


Original Article

Factors Affecting Delay in Diagnosis and Treatment of Pulmonary and Extra pulmonary Tuberculosis in Qom Province during the 2011-2017

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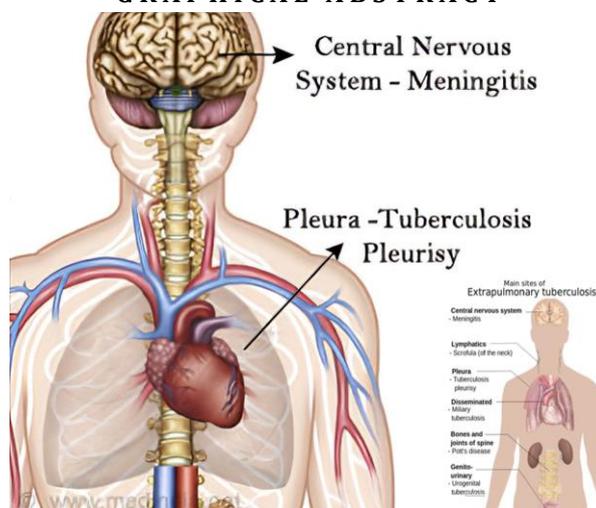
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ABSTRACT

According to the world health organization (WHO), approximately one-third of the world's population is infected with Mycobacterium tuberculosis and is at risk of contracting tuberculosis. About 9 million people are infected with active tuberculosis each year, and 3 million die from the disease. Early diagnosis and initiation of treatment at the beginning of tuberculosis play an essential role on controlling this disease. Delays in diagnosis and treatment may worsen the disease, increasing the risk of mortality, and transmission within the community. The aim of this study was to determine the factors affecting the delay in diagnosis and treatment of pulmonary and extra pulmonary tuberculosis in Qom province, Iran. This work was an observational cross-sectional observational study with available sampling. The findings were analyzed using SPSS software version 24. The results demonstrated that the mean time of diagnosis in Qom province was longer compared with that of the other similar studies. The mean time of delay in referring patients are to medical centers was only significantly related to gender (female) ($p = 0.8$). Non-Iranian nationality, negative smear, extra pulmonary tuberculosis, body mass index more than 25. Also it was found that, improving the knowledge of health center staff about the diagnosis and increasing the public awareness regarding the symptoms of tuberculosis can play a significant role in reducing the time of diagnosis and treatment of pulmonary and extra pulmonary tuberculosis.

GRAPHICAL ABSTRACT


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Introduction

Tuberculosis is the most common cause of death from single-agent infectious diseases in the world. Despite the advances in medical science, it is still a health problem in various countries [1]. Tuberculosis is a chronic infectious disease, most often caused by *Mycobacterium tuberculosis*, affecting the lungs; however, other parts of the body can also be infected [2].

This disease is one of the most important causes of mortality globally and is one of the oldest diseases affecting humans [3]. The prevalence of the infection has led the WHO to declare the disease a global emergency. It is estimated that one-third of the world's population is infected with tuberculosis and is at risk for tuberculosis. The incidence of tuberculosis in 2006 was estimated to be 10.4 million worldwide, and 1.7 million people died of tuberculosis in 2016 [4]. 56% of TB cases in the world are in five countries: India, Indonesia, China, Philippines and Pakistan [5-7]. Immigrants from these two countries to Iran remind us of the need to pay more attention to this disease [8]. The results of studies conducted in the country have shown that in 2016, the number of people infected with various forms of tuberculosis was 9118 people, which were 11.41 people per one hundred thousand people. The incidence of tuberculosis in Qom province in 1995 according to estimates was 13.08 per one hundred thousand people, which is higher than the average incidence of tuberculosis in the country. Tuberculosis is the most common cause of death from single-agent infectious diseases in the world and despite advances in medical science; it is still a health problem in various countries (8, 9). The causative agent of tuberculosis is the bacterium *Mycobacterium*, which usually enters the body in childhood. Over time, due to the weakening of the immune system, the bacilli multiply and cause a recurrence of the disease.

The disease ranks tenth in the global burden of disease and is projected to rise to seventh in 2020. According to the World Health Organization, in 2007 the total number of TB

patients was estimated at 13.7 million. Annually, about 9.3 million people are infected with tuberculosis and 1.7 million die from the disease [9].

According to the Ministry of Health, 14.4 out of 100,000 people in Iran are diagnosed with tuberculosis annually [10]. The incidence of extra pulmonary tuberculosis in Iran has decreased from 5.3% per thousand in 2001 (3382 cases) to 3.6 in 2007 (2604 cases) [11]. According to some reports, 75% of people with tuberculosis are in the age group of 15-45 years, i.e., economically active groups in society, and 95% of patients and 99% of deaths from tuberculosis belong to developing countries. Development [12-14]. The prevalence of tuberculosis in 2012 in the world was 122 per 100,000 populations and the prevalence of HIV infection among patients with tuberculosis in the world is estimated at 13%. At the same time, multidrug resistance, which is the result of poor management of tuberculosis treatment, has become a serious and growing problem in many countries of the world [15]. The total incidence of tuberculosis in 2012 in Iran was 14.4 per 100,000 populations and the incidence and rate of positive smear pulmonary tuberculosis in Iran in 2012 was 7.07 per 100,000 populations [16]. 98% of all TB cases and 98% of TB deaths occur in poor countries, and more than 70% of TB cases occur at productive ages. The most important clinical signs of pulmonary tuberculosis include cough and chronic sputum, weight loss, fever, anorexia, sweating, shortness of breath and chest pain, and the diagnosis is based on sputum smear examination [17].

In Iran, the incidence and prevalence of tuberculosis are not the same in all parts of the country, so that in the peripheral regions of the country such as Sistan and Baluchestan, Gilan, East and West Azerbaijan, Kurdistan, South Coast, and Khorasan has a high prevalence but low in central provinces is more common [18]. Iran was ranked 17th in the world in terms of tuberculosis in 1998. According to the studies conducted in the last report of the Center for Disease Management in 2005, the tuberculosis's total

incidence was 13.5 cases and 11.6 cases for Iranian patients per one percent of the population [19].

The risk of tuberculosis infection in each person depends on two factors: "exposure to infectious particles" and "susceptibility to infection". The risk is higher in a susceptible person in close and prolonged contact with a patient with sputum-positive pulmonary tuberculosis, while the risk of transmitting the infection from a sputum-negative pulmonary tuberculosis patient and from a patient with extra pulmonary tuberculosis is lower. It is also less.

It can affect most tissues and organs in the body, especially the lungs [20]. The chance of developing the disease is at an all-time high shortly after infection, with 50% of patients with pulmonary tuberculosis dying after receiving the disease if left untreated, up to 2% due to an immune defense. Strong recurrence spontaneously and 25% of them will remain with chronic infectious tuberculosis [21].

The more or less high annual incidence of tuberculosis and mortality has made it a major health problem in most developing countries of the world and, in addition to high medical costs, has a high risk of mortality and it is difficult to control [22]. The annual incidence of tuberculosis and the more or less high mortality rate has made it a major health problem in most developing countries of the world and in addition to high medical costs; it has a high risk of mortality and is difficult to control [23]. In Iran, especially in the eastern parts, there are fluctuations in the prevalence of tuberculosis due to the migration of Afghans from Afghanistan [24]. Sputum-positive pulmonary tuberculosis patient is the main cause of tuberculosis transmission in the community; untreated tuberculosis smear patient can infect 10 to 15 people annually.

Transmission occurs through a person's respiratory droplets

The prevalence of tuberculosis infection depends on the tubercle bacillus load in the individual's respiratory secretions, close contact with

patients, and the duration of antimicrobial treatment. According to standard definitions, a patient who has at least 2 positive sputum smear tests for TB bacilli, or a patient who has a positive sputum smear test with chest changes confirming pulmonary tuberculosis, or one positive smear with positive culture Have sputum, tuberculosis is considered positive. In patients receiving the TB mono therapy regimen, a sputum smear at the end of the attack phase (end of the second month) is performed as a rapid indicator of treatment success.

If the smear remains positive, another month is added to the attack phase. According to the National Tuberculosis Guidelines, the negative rate of sputum smear at the end of the attack phase for new positive smear cases and recurrence should be at least 85% and for re-treatment at least 80%. The WHO specifically aims at reducing the tuberculosis mortality by 90% and its incidence by 80% by 2030 compared to 2015. Delays in diagnosis and failure to start appropriate treatment may increase the spread of the disease, increasing its mortality and the emergence of refractory tuberculosis, and its costs and wastage. In this research study, we aimed to identify the factors affecting the delay in the diagnosis and treatment of pulmonary and extra pulmonary tuberculosis in Qom province during the years 2011 to 2017.

Material and methods

This study was an observational type of cross-sectional analysis and sampling was available. The study population consisted of all patients who referred to or were referred to health centers in the province for a period of six years.

The results of the present study were performed on 661 patients with tuberculosis during the mentioned years. All information was collected from the system of recording and analyzing data related to patients with tuberculosis of the Ministry of Health and Medical Education and related to Qom province. Then the questions that were not registered in this system were asked to the patients by phone. In this study, the diagnosis of pulmonary tuberculosis was given according to

the protocol of the World Health Organization, and during the studies performed on these patients, smear with sputum culture was positive or the pathology was consistent with tuberculosis. All people who had pulmonary and extra pulmonary tuberculosis in a certain period and AIDS patients and patients who did not have a contact number to complete the questionnaire were among the exclusion criteria. Finally, the data obtained from this study were analyzed by SPSS software version 24. Descriptive and inferential statistics were used for statistical analysis of data. In descriptive statistics, tables of

frequency distribution, percentage, mean, mean, standard deviation and plotting were used and in accordance with the research hypotheses and questions, T-test and ANOVA (with a significance level of less than 0.05) were used.

Result and Dissection

Table 1 demonstrates the relative and absolute frequency distributions of the variables of age, sex, marital status, place of residence, nationality, body mass index, smear result and type of tuberculosis in patients with tuberculosis.

Table 1: Distribution of relative and absolute frequencies of variables in patients with tuberculosis

Relative and absolute frequency distribution	subset	Variable
34.8 (230) % 31.5 (208)% 33.7 (223) %	Year <35 Year 35-60 Year >60	Age
43.9 (290) % 56.1 (371) %	Male female	Gender
20.9 (138)% 79.1 (523)%	Single Married	marital status
88.2 (583) % 11.8 (78)%	City Village	Address
52 (344)% 48(317)%	Iranian Non-Iranian	Nationality
85.8 (567)% 14.2 (94)%	kg/m ² < 25 kg/m ² > 25	BMI
77.8 (358) % 22.2 (102)%	Positive Negative	The result of the smear
69.9 (462)% 30.1 (199)%	Pulmonary tuberculosis Extra pulmonary tuberculosis	Type of tuberculosis

Variable in Table 1 shows the category in this study. As this table 1 shows, they describe that all categories are related to percentage.

As seen in Table 2, the mean delay time of patients referring to medical centers had a significant relationship only with gender (female) ($p = 0.8$) and this delay in rural patients, non-Iranian nationality, negative smear, tuberculosis. Extra pulmonary, body mass index was more than 25 and ages 60-35 years were higher. Delay

in diagnosis in patients with extra pulmonary tuberculosis, female patients, non-Iranian nationality, rural residents, age over 60 years and body mass index more than 25 and negative smear was longer and delay in treatment in patients with extra pulmonary tuberculosis. Female patients, patients with positive smear and rural residents were shorter and in patients aged 35-60 years, non-Iranian nationality, body mass index was more than 25 (Table 2).

Table 2: Comparison of mean delay in referral, diagnosis and treatment of TB patients based on demographic information

Delay in treatment		p-value	Delay in diagnosis		p-value	Delay in referral		p-value	subset	Component				
Standard deviation	Average		Standard deviation	Average		Standard deviation	Average							
3.028 6.66 2.90	1.41 1.97 1.56	P=0.41	52.64 53.9 58.48	52.1 52.4 57.7	P=0.4	27.29 27.29 26.09	26.6 28.6 28.2	P=0.7	Year <35 Year 35-60 Year >60	Age				
6.04 2.66	1.8 1.51		P=0.41	49.25 59.16		50.15 56.6	P=0.04		27.25 27.88		25.9 29.2	P=0.8	Male female	Gender
4.63 2.93	1.65 1.55			P=0.09		52.17 72.73			52.2 65.05		P=0.05		27.01 25.77	
2.92 5.68	1.43 1.85	P=0.22	52.25 58.06		52.6 55.02	P=0.57	25.06 28.51	25.42 30.3	P=0.018	Iranian Non-Iranian		Nationality		
2.84 9.6	1.5 2.46		P=0.05	53.62 63.22	52.8 59.6		P=0.25	27.29 27.29		26.8 28.6	P=0.43		kg/m ² < 25 kg/m ² >25	BMI
2.84 2.85	1.78 1.24	P=0.08		53.41 63.12	50.7 60.6	P=0.16		24.59 24.48	26.2 27.7	P=0.59		Positive Negative	The result of the smear	
2.84 6.9	1.66 1.57		P=0.8	55.67 53.80	53.15 55.20		P=0.65	24.59 31.38	26.5 30.7		P=0.03	Pulmonary tuberculosis Extrapulmonary tuberculosis		Type of tuberculosis

The mean time of diagnosis in Qom province was longer compared to other similar studies. According to the findings of this study, the delay in referring to medical centers for diagnosis is less in men than women. Also, in rural areas, patients with a diagnosis of extra pulmonary tuberculosis, patients with negative smear, patients with positive smear and patients with non-Iranian nationality are identified for a longer period of time than Iranian patients. It can be inferred that because women are less financially independent than men, rural people and people of non-Iranian nationality can be taken seriously due to low economic status and in patients with negative smear and in patients with extra pulmonary tuberculosis. He did not take the symptoms seriously. Delayed diagnosis in patients with extra pulmonary tuberculosis, female patients, non-Iranian nationality, rural residents, age over 60 years and body mass index more than 25 and negative smear was longer and delay in treatment in patients with extra pulmonary tuberculosis, Female patients, patients with positive smear and rural residents were shorter and in patients aged 35-60 years,

non-Iranian nationality, body mass index was more than 25.

Wondimu *et al.* [8] reported that people in Kenya, in urban areas were diagnosed 54% faster than in rural areas, and women were 63% more likely to be diagnosed later than men. They argued that as women are less financially independent than men and depend on men to see a doctor. Also there is a greater delay in their referrals and also a delay in diagnosis in rural areas due to less access to health care. Hence inadequate education, which is consistent with our study, except that access to health centers in our rural areas is possible. In addition the reason for the long delay in these patients in Iran can be attributed to the unfavorable economic situation and inadequate education.

In the present study, the delay in diagnosis in the age group of 35-60 years was more than the ages less than 35 and more than 60 years. The cause can also be attributed to work and marriage and less tendency to express the disease. In Egypt, Yemen, and Somalia, lower age groups are identified, but this difference was not statistically significant, which is consistent with our study.

According to the report of the WHO, the average delay in patient referral and diagnosis by our country's health system is 51 and 75 days, respectively, which is more than most countries in the EMRO region (29), which in our study, the average delay in the referral was 27.8 days and the mean time of diagnosis was 53.7 days and the mean time of starting treatment was 1.64 days. According to the study, the mean time of delay in referral was longer than the present study. Iran can be attributed to education and diagnosis. In a study by Zerbini on 243 patients with positive pulmonary tuberculosis, the overall mean delay was 92.1 days, with a patient delay of 58 days and a health system delay of 34.1 days. The most important risk factors associated with delay. These were: long distance from health centers and age over 50 years. In our study, the average delay of patients was 27.8 days, which is shorter than this study and there is a significant relationship between patients' delay with age and place of residence. There was no significant relationship and only a significant relationship with patients' gender.

A study in which Reza Talab et al. [24] reported a total delay of 99 + 44 days and a patient delay of 14 + 10 days. In this study, there was no relationship between age, gender, occupation, urban residence, nationality and literacy level with the rate of delay, the patient delay time in our study was longer than the above study, which can be argued that Insufficient education has been provided to the people about this disease in Qom province.

In the study of Sadegh Nejad et al. In Kurdistan, the total mean of each of the delay times in diagnosis, treatment delay and total delay time were 36.6 + 45.6, 22.2 + 16.8, and 1.7, respectively. +9/0, 64.2 + 46.2 days. The mean patient delay and total latency were lower in single individuals than in married individuals. The mean patient delay was lower in men than women. In this study, each of the latency was less and acceptable compared to other studies in Iran and other parts of the world.

In the findings of our study, the delay in diagnosis was long compared to this study and other findings of this study are consistent with it. In Habibzadeh's study, the delay in diagnosis in patients with negative smear was significant compared to patients with positive smear, and the highest time delay in the diagnosis of tuberculosis was related to the delay in patient's visit and the average delay in all cases of patients the onset of symptoms until treatment was 72.02 days and the mean delay in referral was 43.4 days and the mean delay in diagnosis from referral to diagnosis was 28.9 days. In our study, the mean latency of the patient was 27.7 days and the mean time of diagnosis was 53.7 days and the total latency was 82.5 days. The present study is part of a professional medical doctoral dissertation that has an ethics code from the ethics committee of the Islamic Azad University, Qom branch.

Conclusion

This research study found that, to improve the diagnosis and subsequent treatment of pulmonary and extra pulmonary tuberculosis; increasing the knowledge of health center staff. Also physicians in timely diagnosis of patients with tuberculosis retraining courses, increasing public awareness about the symptoms of tuberculosis, to identify factors related to delays in identifying patients, both individual and the health system is recommended. It is suggested that in other studies, influential variables such as socio-economic level, income and education be considered to reduce the limitations of the generalized findings.

Conflict of Interest

We have no conflicts of interest to disclose.

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