Tuberculosis in Iran: a historical overview from al-Tabari, Rhazes, Avicenna and Jorjani to Abolhassan Ziyā-Zarifi. Old and new pioneers in the fight against tuberculosis: challenges, pitfalls and hopes

Ma. BEHZADIFAR[1], M. MARTINI[2,3], Me. BEHZADIFAR[4], N.L. BRAGAZZI[2,3,5,6]

[1] Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran; [2] Department of Health Sciences (DISSAL), University of Genoa, Italy; [3] UNESCO Chair, Health Anthropology Biosphere and Healing Systems, University of Genoa, Italy; [4] Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran; [5] Postgraduate School of Public Health, Department of Health Sciences (DISSAL), University of Genoa, Italy; [6] Department of Mathematics and Statistics, Laboratory for Industrial and Applied Mathematics (LIAM), York University, Toronto, Canada

Keywords

Tuberculosis • History of tuberculosis • Iran • History of medicine

Summary

Tuberculosis is a serious respiratory infectious disease, caused by Mycobacterium tuberculosis bacteria. It has always represented a permanent, serious public health challenge over the course of human history, because of its severe epidemiological, clinical and societal implications. The present review aims at over-viewing the contributions of the Iranian medicine to the control, management and treatment of tuberculosis, from the glorious past of the eighth-ninth centuries to the present, from Ali Abu al-Hasan Ahmad ibn Sahl-e Rabban al-Tabari to Rhazes, Avicenna, Jorjani and Abolhassan Ziyā-Zarifi. However, despite the efforts, tuberculosis and, in particular, multidrug-resistant tuberculosis still represent a great public health concern in Iran. On the other hand, this country can capitalize on its millennial, incredibly rich story of major achievements in the battle against tuberculosis to develop and implement ad hoc public health programs for the control of the disorder, including targeted and specialized interventions.

Introduction

Tuberculosis is a serious respiratory infectious disease, caused by *Mycobacterium tuberculosis* bacteria. It has always represented a permanent, serious public health challenge over the course of human history, because of its severe epidemiological, clinical and societal implications [1]. The present review aims at overviewing the contributions of the Iranian medicine to the control, management and treatment of tuberculosis, from the glorious past of the eighth-ninth centuries to the present.

Tuberculosis and the glorious past of the Iranian medicine

The Iranian medicine has a rich, glorious millennial past. Ali Abu al-Hasan Ahmad ibn Sahl-e Rabban al-Tabari (born in Merv, in the Khorasan, or in Toranja, in the province of Tabaristan in 783, 808, 810 or 838, and dead in Baghdad or in Samarra, in 855, 858, 864 or 870, according to other scholars) was an erudite Persian Muslim scholar, son of a prominent Syrian Christian physician, Sahl ibn Bishr, who was also a mathematician and astronomer. al-Tabari was erroneously considered Jewish by some researchers because of the nickname of the father ("*Rabban*", meaning "master"), whereas other scholars thought he was Christian ("*al-Katib al-Nasrani*", meaning "the Christian writer"). According to other sources, he was Zoroastrian. He was the secretary of the Persian prince Mazyar from the Qarinvand dynasty ("*katib Mazyar*"), who, in 839, guided the rebellion against the Abbasids. This rebellion failed and al-Tabari converted to Islam, serving as personal physician of various Caliphs, including al-Mu'tasim (833-842) and al-Mutawakkil (847-861). He cultivated different medical disciplines and specialties, including pediatrics and pediatric infectious disorders [2-4]. He was the author of one of the first most comprehensive treatises of medical knowledge and pharmacopeia, known as "*Firdous al-Hikmah*" ("The Paradise of Wisdom") or "*al-Kunnash*". A chapter of his seven-volume encyclopedia was entirely devoted to the description of tuberculosis, the etiopathogenesis of which, according to the author, should be attributed to the adoption of unhealthy lifestyle behaviors, characterized by excessive sexual desire and grief. Socio-economic status, such as poverty, could as well be a facilitating condition for an increased risk of development and/or transmission of tuberculosis. Once being infected, the pathogen could erode heart's veins creating cavities. Moreover, al-Tabari described in detail tuberculosis cases affecting the skin (*lupus vulgaris*) as well as involving the lymph nodes (*Khanazir* or scrofula) [4].

Abu Bakr Mohammad Ibn Zakariya Al-Razi, known as "Rhazes" (born in Rey, formerly known as Arsacia, Iran,

in 854/865 and dead in Rey in 925/930 or 932 according to other scholars), compiled a prominent collection of medical case-reports and case-series, termed "*Kitab Al-Hawi Fi Al-Tibb*". In this treatise, the author reported a case of a patient who had bloody sputum (*nafeth-o-damm*), speculating that the most probable cause was pulmonary tuberculosis, in that it rarely occurred in other pulmonary diseases (such as pleuritis or pneumonia). Furthermore, Rhazes was one of the first to describe in detail tuberculosis of the joints [5, 6].

In the "Canon of Medicine" (*al-Qānūn fi al-Ṭibb*), Avicenna, known also as Ibn Sina, Abu Ali Sina or Pur Sina (born in Afshona, Uzbekistan, in 980 and dead in Hamadan, Iran, in 1037), dedicated two chapters to the description of tuberculosis, the fourth and the fifth of his medical encyclopedia addressing, respectively, the etiopathogenesis, the differential diagnosis and the pharmacological treatment and management of this communicable disorder. Avicenna maintained that pulmonary tuberculosis (*sil*) should be differentiated from other respiratory diseases, including pleuritis (*zaat al-janb*), and asthma (*rabv*), because all these disorders may clinically result, for different etiopathogenetic reasons, in cough and shortness of breath. However, tuberculosis is uniquely characterized by symptoms such as chronic fever that is more severe and relevant at night, sweating, sputum that may be bloody (hemoptysis) or contain plaster-like material (lithoptysis), dyspnea, and severe weakness, among others. Avicenna added that in advanced cases of pulmonary tuberculosis, a potential danger would be represented by the insurgence of lung hemorrhage, which may ultimately lead to death. Furthermore, from an etiopathogenetic standpoint, Avicenna believed that tuberculosis has three stages including i) pre-inflammatory, ii) ulcerative, and, finally, iii) cavernous stage. According to the author, some aggravating factors are seasonality (in particular, autumn), and eating garlic. Moreover, Avicenna listed 21 potentially beneficial herbs, including plantain (*Plantago ovata*), grey oak (*Quercus baloot*), almond (*Prunus amygdalus*), dried sponge, oligochaeta (*Volutarella divaricata*), and opium (*Papaver somniferum*).

In another famous Persian medical text, "*Zakhireh-ye Kharazmshahi*" (Treasure of Kharazm Shah), Ismail Jorjani (born in Urganj, Uzbekistan, in 1040 and dead in Chorasmia, Northeastern Iran, in 1136) claimed that tuberculosis was a contagious illness characterized by a rather prolonged and marked fever.

Modernity and the fight against tuberculosis in Iran

During the last decade of the Qajar dynastic period (1789-1925) [5], in 1921, the "Pasteur Institute of Iran" was established for the proper and effective control of tuberculosis. It represented "the most significant medical establishment partly endowed by *waqf*" (in Persian language, a Muslim religious/charitable foundation created by a trust fund) [5]. The first physician who visited tuberculosis patients in his private clinic facility was Dr. Siavash Shaghaghi, a physician trained in Switzerland and an authentic Iranian pioneer in the management and treatment of tuberculosis [6, 7].

Another prominent physician in the battle against tuberculosis was Dr. Masih Daneshvari (born in 1899 and dead in 1976), a pulmonologist that studied in various European countries, especially in France, and who, after a long period of training, returned to Iran in October 1934 and founded the first Iranian tuberculosis sanitarium, known as "Shah Abad Tuberculosis Patients' Hospital". This major healthcare facility, entirely devoted to the treatment of tuberculosis patients, was finally settled in 1937 due to his efforts. However, due to a shortage of healthcare staff, Daneshvari decided in 1939 to write a letter to the Prime Minister, in which he explained the urgent need to strengthen and considerably expand an ambitious tuberculosis control and mitigation program at the Shah Abad Tuberculosis Patients' Hospital. The Prime Minister was convinced by this letter and ordered the responsible authorities of the Ministries of Interior and of Health to provide support to him [6, 7].

Several medical doctors and directors of the Pasteur Institute of Iran have continued these efforts, achieving fundamental results in terms of vaccination coverage against tuberculosis as well as diagnosis and treatment of the disorder. Among these prominent and outstanding professional figures, Dr. Abolhassan Ziyā-Zarifi (born on 20 August 1926 and dead on 4 October 2010) undoubtedly represents the most famous one. He pursued his degree at the School of Pharmacy of Tehran University and he started his professional career in 1952 at the Health Ministry, to later join the academy. His research and clinical interests were mostly represented by communicable disorders, and, in particular, respiratory infectious diseases, including tuberculosis and legionnaires' disease or legionellosis. In 1956, he worked at the First tuberculosis diagnostic laboratory supervised by Dr. Mehdi Zolriassatian, and, later, he decided to go to England in order to strengthen his expertise in the field of the clinics of infectious diseases and microbiology. Once returned to Iran, he managed to settle the "National Reference tuberculosis Laboratory" in 1963. In the same year, Dr. Zia-Zari became a member of the "International Union against Tuberculosis and Lung Diseases" (IUTLD), of which later he was appointed Director. In 1968, Dr. Zia-Zari went abroad to continue his training at the Pasteur Institute of Paris and in 1971 he completed his studies on medical laboratory management at the University of Maryland as well as the Centers for Disease Control and Prevention (CDC) in the USA that had been recently founded in 1942. Between 1975 and 1979, Dr. Zia-Zari was appointed as the Director General of the Laboratories of the Ministry of Health and during these years with the support of the "World Health Organization" (WHO) he was able to establish more than 400 medical laboratories, including facilities in remote, rural, generally underserved regions of Iran, significantly expanding laboratory coverage.

Due to his strenuous efforts and major achievement, he was nominated as a consultant to the WHO in the Middle East, Asia and Africa. Furthermore, he wrote several pa-

pers and books on tuberculosis, including "Bacteriology of Tuberculosis" (1973), "A Short History of Robert Koch" (1984) and "History of Tuberculosis" (1984) [6, 7].

Tuberculosis in Iran: the current situation and future prospects

In Iran, tuberculosis still represents a public health concern, with an incidence rate on the rise, because of different factors, including immigration [8], poor economic-financial conditions, co-morbidities (such as diabetes and HIV/AIDS), high-risk behaviors and unhealthy lifestyles, like drug abuse and smoking [9].

Also the incidence of multidrug-resistant (MDR) tuberculosis is increasing [10, 11]. According to Jimma and coworkers [12], the overall pooled prevalence rate of MDR tuberculosis in Iran and neighboring countries (including Iraq, Turkey and Pakistan) was 16% (with a 95% confidence interval or CI of 11-20%). Having received a previous tuberculosis treatment, being aged less than 45 years and being males were significantly associated with an increased pooled risk of developing MDR tuberculosis with an odds-ratio, OR, of 2.01 [95% CI 1.65-2.36%].

Despite the efforts, tuberculosis and, in particular, MDR tuberculosis still represent a great public health concern in Iran. On the other hand, this country can capitalize on its millennial, incredibly rich story of major achievements in the battle against tuberculosis to develop and implement *ad hoc* public health programs for the control of the disorder, including targeted and specialized interventions.

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

MaB and NLB conceived the study, MaB and NLB drafted the manuscript, MM and MeB revised the manuscript. NLB performed a search of the literature. All authors critically revised the manuscript. All authors have read and approved the latest version of the manuscript.

References

[1] Barberis I, Bragazzi NL, Galluzzo L, Martini M. The history of tuberculosis: from the first historical records to the isolation of Koch's bacillus. J Prev Med Hyg 2017;58:E9-E12.

[2] Hamarneh S. Contributions of 'Ali al-Tabari to ninth-century Arabic culture. Folia Orient 1970;12:91-101.

[3] Ghaffari F, Naseri M, Asghari M, Naseri V. Abul- Hasan al-Tabari: a review of his views and works. Arch Iran Med 2014;17:299-301.

[4] Khan MS. Ali ibn Rabban at-tabari, a ninth century Arab physician, on the āyurveda. Indian J Hist Sci 1990;25:20-33.

[5] Ebrahimnejad H. Medicine in Iran, profession, practice and politics, 1800-1925. New York, USA: Palgrave Macmillan 2014.

[6] Fallah F, Abdolghafoorian H. The History of tuberculosis and Bacillus Calmette–Guérin vaccine in Iran, Arch Pediatr Infect Dis 2015; 3:e59840.

[7] Azizi MH, Bahadori M. A brief history of tuberculosis in Iran during the 19th and 20th centuries. Arch Iran Med 2011;14:215-9.

[8] Pourhossein B, Irani AD, Mostafavi E. Major infectious diseases affecting the Afghan immigrant population of Iran: a systematic review and meta-analysis. Epidemiol Health 2015;37:e2015002.

[9] Fadaee M, Rashedi J, Arabi S, Poor BM, Kafil HS, Pourostadi M, Kazemi A, Asgharzadeh M. Stopping of the downtrend of Tuberculosis in Iran, a systematic review of associated risk factors. Infect Disord Drug Targets 2018. https://doi.org/10.2174/1871526519666181228162837

[10] Nasiri MJ, Dabiri H, Darban-Sarokhalil D, Rezadehbashi M, Zamani S. Prevalence of drug-resistant tuberculosis in Iran: systematic review and meta-analysis. Am J Infect Control 2014;42:1212-8.

[11] Javad Nasiri M, Chirani AS, Amin M, Halabian R, Imani Fooladi AA. Isoniazid-resistant tuberculosis in Iran: a systematic review. Tuberculosis (Edinb) 2016;98:104-9.

[12] Jimma W, Ghazisaeedi M, Shahmoradi L, Abdurahman AA, Kalhori SRN, Nasehi M, Yazdi S, Safdari R. Prevalence of and risk factors for multidrug-resistant tuberculosis in Iran and its neighboring countries: systematic review and meta-analysis. Rev Soc Bras Med Trop 2017;50:287-295. https://doi.org/10.1590/0037-8682-0002-2017

Received on September 1, 2019. Accepted on October 24, 2019.

Correspondence: Nicola Luigi Bragazzi, Department of Mathematics and Statistics, Laboratory for Industrial and Applied Mathematics (LIAM), York University, Toronto, Canada - E-mail: bragazzi@yorku.ca

How to cite this article: Behzadifar M, Martini M, Behzadifar M, Bragazzi NL. Tuberculosis in Iran: a historical overview from al-Tabari, Rhazes, Avicenna and Jorjani to Abolhassan Ziyā-Zarifi. Old and new pioneers in the fight against tuberculosis: challenges, pitfalls and hopes. J Prev Med Hyg 2020;61(Suppl.1):E13-E15. https://doi.org/10.15167/2421-4248/jpmh2020.61.1s1.1384