryside.
Mortality rates varied enormously according to the geographical area affected, ranging from a minimum of 7.8% in Rome to horrendous levels in Naples and Genoa, where more than half of the population perished [5].

Fig. 1. Canvas of Domenico Fiasella (1589-1669) entitled: "The story of the plague in Genoa, Italy, (1656-1657)"*

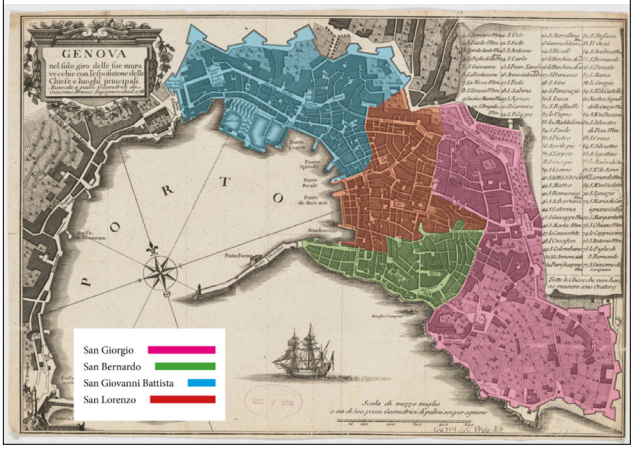
*(Archivio Fotografico Fondazione Franzoni onlus– Genova)

This disparity, however, did not stem from a lack of attention or preparation on the part of those responsible for tackling the emergency, as is well demonstrated by the case of the Republic of Genoa, the only one of the four above-mentioned states that had had a permanent and well-organised body dedicated to public health since the first half of the 16th century. Indeed, as Giovanni Assereto pointed out, the plague did not catch the city off its guard; the public health system, which had already been tested by the 1648-1650 epidemic of exanthematous typhus, was activated as soon as the plague manifested itself in Sardinia. Nevertheless, the attempt to cordon off the city, to impose quarantine and to ban the importation of goods coming from infected areas did not meet with success, and in May 1656, the disease reached Genoa's neighbouring villages in the Bisagno Captaincy [6].
According to some sources, the plague had been brought in by a few sailors arriving from Sardinia, who, having come ashore at Sturla, had sold "certain infected stuff" without respecting the hygiene regulations issued by the Magistrate [7]. According to others, the disease had been brought into the "marinas of Albaro" by Neapolitan refugees [8]. Whatever its vector was, however, the plague raged in the area and, despite efforts to protect Genoa (the capital), penetrated within the city's walls in July of the same year. The trend in contagion, which was initially fairly constant, displayed a downturn during the winter months; subsequently, however, it rose again, reaching its peak of morbidity and mortality as the weather warmed up in 1657, reflecting the life-cycle of fleas [8].

Public health measures and the role of the "Health Magistrate": hygiene regulations and sanctions

The measures implemented by the Health Magistrate roughly retraced the model that had already been tried and tested during the plague of 1579: public health officers were deployed to guard the coasts; the city gates were garrisoned, and a network of secondary hospitals was created to relieve the pressure on the Lazaretto at the Foce [6]. Paradoxically, the place where these measures differed most markedly from the previous intervention was the city of Genoa itself, which was divided into smaller districts in order to facilitate the application of the public health measures. In September 1656, the city authorities identified four areas (Fig. 2) inside the ancient walls; named after the patron saints of the city (St Laurence, St George, St John the Baptist and St Bernard), each of these areas was subdivided into five zones, denominated by the letters A to E [9]. Administration of these zones was entrusted to "Commissioners", who were randomly selected from among all the patricians aged between 25 and 70 years, excluding those already engaged as health officers in the coastal areas.
The Commissioners of the zones were called upon to enforce the regulations of the Health Magistrate and to maintain public order. However, they also had duties in the sphere of public health and assistance [3]. For instance, they were to ensure cleanliness of the streets, supervise the burning of infected material, coordinate health personnel, seal warehouses containing precious goods in order to avoid their contamination, and authorise all movement of persons and things within their zone. In particular, they had to make sure that the physician and surgeon assigned to the zone did not leave it, even during the night, and to check that the procedures of quarantine and conveyance to the plague hospitals were meticulously implemented. Anyone who did not obey the Commissioner's orders was liable to be imprisoned or sentenced to serve as a galley slave, at the discretion of the Commissioner himself.
In order to carry out his duties, each Commissioner was assisted by a Chancellor and 6-8 "*Capistrada*" (neighbourhood watchmen), who were appointed at the moment of the Commissioner's election [3]. These latter constituted the Commissioner's network of informers and executors on the ground; they verified the proper functioning of "sewers and wash-houses", visited people in quarantine, and distributed bread and alms to the poorest. Their principal task, however, was to carry out a

Fig. 2 Division of the city of Genoa into areas.



census of the population living in the streets under their jurisdiction and to record, for each house:

- the surname and first name of the master […]; whether he had a wife; how many sons and daughters he had and the age of each one; and, if the family kept servants, how many of each sex […]. Regarding persons of inferior condition, the quality of the house was to be recorded (*i.e.* whether it had its own entrance), and, if such persons worked for a living, *whether on a large or small scale)* [3].

In the case of strangers, it was to be ascertained how long they had been in Genoa and whether they were vagabonds. The *"Magistrato di consegna"*, who was responsible for checking on outsiders, was to facilitate this operation by not permitting "strangers, vagabonds, ne'er-do-wells and scroungers to remain in the city" [3]. This diffidence towards marginalised individuals stemmed from the ambivalent nature of the pauper, who was regarded both as an image of Christ and as a public health risk. Indeed, the conviction that the plague was caused by corrupted air aroused suspicion that the disease might be spread by poor individuals, who were typically dirty [13]. Thus, during the 1656 plague, the Magistrate for the poor suspended the Sunday distribution of "charity" bread in order to avoid dangerous gatherings of paupers, and the Commissioners took over the task of distributing alms door-to-door [3]. At the same time, the neighbourhood watchmen were called upon to report those who lived in hovels or makeshift accommodation, so that the Magistrate could find adequate housing for them. As pointed out by Maria Francesca Raggi in a letter, a good proportion of the lower orders lived "*in houses of 10 or 12 families, where the plague was to be found even in healthy periods, owing to the filth and infected air therein*" [8].

To study the social impact of the measures implemented, we consulted the deeds of the notary Giovanni Battista Lavagnino, Chancellor to Felice Spinola, the Commissioner of zone D of the St Laurence district. This documentation enabled us to investigate the everyday activities of the Commissioner and to sample the difficulties encountered in applying the public health provisions regarding the burning of infected materials and the limitation of the movement of inhabitants. Silk, velvet and leather were considered to be particularly dangerous, as the particles of contagion could easily adhere to these materials and remain active for years. According to one coeval source: *Such materials, albeit not easily receiving contagion, conserve it for two or more years, as it is closed within and forms over time, becoming more active and efficacious than it was at the beginning. Merely by using an infected cotton cloth that covered a diamond, many people have died, and also after opening a trunk full of infected garments* [11].

The only way to get rid of the danger was to burn any goods that had been in contact with plague victims, regardless of their financial value. To prevent this potential loss of property, several patricians and merchants asked the Commissioner to seal rooms in their houses and warehouses where they kept precious furnishings, unsold goods and semi-finished raw materials. Dealers in silk and wool regarded this freezing of their activities as a necessary evil that could save them from the much greater loss of having all their material burnt. At the moment when the room was sealed, the Chancellor drew up a deed describing the room, its contents and the paper seal, in order to be able to check that it was not broken too soon.

Most people, however, could not afford to avail themselves of these procedures and, heedless of the risks involved, appropriated furniture and materials that had belonged to plague victims and hid them from the neighbourhood watchmen. Giovanni Battista Lavagnino's papers include about 20 accusations, excerpts from trials and witness accounts that testify to this type of fraud and misappropriation. Sometimes, penal proceedings were initiated after a case of plague and the reconstruction of the network of contacts of the deceased. For instance:

- the death of Bastiana, a washerwoman from Bastia, helped to unmask a ring of smugglers of "*pepper, cloves… and Barbary wool*" run by Corsican soldiers billeted at the plague hospital at the Foce, together with compatriots of theirs who washed clothes in the river Bisagno [12];
- in the case of the trial of Faustina Giannina, who was accused of keeping on her balcony a trunk of clothes that had belonged to her daughter and son-in-law, both of whom had died of the plague, it was one of the woman's neighbours who reported the fact [13].

The information network of the local Commissioners and their neighbourhood watchmen was supported by part of the citizenry, alarmed by the high mortality of the epidemic and its economic consequences. The population was particularly sensitive to the issue of adherence to quarantine, so much so that accusations were made which subsequently proved unfounded:

- on 3 October, Cesare Corte, "*prompted by the interest of the public good […] reported seeing a boy come out of the Torre Tavern situated in Sosilia and then go back in through the same door after buying a little tobacco from a spicer who was standing in the vicinity of the said tavern*" [14]. The tavern had been placed under quarantine a few days earlier, but, according to Corte, the boy had gone in and come out through a small aperture in the façade of the building. Although the report had been made "*quite late*" in the evening, the Commissioner ordered that "*due information*" should immediately be gathered by the neighbourhood watchman and the notary; the boy, who was blind in one eye, was immediately identified, and both he and the spicer were interrogated. The boy swore that the tobacco and the money (soaked in vinegar) had only been passed under the door of the tavern. Unconvinced, the investigators insisted on testing whether it was physically possible for the boy to enter the tavern by passing through the aperture. After ascertaining that, "*having made the said boy lie on the ground and having tried to push him through the aperture*", it was not possible for the boy to get in that way, even "*by pushing him hard*", his questioners accepted the hapless lad's version;

- equally unfounded was the allegation made in an anonymous letter sent to Francesco Invrea, the Commissioner of zone E of the St George district, in February 1657. The writer claimed that the baker's assistant Bernardo Musso had the plague […]. After investigation by the neighbourhood watchman and medical examinations by the physician and the surgeon, the Commissioner was obliged to admit that the report was groundless.

The Genoese plague hospitals: structure, organisation and location

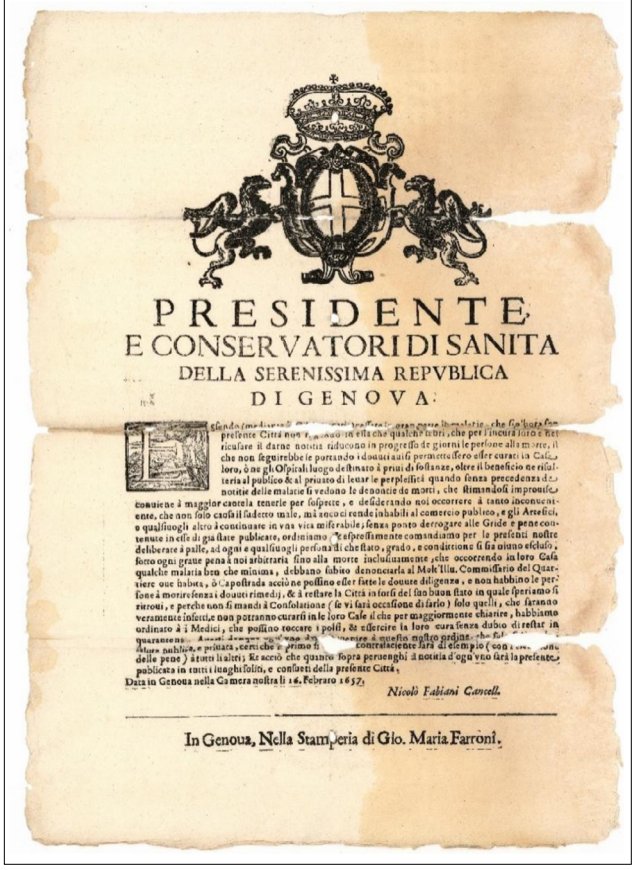
Unfortunately, analysis of the available sources does not enable us to determine whether the accusations made were prompted by mass hysteria or by a desire for personal vendetta. Nevertheless, what emerges is that the system was efficient, well-tested and generally appreciated by the citizenry. Only a few anonymous denunciations of the woeful state of the plague hospitals and of the abuses perpetrated by the neighbourhood watchmen in some zones testify to a more variegated picture.

Some of the patricians openly opposed conveyance to the plague hospital at the Foce, as this facility did not ensure a treatment worthy of their social class; indeed, nobles were obliged to share the same spaces with members of the lower orders. Moreover, numerous informers pointed to the scant efficacy of the therapy offered, and even claimed that transferring a sick person to the plague hospital at the Foce was tantamount to issuing a death sentence (Fig. 3). Likewise, the Consolazione plague hospital was dubbed by the author of one missive as the "Desolation Hospital", as it was "infected" and its beds were "diseased and plague-ridden" [15].

In addition, corpse-gatherers and neighbourhood watchmen were accused of exploiting their position in order to commit theft and perpetrate violence. Indeed, surveying the population, questioning people and assisting the sick gave them the opportunity to examine the premises and to spot the most attractive objects to steal. Moreover, when a new Commissioner was appointed in zone E of the St George district in 1657, the previous neighbourhood watchmen were accused of stealing bread and arms intended for the poor and of taking bribes in order to close one eye to quarantine violations. Some of these abuses were reported shortly after they had been perpetrated, while others came to the attention of the Health Magistrate only in 1658, when the epidemic was over.

Despite these distortions, the end of the plague did not mark the end of the city's subdivision into districts; on the contrary, this scheme was adopted several times during the course of the 17th century, in order to carry out censuses of the population and other operations, such as the assignment of street numbers to buildings and the maintenance of public lighting [16]. Indeed, the dense information network utilised by the Commissioners proved to be a perfect means of controlling the territory and implementing measures aimed at safeguarding the citizenry.

Fig. 3. State archive of Genoa, Health Office n. 1881 (Archivio di Stato di Genova, Ufficio di Sanità, N. 1881).



PRESIDENTE
E CONSERVATORI DI SANITA
DELLA SERENISSIMA REPVBLICA
DI GENOVA.

Nicolò Fabiani Cancell.

In Genoua, Nella Stamperia di Gio. Maria Farroni.

Conclusions

The experience of the plague in Genoa in the 17th century once again testifies to the importance of adopting measures of safety and prevention in the field of hygiene and public health [17, 18]. This testimony is interesting from both the historical-social and public health standpoints, in that it dates back to a period in which public health legislation was not particularly advanced and the population was often scantly informed of the regulations to be respected and the measures to be implemented [19].

Indeed, in terms of hygiene, people's behaviours and habits, not only at that time but also even later, left much to be desired and were certainly not sufficient to ensure proper compliance with the principal rules of public health [20, 21].

This was the case even in "uneventful" conditions, and all the more so when such aggressive, devastating and, above all, rapid events occurred, as in the case described above.

And yet, albeit with due caution and considering the standards of large cities in the middle of the 17th century, we can claim that Genoa was well organised from the public health standpoint; its planning was innovative and its set of dedicated norms and system of sanctions proved to be fairly efficacious. In order to curb the diffusion of the plague, the city was subdivided into restricted areas,

which were placed under the control, management and organisation of local Commissioners.
This helped to limit the further spread of contagion, providing greater equilibrium and more efficient organisation. This approach gained the approval of the citizenry, so much so that, once the emergency was over, the subdivision of the city into districts was maintained, being adopted for various purposes on other occasions during the course of the 17th century [20]. Indeed, it was an efficient structure that utilised a robust information network in order to control the territory and to implement measures aimed at protecting the city and its inhabitants.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare no conflict of interest.

Author's contribution

FF and MM designed the study, conceived and drafted the manuscript; PC, FB and MM revised the manuscript, FF performed a search of the literature. All authors critically revised the manuscript. All authors have read and approved the latest version of the paper for publication.

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Received on March 11, 2022. Accepted on November 25, 2022.

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How to cite this article: Martini M, Calcagno P, Brigo F, Ferrando F. The Story of the plague in the Maritime Republic of Genoa (Italy) (1656-1657): An innovative public health system and an efficacious method of territorial health organization. J Prev Med Hyg 2022;63:E625-E629. https://doi.org/10.15167/2421-4248/jpmh2022.63.4.2781


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