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Factors associated with patient and healthcare system delay in diagnosis and treatment of tuberculosis

Abolfazl Mozafari, Reza Kianifar

1 Department of Internal Medicine, School of Medicine, Islamic Azad University, Qom Branch, Qom, Iran

Original Article

Abstract

BACKGROUND: More than 90% of the worldwide tuberculosis (TB) cases and deaths arise in the developing world. Delay in the diagnosis and treatment of TB potentially extents and aggravates the infection in the public leading to increased risk of death. Identifying the delays in the diagnosis of TB is indispensable to the health system to prevent spread of the disease. The current study was conducted to identify the factors related to patients and health care systems which delay diagnosis and treatment of TB in Qom Province, Iran.

METHODS: A cross-sectional survey was conducted on 661 patients with TB registered in healthcare units of Qom during 7 years (April 2011 to March 2017). Data regarding the patients' demographic characteristics and clinical factors associated with diagnosis and treatment delay and total delay were analyzed using Student's t-test and one-way analysis of variance (ANOVA). Multivariate logistic regression was also employed to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) using SPSS software.

RESULTS: The means of patient, healthcare, treatment, and total delay were 27.7 days, 53.7 days, 1.64 days, and 82.5 days, respectively. Additionally, 550 (83.2%) cases had total delay. It was determined that inhabitance, nationality, and type of extrapulmonary TB were significantly associated with diagnosis delay ($P < 0.05$).

CONCLUSION: Diagnostic delay in this study was mainly due to healthcare systems' facilities. Modern and efficient facilities would contribute a lot to early diagnosis of TB and improve the quality of TB management.

KEYWORDS: Tuberculosis; Diagnosis; Treatment; Risk Factors; Delay

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Introduction

Tuberculosis (TB) is an infectious disease caused by the bacillus, Mycobacterium tuberculosis. It usually resides in the lungs (pulmonary TB), but can also be found in other organs (extrapulmonary TB). The disease is spread when patients with pulmonary TB expel the bacteria into the air. Unfortunately, a relatively small portion (5%-15%) of the infected people manifest clinical signs during their lifetime.[1]

Corresponding Author:
Abolfazl Mozafari; Department of Internal Medicine, School of Medicine, Islamic Azad University, Qom Branch, Qom, Iran
Email: a_mozafari@hotmail.com

TB is still a major public health concern; as evidence shows, it is one of the top 10 causes of death and the leading cause from a single infectious agent [above human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS)]. TB occurs in every part of the world. In 2018, the largest number of new TB cases occurred in the South-East Asian region, with 44% of new cases, followed by the African region, with 24% of new cases and the Western Pacific with 18%. Globally, 2450000 TB cases were recorded in 2018 and the infection rate was estimated to be 231000 per 100000 population. Multidrug-resistant TB (MDR-TB) remains a public health

crisis and a health security threat. World Health Organization (WHO) estimates that there were 484000 new cases with resistance to rifampicin – the most effective first-line drug. However, it is anticipating that more than one third of cases either went undiagnosed or unreported.[2] According to World Bank report, an annual prevalence of TB in Iran is 14 per 100000 population in 2018, but in Afghanistan and Pakistan, it is 189 and 270 per 100000 population, respectively.[3]

Early diagnosis and prompt active treatment is critical for TB control program. Delay in diagnosis eventuates in increased infection in the community and it is predicted that an untreated smear-positive patient can infect 10 contacts yearly and more than 20 throughout the natural history of the disease until death. Delay in TB diagnosis could also lead to a further progressive disease state at presentation which contributes to late squeal and total death.[4]

Farzianpour and Kooshad studied the status of TB control program based on the implementation of the directly observed treatment short-course (DOTS) strategy in Iran and found that successful treatment rate was increased to 84% (88% in Eastern Mediterranean region and 87% all over the world), but case detection rate was about 70% (63% in the region and 67% in world). Timely and accurate detection is important because identifying new cases of the infection and clinical disease is crucial for diminishing the load of disease and death.[5]

Several factors contribute to the delayed diagnosis of TB in various parts of the world. In low-prevalence countries, delay occurs mainly due to the fact that TB is not suspected, or the previous infrastructure for TB control is disintegrated. In high-prevalence countries, delays are usually long and can be attributed to both patients in seeking treatment, and physicians in establishing diagnosis.[6] A national survey conducted in Iran, in 2003, revealed that the median delay in diagnosis and treatment in patients with sputum-positive pulmonary TB was 92 days and the median patient and physician delays in diagnosis were 20 and 46 days, respectively.[7] The main determinants of delay include being part of specific patient groups such as men, old age, some professions and unemployment, low education, low income, rural versus urban residents, nationality, or the availability, cost, and long travel time/distance to health services.[8]

Considering that the delays in TB diagnosis and treatment may exert adverse effects on the wellbeing of the society, the current study was undertaken to assess the extent of delay in diagnosis and management of patients with TB and determine the major contributors to such delays (whether patient or health organizations). It is expected that the obtained information will assist with TB control program targets in Qom Province, Iran.

Methods

Study participants and data collection: This cross-sectional study was carried out in Qom City located in central Iran (34°38′24″N 50°52′35″E). Medical records of 1200 patients suffering from both pulmonary and extrapulmonary TB during a period of 7 years (April 2011 to March 2017) who referred to Tuberculosis and Leprosy Control Office of Communicable Disease Management Center were analyzed. All the obtained information was kept confidential. Pulmonary and extrapulmonary TB cases were defined according to WHO and Iran's national TB guideline.[9] Sputum smear was positivity graded by direct microscopic examination as a 1-9 bacilli, 1+, 2+, and 3+ scales. Smear-negative pulmonary TB was defined as a pulmonary TB case with negative sputum smears but growth positive in cultures and the patients who meet all of the four criteria stated as follows: at least two negative sputum smears, radiological findings consistent with radiologically active pulmonary TB, no response to a course of broad-spectrum

antibiotics, and a decision made by a clinician for the treatment with anti-TB medication.[10] Inclusion criteria were pulmonary and extrapulmonary TB and age over than 15 years old. Exclusion parameters were HIV-positive patients, intravenous (IV) drug abuser, previous history of gastric bypass surgery, end-stage renal disease, cancer, leukemia, and lymphoma, immunocompromised patients, and patients on oral corticosteroid or immunosuppressant drugs. Patients whose first symptom date, diagnosis date, or treatment date were unknown were considered as censored data. According to inclusion and exclusion criteria, finally 661 patients were inserted into study. The sociodemographic parameters including marital status (single, married), age, gender, nationality, residence (urban, rural), and body mass index (BMI) were also analyzed.

Data analysis: Descriptive statistics including mean or median with interquartile range (IQR) were used to present data. Comparisons between groups were made using the chi-square test or Fisher's exact test as appropriate for qualitative/categorical variables. Univariate analysis was done with Student's t-test and one-way analysis of variance (ANOVA) to find significant factors related to delay. Multivariate logistic regression was used to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for associations between patient delay > 2 weeks, health system delay > 2 weeks, treatment delay > 4 days, and total delay over than 30 days. All analyses were performed using SPSS software (version 20, IBM Corporation, Armonk, NY, USA) and P-value less than 0.05 was considered to be statistically significant. The study was initiated after the approval from the Ethics Review and Research Committee of Islamic Azad University, Qom Branch. Permission from the health authorities was also taken prior to the study (code of ethics: IRIAUTMU.REC.1398.019).

Results

Table 1 represents demographic characteristics of patients with TB included in the study. As can be seen, of the 661 patients with TB, 462 (69.9%) had pulmonary TB and 199 (30.1%) had extrapulmonary TB. Moreover, 77% (358) of the participants were smearing positive. The median age of cases was 48.1 years (IQR: 27-65) which 290 (43.9%) were men. Additionally, the majority of patients (85.8%) had normal weight (BMI < 25).

Univariate analysis of potential factors related to delay in diagnosis and mean corresponding patient, healthcare, treatment, and total delays are depicted in table 2.

Table 1. Demographic characteristics of patients with tuberculosis (TB)

Variable		n (%)	Variable		n (%)
Gender	Men	290 (43.9)	TB	Pulmonary	462 (69.9)
	Women	371 (56.1)		Extrapulmonary	199 (30.1)
Age (year)	< 35	230 (34.8)	Smear	Positive	358 (77.0)
	35-60	208 (31.5)		Negative	103 (23.0)
	> 60	223 (33.7)	Extrapulmonary	Pleural	51 (25.6)
BMI (kg/m^2)	< 25	567 (85.8)		Lymph node	44 (22.1)
	> 25	94 (14.2)		Genitourinary	33 (16.6)
Residence	Urban	583 (88.2)		Others	71 (27.0)
	Rural	78 (11.8)	Pulmonary	Smear positive	358 (77.0)
Nationality	Iranian	344 (52.0)		Smear negative	104 (23.0)
	Foreigner	317 (48.0)	Smear positive	1+	151 (42.1)
Marital status	Single	138 (20.9)		2+	74 (20.7)
	Married	452 (68.4)		3+	47 (13.1)
	Widow	71 (10.7)		1-9 bacilli	86 (24.1)

BMI: Body mass index; TB: Tuberculosis

Table 2. Univariate analysis of factors correlated to patient, healthcare, treatment, and total delay

Variable		Patient delay		Healthcare delay		Treatment delay		Total delay	
		Mean delay (day)	P	Mean delay (day)	P	Mean delay (day)	P	Mean delay (day)	P
Age (year)	< 35	26.6	0.700	51.0	0.910	1.4	0.880	78.6	0.480
	35-60	28.6		52.4		1.9		82.6	
	> 60	28.2		57.7		1.5		86.4	
Gender	Men	25.9	0.120	50.1	0.130	1.8	0.410	77.8	0.120
	Women	29.2		56.6		1.5		86.2	
BMI (kg/m^2)	< 25	27.4	0.430	52.8	0.260	1.5	0.540	81.1	0.180
	> 25	29.8		59.6		2.4		91.1	
Residence	Urban	27.4	0.320	52.2	0.050	1.6	0.860	80.5	0.045
	Rural	30.5		65.0		1.5		97.1	
Nationality	Iranian	25.4	0.018	52.6	0.310	1.4	0.220	79.4	0.220
	Foreigner	30.3		55.0		1.8		85.9	
Marital status	Single	28.6	0.200	45.6	0.150	1.3	0.590	75.1	0.300
	Married	26.7		55.8		1.6		83.8	
	Widow	32.6		56.6		1.9		89.2	
TB	Pulmonary	26.5	0.062	53.1	0.650	1.6	0.065	80.8	0.900
	Extrapulmonary	30.7		55.2		1.5		86.4	
Smear	Positive	26.2	0.280	50.7	0.110	1.7	0.086	78.6	0.210
	Negative	27.7		60.6		1.2		88.1	
Extrapulmonary	Pleural	22.5	0.110	38.1	0.021	2.4	0.600	63.2	0.019
	Lymph node	30.2		54.1		0.7		83.2	
	Genitourinary	38.5		73.1		1.0		19.8	
	Others	33.3		60.9		1.7		94.8	

BMI: Body mass index; TB: Tuberculosis

As indicated, the mean and median of patient delay were 27.7 and 20 days (IQR: 10-30), respectively, while these values for healthcare delay were 53.7 and 40 days (IQR: 22-60). Additionally, mean of treatment delay was calculated to be 1.64 days. Moreover, mean and median of 82.5 and 61 days (IQR: 38-91) were recorded for total delay. The obtained data also demonstrated that 411 (62.2%) of cases had patient delay, while 590 (89.3%), 58 (8.8%), and 550 (83.2%) patients had healthcare, treatment, and total delay, respectively.

Multivariate analysis of patients, healthcare, treatment, and total delay according to age, sex, nationality, and other parameters showed that there was a significant relationship between delay and some of these parameters (Table 3). As can be seen, extrapulmonary TB significantly influenced patient delay (P = 0.006), but healthcare delay was significantly influenced by pulmonary TB (P = 0.012).

Discussion

The delays in TB diagnosis and treatment can increase the disease burden and death in society. Therefore, it is of crucial importance to identify the origins of such delays. With this aspect, the current study was conducted to identify delays in diagnosis and treatment of TB in Qom Province. We studied patient delay and healthcare system delay as well as the associated factors. An important epidemiological challenge for TB control in Iran is inadequate and late case detection.[7] Understanding the factors that strengthen delays in accessing TB services as well as delays in in-time rapid diagnosis and management is important for effective control of the disease. Results of this study revealed that the median lengths of patient and health system delays in Qom were 20 and 40 days, respectively. Furthermore, prolonged delay was observed on the value of the 75th percentile of maximum median delay measurement which accounted for 30 days between patients and 60 days in the healthcare system.

Table 3. Multivariate analysis (logistic regression) of factors related with patient, healthcare, treatment, and total delay

Variable	Patient delay		Healthcare delay		Treatment delay		Total delay	
	Adjusted OR (95% CI)	P	Adjusted OR (95% CI)	P	Adjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Gender	0.80 (0.58-1.10)	0.180	1.60 (0.42-6.70)	0.450	0.39 (0.11-1.40)	0.150	0.75 (0.32-1.70)	0.500
Residence	0.81 (0.48-1.30)	0.440	1.50 (0.17-1.40)	0.690	0.73 (0.12-4.10)	0.720	1.90 (0.50-7.40)	0.330
Nationality	0.71 (0.50-1.00)	0.050	0.83 (0.20-3.30)	0.790	1.30 (0.37-4.90)	0.640	0.76 (0.33-1.70)	0.530
BMI	0.68 (0.42-1.10)	0.120	0.94 (0.80-1.10)	0.500	1.00 (0.93-1.20)	0.300	0.98 (0.88-1.00)	0.770
Age	1.00 (1.00-1.01)	0.050	1.00 (0.98-1.00)	0.210	0.95 (0.91-1.00)	0.050	1.00 (0.98-1.00)	0.370
Marital status	1.00 (0.68-1.70)	0.700	0.70 (0.12-3.90)	0.690	7.50 (1.10-48.00)	0.035	0.78 (0.27-2.20)	0.650
Smear	0.62 (0.39-1.00)	0.050	0.67 (0.32-1.30)	0.270	0.96 (0.46-2.00)	0.920	0.90 (0.49-1.60)	0.740
Pulmonary TB	1.10 (0.80-1.60)	0.450	2.20 (1.10-4.30)	0.012	0.71 (0.38-1.30)	0.300	0.97 (0.62-1.50)	0.800
Extrapulmonary TB	1.40 (1.10-1.80)	0.006	1.70 (0.96-3.00)	0.067	1.20 (0.75-2.00)	0.380	1.30 (0.96-1.80)	0.080

BMI: Body mass index; TB: Tuberculosis

In addition, global mean delay accounts for 62.2% of patient delay and 89.3% of health system delay. It can be concluded that both patient and healthcare system associated reasons influence diagnostic delays. Nearly similar distribution of delays between patients and health system has previously been reported.[11] Getnet et al. have claimed that following patient and healthcare delays in low-income countries, the median diagnostic delay has been increased from 30 to 366.5 days, through a 4-199 days and 2-128.5 days, respectively. This meta-analysis indicated that 42% of patients with pulmonary TB delayed looking for care at least one month; uneducated patients (OR = 1.5) and those who required initial care from informal providers had more odds of patient delay (OR = 3).[11] However, differences among our and previous studies may be attributed to inconsistent recording of data or different levels of socioeconomic status (SES).

Our study indicated that rural inhabitance, nationality (foreigner), type of involvement (pulmonary or extrapulmonary), and site of extrapulmonary TB were factors associated with both patient and healthcare delays. In a study done by Li et al., it was noticed that living in rural areas was a risk factor for patient delays [OR (95% CI): 1.79 (1.62-1.98)] and diagnostic delays [OR (95% CI): 1.40 (1.23-1.59)]. Moreover, female patients had higher risk of patient delay [OR (95% CI): 1.94 (1.13-3.33)]. Low educational attainment (primary school and below) was also a risk factor for patient delay.[12]

Reasons for patient delay have been claimed to be complex and the described causes include: diverse level of health information, patients' poor knowledge and awareness of TB symptoms and the need for prompt consultation with healthcare services for diagnosis and treatment, or differences in access to healthcare.[13] Furthermore, patients who suffered from chronic cough, pulmonary comorbidity, and mild to severe illness and extrapulmonary TB intentionally postponed looking for care. Perhaps, this is due to the fact that patients with such type of symptoms may be suspicious to other common respiratory and none-respiratory diseases which are not considered serious. Nevertheless, the existence of hemoptysis, chest pain, and multiple symptoms decreases the possibility of patient delay.

We observed that people with older age were more likely to experience patient delays compared to younger ones. Older persons were less likely to pursue for a doctor or healthcare provider contrary to young people who usually have minor respiratory complaints, cough, hemoptysis, and classic constitutional symptoms. In addition, TB diagnosis in older individuals probably is more difficult. One of the probable explanations can be that in the elderly, respiratory problems such as cough are less pronounced, which makes it difficult to get samples and bacilli isolation, leading to prolonged diagnosis. Another reason is higher incidence of diseases like pneumonia, asthma, bronchitis, and lung cancer, in addition to TB, in old people, which increases the probability of diagnostic errors due to low suspicion of TB in these patients.[14] Consistent with our results, Lee et al. have found that older age, comorbidities, and not undergoing rapid molecular diagnostic tests are independently associated with longer treatment delays.[15]

Contrary to our research which showed that there was an insignificant relationship between the sex and patient delay, Saldana et al. have reported that the delay is more common among women than men probably due to fear of diagnosis and treatment as well as social influence on health decision making that might differ through cultures and countries.[16] In another study, men postponed care-seeking longer than women probably because of distress of cost of diagnosis and

management or perhaps men were more likely to neglect symptoms longer until the symptoms were aggravated.[17]

In this study, the period from patients' initial reference to public health services to definite diagnosis is unfortunately long (53.7 days) and approximately twice higher than patient delay which meaningfully contributes to total diagnostic delay. Similar findings have been reported in other countries such as Ethiopia, Uganda, and Pakistan in which median healthcare system delay varies from 61 to 87 days, however, longer than that of report from Nigeria.[18] This variation can probably be secondary to the difference in the definition of healthcare system delay. Some projects defined it as the duration between diagnosis and beginning of TB management. In addition, in spite of TB control programs' recommendation that diagnosis should be made at the primary health care level, most patients are still diagnosed in private clinics and hospitals, especially general hospitals which probably are not well equipped for TB diagnosis.[19,20]

The cross-sectional nature of this study may have potentially influenced our results, mainly due to extensive range of confounding factors. Even though the study has tightly been controlled for confounding factors in the multiple logistic regression models, we could not omit the effect of residual factor. Additionally, some patients could not remember the exact information of manifesting symptoms. One of the most important advantages of our study was that the participants were representative of the population who really had TB, because all the treated patients were registered at one TB reference center in Qom City. The identified risk factors should be further explored and specific strategies aimed at addressing these issues to decrease patient and health system delays should be covered in future studies.

Conclusion

Taking together, it was found that the mean total delay was almost 3 months mainly depending on healthcare delay (two months). To decrease patient delay, strategies aimed at promoting timely seeking for appropriate medical consultation among presumptive TB patients should be adopted. More efforts should be made on building effective collaboration between the national TB control program and the private sector, often the recipient of the first health-seeking action of the community, to decrease delays related to healthcare system.

Conflict of Interests

Authors have no conflict of interests.

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