

RESEARCH ARTICLE

Delay in diagnosis of Pulmonary Tuberculosis: Study of factors related to patients and health care system

Usman Ali¹, Usama Bin Zubair², Asma Ambreen³, Husnain Yousaf⁴, Fatima Kaleem⁵, Kanwal Fatima Khalil⁶

¹Department of Oncology, Fauji Foundation Hospital, Rawalpindi, Pakistan

²Department of Psychiatry Pakistan Institute of Medical Sciences, Islamabad, Pakistan

³Department of Medicine, Foundation University Medical College, Islamabad, Pakistan

⁴MBBS, Department of Cardiology, Armed Forces Institute of Cardiology, Rawalpindi, Pakistan

⁵Department of Microbiology, Foundation University Medical College, Islamabad, Pakistan

⁶Department of Pulmonology, Foundation University Medical College, Islamabad, Pakistan

ABSTRACT

Objective: To find factors related with delayed diagnosis of pulmonary tuberculosis in patients presenting to the hospitals of Rawalpindi.

Methods: A cross sectional observation study was carried out in Benazir Bhutto Hospital, District head quarter Hospital, Fauji Foundation Hospital, Military Hospital and Holy Family Hospital, Rawalpindi from February 2016 to September 2016. A total of one hundred ninety patients of pulmonary tuberculosis were interviewed through convenient sampling by a formulated questionnaire.

Results: Mean total delay was 114.48 days whereas median total delay was 53.5 days. Mean patient delay was 33.25 days and mean health care delay was 81.23 days. On multivariate analysis unemployment was associated with patients delay whereas healthcare delay was associated with smear negative TB and patients self-realization that there is delay in diagnosis.

Conclusion: This study shows that there is a long delay in the diagnosis of pulmonary tuberculosis in our country. Unemployment is main factor related to patient delay. Improving TB knowledge and socio-economic status of individuals may help in the earlier diagnosis. Adequate training of healthcare workers in diagnosing smear negative TB and improvement in health care services may also help to reduce the long healthcare delays. *J Microbiol Infect Dis* 2017; 7(3):119-124

Keywords: delay; diagnosis; pulmonary tuberculosis

INTRODUCTION

Tuberculosis is a major health problem worldwide. TB is the second most common cause of infection related deaths in human beings, preceded only by Human Immunodeficiency Virus (HIV) infections [1]. Despite the exhaustive strategies of World health organization for controlling this disease, millions of people is still infected annually [2]. It is estimated by WHO that 9.6 million people fell ill with tuberculosis in 2014 but only 6 million out of them reported to WHO during this time, anticipating that the other 37% cases either went undiagnosed or unreported [2]. Early diagnosis of tuberculosis can reduce the mortality

associated with this disease [3]. Whereas delayed diagnosis, is not only associated with increased mortality but also with the increased risk of transmission of disease to the non-infected individuals [4].

According to a survey conducted in 2015, Pakistan ranks fifth amongst the TB high-burden countries worldwide [5]. World Bank reports an annual prevalence of tuberculosis in Pakistan to be 270 per 100,000 population in 2014. This is more than its neighboring countries; India, Iran and Afghanistan where prevalence is 167, 22 and 189 per 100,000 population respectively [6]. After the introduction of National Tuberculosis control program in Pakistan, the treatment

Correspondence: Usman Ali, House Officer, Fauji Foundation Hospital, Rawalpindi, Pakistan, Email: ali.osmani0987@gmail.com

Received: 04 February 2017 Accepted: 25 June 2017

Copyright © JMID / Journal of Microbiology and Infectious Diseases 2017, All rights reserved

success rate is 91% but case detection rate is 63%, much lower than 70% recommended by the WHO [5]. In fact most of low case detection in Eastern Mediterranean region is contributed by Pakistan and Afghanistan [7].

Various factors have been noted that contribute to the delayed diagnosis of this chronic infection in various parts of the world. These factors include place of residence of the patient, level of education, waiting time of patients at health care facility, place of consultation etc.[8]. A study conducted previously in Rawalpindi has concluded that age and profession of the subjects contribute to the delayed diagnosis of Tuberculosis [9]. In a study conducted in Karachi living in suburbs, lack of trust on low-cost services, diagnosis in health facilities not belonging to the National TB program, visiting many health care providers before diagnosis, inadequate knowledge regarding the disease and poor satisfaction with care were factors related to high total delay in diagnosis [7].

The current study is carried out at five tertiary care hospitals of Rawalpindi to assess the factors related to patients or health care system which cause delayed diagnosis of this deadly but treatable disease.

METHODS

After Ethical approval from Ethics Review and Research Committee (ERC), Foundation University Medical College this cross-sectional study was carried out from February 2016 to September 2016. A total one hundred and ninety cases of pulmonary tuberculosis were interviewed by convenient sampling at five tertiary care hospitals of public sector namely; Benazir Bhutto Hospital, District head quarter Hospital, Fauji Foundation Hospital, Military Hospital and Holy Family Hospital.

Patients of pulmonary tuberculosis of both genders with age above 15 years with or without extra-pulmonary tuberculosis under anti-tubercular chemotherapy were included in the study. Non-consenting patients, Immuno-compromised patients, patients on immuno-suppressant drugs, patient undergoing cancer chemotherapy or radiotherapy and patients with asthma or COPD were excluded from the study. Patients who were receiving anti-tubercular

therapy after relapse of tuberculosis or treatment failure were also excluded from study.

A structured questionnaire in the national language was made after detailed literature review including the World Health Organization report of 2003-2004 on factors contributing to delayed diagnosis of tuberculosis in Eastern Mediterranean region. The questionnaire covered socio-demographic aspects, knowledge about tuberculosis of patients and various factors speculated to cause the delay in diagnosis. All interviewers were briefed and trained before the data collection to streamline the process.

To assess the duration of delay from onset of symptoms to the diagnosis of TB, total delay was broken down in two categories. Patients delay was defined as the time (in days) after onset of symptoms to the first encounter with any health care provider. Health system delay is taken as time lapsed (in days) after the encounter with health care facility to the diagnosis of tuberculosis. Patient's records were checked. If records were not available, delays were directly asked from the patient. To minimize the recall bias, patients were asked these questions at least twice [8].

Data obtained from the patients was compiled using the statistical software for social sciences version 21. Age, gender, occupation, education, marital status, monthly income, residence, knowledge about TB, perception about TB, BCG vaccination, treatment before diagnosis, first healthcare facility visited after onset of symptoms, no. of encounters with healthcare facility before diagnosis, self-realization of patient about delayed diagnosis, being dependent on family members for visiting healthcare facility, transportation issue to healthcare facility, financial problems of patients, thinking that disease will go on its own, familiarity with symptoms of TB, active smoking, place of diagnosis and smear status were considered as potential factors associated with delayed diagnosis. Univariate analysis was done with chi-square test to find significant factors related with delay. To test the independence of the factors related with more than mean patient and healthcare delay in diagnosis for TB, the significant variables on univariate analysis ($p < 0.05$) were entered into a multivariate logistic

regression model with backward selection of independent variables.

RESULTS

Out of total one hundred and ninety subjects 41.1% were males and 58.9% were females. Patients delay and healthcare delay was assessed. Mean total delay was 114.48 days whereas median total delay was 53.5 days. Mean patient delay was 33.25 days and mean health care delay was 81.23 days. Univariate analysis of potential factors related to delay in diagnosis and mean corresponding patient and healthcare delay is given in Table 1. Illiteracy, unemployment, rural residence, no knowledge of TB and smear negative status was some of the factors related with delayed diagnosis. On multivariate analysis unemployment was related to significant patients delay in diagnosis whereas less no. of encounters with healthcare facility, smear negative TB and patients self-realization about delayed diagnosis was related to healthcare delay (Table 2).

DISCUSSION

Pakistan is a middle-income country with a high prevalence of tuberculosis [6]. Our study aimed at finding the factors associated with the delayed diagnosis of this deadly but curable disease in a cosmopolitan city of Pakistan with numerous public and private sector tertiary care hospitals. Previously a similar study was conducted in Rawalpindi but it was limited to the patients presenting in National Tuberculosis Centre, so we planned this study in five tertiary care hospitals of the city to broaden the spectrum of patients and reduce the bias. A total median delay of 56 days was reported in a local study done in recent past, which is consistent with our findings [9]. Delays in the diagnosis of TB are quite less in other populations of the world. An African study showed the mean and median delay of 45 days and 100.43 days respectively [8]. Another similar study from our neighboring country China had reported much shorter median delay of 36 days [10].

Mean patients delay and median patient delay was 33.25 and 14 days respectively. This is consistent with the findings of Lusignani et al, who reported a 30-day mean patient delay [8]. A recent study from Zimbabwe has also shown

similar results [11]. Another similar study from low and middle income countries also supported our findings [12]. Illiteracy, unemployment, income less than 20, 000 PKR, less knowledge of TB, visiting traditional medical centers, more number of encounters with healthcare workers, transportation and financial issues were the factors associated with the patients delay. This association is also in accordance with a recently published literature review [13]. However, in our study negative sputum smear was associated with more delay than the positive smear as opposed to findings of Cai et al [13]. Female gender was not significantly associated with more delay as opposed to findings reported in a recent Chinese study [14]. Female gender and urban residence was also associated with much longer delay in a study on smear positive TB patients from Iran [15]. Mean health care delay and median health care delay was 81.23 and 31 days respectively. The median delay reported in a study done in Ethiopia was 33.5 days [16]. Among low and middle-income countries Pakistan has the longest healthcare delay of 87 days in the diagnosis of TB [12]. The average delay in low and middle-income countries is much less i.e. 28.4 days [12]. This signifies the lapse of poor health care system, which instead of doing good to the patient adds to the delay in diagnosis. This may lead to the increase in burden of disease, cost of treatment and poor prognosis due to complications of the delayed diagnosis and treatment. Less no. of encounters with healthcare facility and self-realization of delay were related to delay in diagnosis on multivariate analysis. Smear negative TB was also related longer delay in diagnosis. This may be attributed to ignorance of disease by healthcare professional, looking for alternative diagnosis or time taken in running more investigations like bronchoscopy and gene Xpert to reach diagnosis [17,18].

The major limitation of our study is that it was not a prospective study so we cannot hypothesize that delayed diagnosis was really the consequence of the factors found significant in the study. The sample size and use of self-administered questionnaires pose methodological issues as well. The findings cannot be generalized as this was not a population based study.

Table 1. Univariate analysis of potential factors related to delay in diagnosis and mean corresponding patient and healthcare delay (n=190).

Variables	Frequency (%)	Patient delay		Healthcare delay	
		Mean delay (days)	p-value	Mean delay (days)	p-value
Age					
15-29	75 (39.5%)	23.49	0.515	73.55	0.531
30-39	32 (16.8%)	28.44		92.09	
40-49	25 (13.2%)	19.12		67.76	
50-59	32 (16.8%)	65.63		98.13	
Above 60	26 (13.7%)	41.08		82.15	
Male	78 (41.1%)	29.47	0.233	85.36	0.166
Married	111 (58.4%)	40.93	0.537	83.79	0.503
Illiterate	60 (31.6%)	43.48	0.020	90.52	0.024
Un-employed	114 (60%)	20.47	0.030	84.12	0.111
Low income (less than 20,000PKR)	162 (85.3%)	33.61	0.077	82.6	0.044
Rural residence	162 (85.3%)	19.73	0.200	96.9	0.727
No knowledge about TB	90 (47.4%)	27.49	0.005	102.17	0.02
Not considering TB a serious ailment	50 (26.3%)	30.60	0.738	83.9	0.748
Not BCG vaccinated	95 (50%)	82.98	0.037	39.81	0.142
Treatment before diagnosis of TB	162 (85.3%)	33.25	0.247	84.59	0.104
First healthcare facility visited on onset of symptoms					
Traditional Medicine	17 (8.9%)	31.42	0.000	120.25	0.006
General physician	74 (38.9%)	40.92		118.32	
Tertiary care hospital or Pulmonologist	99 (52.1%)	28.09		49.70	
No. of encounter with healthcare facility before diagnosis					
1	38 (20%)	28.29	0.000	29	0.000
2	70 (36.8%)	20.29		50	
3	34 (17.8%)	28.56		59	
4	10 (5.26%)	33.80		126	
5	10 (5.26%)	28.70		95	
6	5 (2.63%)	67.4		150	
More than 6	22 (11.5%)	85.27		203	
Self-realization of patient that there is a delay in diagnosis	96 (50.5%)	42.46	0.000	124.26	0.00
Being dependent on family member for visiting health care facility	123 (64.5%)	37.42	0.70	94.62	0.305
Transport issue in visiting healthcare facility	95 (50%)	31.82	0.18	104.39	0.10
Financial issues that intervenes in treatment	123 (64.7%)	28.53	0.012	94.04	0.011
Busy occupational life intervenes in consulting healthcare facility	115 (60.5%)	26.01	0.789	84.50	0.835
Perception that disease was of lesser intensity	74 (39.8%)	31.49	0.757	89.94	0.588
Thinking that disease will go on its own	69 (36.3%)	25.02	0.592	66.06	0.492
Not familiar with symptoms of TB	115 (60.5%)	37.11	0.237	89.89	0.082
Active smokers	43 (23.3%)	32.57	0.086	45.93	0.122
Place of diagnosis					
Specialist	27 (14.2%)	12.85	0.006	88.63	0.017
General physician	11 (5.8%)	23.18		65.82	
Rural and basic health care units	5 (2.6%)	13		68.0	
Tertiary care hospitals	147 (77.4%)	38.44		81.47	
Smear negative TB	66 (34.7%)	45.75	0.005	138.0	0.021

Table 2. Multivariate analysis (logistic regression) of factors associated with patient and healthcare delay (n=190).

Variables	Patient delay		Healthcare delay	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Illiteracy	0.707(.264-1.896)	0.491	0.896(.349-2.302)	0.894
Unemployed	2.43(1.115-5.311)	0.026	-	-
No knowledge about TB	0.844(.367-2.111)	0.717	0.650(.241-1.753)	0.395
Not BCG vaccinated	1.079(.391-2.978)	0.884	-	-
First healthcare facility visited after onset of symptoms	2.068(.919-4.654)	0.079	2.011(.938-4.341)	0.072
More no. of encounters with healthcare facility before diagnosis	0.422(.090-1.976)	0.345	0.016(.2-2.104)	0.001
Self-realization of patient that there is a delay in diagnosis	0.607(.225-1.636)	0.324	0.189(.58-.620)	0.006
Financial issues that intervenes in treatment	2.394(.977-5.853)	0.56	0.508(.175-1.471)	0.212
Place of diagnosis	0.026(.291-1.343)	0.225	2(.882-4.842)	0.0924
Smear negative TB	0.668(.307-1.454)	0.309	4.192(1.916-9.171)	0.000

A specific group of patients in five tertiary care hospitals were targeted instead of a randomized sample of all TB patients at various hospitals of Pakistan. We suggest further studies on a broader based and a more representative sample size using standardized tools in subsequent studies on the subject.

Conclusion: This study shows that there is a long delay in the diagnosis of pulmonary tuberculosis in our country. Unemployment is main factor related to patient delay. Improving TB knowledge and socio-economic status of individuals may help in the earlier diagnosis. Adequate training of healthcare workers in diagnosing smear negative TB and improvement in health care services may also help to reduce the long healthcare delays.

ACKNOWLEDGMENTS

The authors thank the department of Community Medicine, Foundation University Medical College, Islamabad for supporting this study.

Conflict of interest: The authors declare no personal or financial conflict of interest.

Funding disclosure: Non to declare

REFERENCES

1. WHO fact sheet Tuberculosis :2014.
2. Global Tuberculosis report 2015.
3. Keeler E, Perkins MD, Small P, et al. Reducing the global burden of tuberculosis: the contribution of improved diagnostics; Nature 2006; Suppl 1:49-57.
4. Golub JE, Bur S, Cronin WA, et al. Delayed tuberculosis diagnosis and tuberculosis transmission. *Int J Tuberc Lung Dis* 2006; 10:24-30.
5. WHO Regional Office for Eastern Mediterranean, Available at <http://www.emro.who.int/pak/programmes/stop-tuberculosis.html>
6. World Bank Indicators, <http://data.worldbank.org/indicator/SH.TBS.INCD/countries> accessed: 2 Jan 2016.
7. Bassili A, Seita A, Baghdadi S, et al. Diagnostic and treatment delay in tuberculosis in 7 countries of the Eastern Mediterranean Region. *Infect Dis Clin Pract* 2008; 16:23-35.
8. Lusignani L, Quaglio G, Atzori A, et al. Factors associated with patient and health care system delay in diagnosis for tuberculosis in the province of Luanda, Angola. *BMC Infect Dis* 2013; 13:168.
9. Saqib MA, Awan IN, Rizvi SK, et al. Delay in diagnosis of tuberculosis in Rawalpindi, Pakistan. *BMC Res Notes*. 2011; 4:165.
10. Meyssonier V, Li X, Shen X, et al. Factors associated with delayed tuberculosis diagnosis in China. *Eur J Public Health* 2013; 23(2):253-257.
11. Takarinda KC, Harries AD, Nyathi B, et al. Tuberculosis treatment delays and associated factors within the Zimbabwe national tuberculosis programme. *BMC Public Health* 2015; 15:29.
12. Sreeramareddy CT, Panduru KV, Menten J, Van den Ende J. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. *BMC Infect Dis* 2009; 9:91.
13. Cai J, Wang X, Ma A, Wang Q, Han X, Li Y. Factors associated with patient and provider delays for tuberculosis diagnosis and treatment in

- Asia: a systematic review and meta-analysis. *PLoS One* 2015; 10: e0120088.
- 14: Li Y, Ehiri J, Tang S, et al. Factors associated with patient, and diagnostic delays in Chinese TB patients: a systematic review and meta-analysis. *BMC Med.* 2013; 11:156. doi: 10.1186/1741-7015-11-156.
- 15: Nasehi M, Hassanzadeh J, Rezaianzadeh A, Zeigami B, Tabatabaee H, Ghaderi E. Diagnosis delay in smear positive tuberculosis patients. *J Res Med Sci* 2012; 17:1001-1004.
- 16: Belay M, Bjune G, Ameni G, Abebe F. Diagnostic and treatment delay among Tuberculosis patients in Afar Region, Ethiopia: a cross-sectional study. *BMC Public Health* 2012; 12:369.
- 17: Bachh AA, Gupta R, Haq I, Varudkar HG. Diagnosing sputum/smear-negative pulmonary tuberculosis: Does fibre-optic bronchoscopy play a significant role? *Lung India* 2010; 27(2): 58-62.
- 18: Lombardi G, Di Gregori V, Girometti N, Tadolini M, Bisognin F, Dal Monte P. Diagnosis of smear-negative tuberculosis is greatly improved by Xpert MTB/RIF. *PLoS One* 2017; 12(4):e0176186.