



The Egyptian Society of Chest Diseases and Tuberculosis
Egyptian Journal of Chest Diseases and Tuberculosis

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Determinants of delay in tuberculosis diagnosis in Hamadan province, 2006–2014



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Received 31 May 2016; accepted 26 June 2016

Available online 14 July 2016

KEYWORDS

Tuberculosis;
Delayed diagnosis;
Iran

Abstract *Introduction:* Identifying factors that delay diagnosis of tuberculosis (TB) are important for the health system when timely patient treatment and reducing TB transmission are desirable goals. Aim of this study was to investigate the prognostic factors that delay TB diagnosis.

Material and methods: This retrospective cohort study used National TB Program (NTP) data from 1056 TB patients during 2006–2014 in Hamadan province, western Iran. The Cox regression model was performed to determine associations between baseline explanatory variables and survival outcome with Hazard Ratio HRs (95% CIs).

Results: N (%) of delay in TB diagnosis more than 90 days was significantly higher in male patients, new case patients and pulmonary positive cases. After adjustment for covariates, HR (95% CI) in relapsed TB compared to new cases was 0.67 (0.53, 0.85) and these figures for positive pulmonary cases and extra pulmonary cases in compared to negative pulmonary cases were 0.80 (0.68, 0.94) and 0.84 (0.73, 0.98) respectively.

Conclusion: A high proportion of patients had delays in diagnosis exceeding three months. Our findings suggest that male gender, new cases, positive and extra pulmonary cases might increase the risk for delayed diagnosis among TB patients.

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

<http://dx.doi.org/10.1016/j.ejcdt.2016.06.003>

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Introduction

Tuberculosis (TB) is known as a global public health problem accounting 9.4 million incident cases and 1.4 million deaths in 2012 [1]. Many factors including HIV epidemics, population growth, socio-economic changes and emergence of resistant new strains of *Mycobacterium Tuberculosis* (such as *W* and *Beijing*) lead to re-emerging of TB. In 1993, due to the steady increase in TB cases WHO declared a state of global emergency for TB and called it as a global enemy in addition to HIV and malaria [2].

The main goal of TB control programs is to arrest the transmission within the community. An effective TB control program requires early diagnosis and immediate initiation of treatment. Delay in diagnosis in individuals and community plays a crucial role in terms of disease prognosis and disease transmission respectively [3].

Delay in the diagnosis and treatment of pulmonary tuberculosis results in increasing severity, mortality, and transmission of TB. Most transmissions occurs when the appearance of cough in initiation of treatment. A published study reported that patients become more contagious as the delay progresses. In other words, the longest delays are associated with the highest bacillary numbers in sputum smears. On the other hand, patients with delay in TB diagnosis are more likely to develop pneumonia, other respiratory infections, and mortality in emergency departments [4].

A systematic review on delay in TB diagnosis is shown regardless of low or high endemic settings, a range of 60–90 days for total delay in TB diagnosis [5]. Eastern Mediterranean region of WHO (EMRO) also reported that the highest time between onset of symptoms and disease diagnosis in Iran was 127 days in 2006 [6]. Moreover, one other study argued that the main cause of delay in TB patients in Iran is health-care system oriented. In other words, the main delay was the time taken by physicians to diagnose symptomatic patients [7]. It suggested that the reasons for delay in diagnosis embedded in cultural or educational deficiencies. However, postponed treatment initiation is rooted in the ability of the national program of TB control in establishment of technical and therapeutic facilities and providing the efficient control system in a given country [7].

Delay in the diagnosis and treatment of TB patients will result in spreading of infection in the community, increase in severity of the disease and also a higher risk of mortality. Therefore understanding the factors causing delay between TB symptoms and therapy initiation is crucial to combatting against the increasing TB epidemic, and to help healthcare system in designing and implementing TB control programs. Thus, aim of the present study is to determine the prognostic factors that delay TB diagnosis.

Material and methods

This retrospective cohort study was conducted involving 1056 TB patients in Hamadan province, western Iran, from 2006 to 2014. The cohort involved all registered TB patients with smear-positive, smear-negative or extra pulmonary. TB cases were defined according to WHO and Iran's national TB guidelines [8]. To reach a homogenous sample and generalize results to Iranian population, records of Afghan

immigrants, patients with probable diagnosis of TB and non-native born citizens were excluded.

Data were extracted from the National TB Program (NTP) as follow: background *characteristics* (gender, age, time of diagnosis, source of reporting, *place of residence* (urban and rural), and *type of TB*. Survival time was defined by symptom onset until diagnosis. Delay time was categorized into less than 30 days, 31–90 days, and more than 90 days (which was hypothesized as problem oriented delay).

The Log-rank test was used for comparison of survival curves. The Kaplan–Meier curves were tested under the null hypothesis that there is no significant difference between median of delay times. Null hypothesis is tested by Log-rank test. The Cox regression model was used to evaluation simultaneous effects of prognostic variables on survival outcome. Proportionality of hazards was tested using the *Schoenfeld* test and graphical schemes. *P*-value ≤ 0.05 was considered a significant level for all mentioned statistical tests. All analyses were conducted in Stata software version 11 ((StataCorp, College Station, TX, USA).

Results

Of the 1056 cases, N (%) of male and urban residence were 519 (49) and 649 (61) respectively. Table 1 shows the baseline characteristics of the patients. The results showed that male patients, relapse cases, and pulmonary positive patients compared to the references had a significantly higher percent of delay in diagnosis more than 90 days; but a significant difference was found between median delays for disease type (Table 2).

The results of Cox's proportional hazards model are demonstrated in Table 3. The adjusted hazard ratios (HRs) were statistically significant for treatment group, disease type, and year of diagnosis. Hazard Ratio HR (95% CI) of patients with pulmonary positive TB and extra pulmonary TB compared to negative pulmonary TB patients was 0.8 (0.68, 0.94) and 0.84 (0.73, 0.98) respectively. This figure for relapsed cases compared to new cases was 0.67 (0.53, 0.85).

Fig. 1 shows Kaplan–Meier curves for survival adjusted for gender, residency, disease type, and treatment group. Based on Fig. 1, there are satisfactory conditions to use the Cox Proportional models.

Discussion

Delay in TB case detection may worsen the disease and also increase TB transmission in the society. The results of this study showed that the median delay time in TB is higher in females, and negative smear cases, also relapse cases and pulmonary smear positive and extra pulmonary patients have lower hazard for delayed diagnosis compared to other groups. Results of other studies have shown that females [8–10], and negative sputum smear cases [11,12] have experienced increased diagnostic delay compared to males and other types of TB. Specifically, the given negative smear results might lead to a spurious confidence regarding not seeking further medical attention [13].

Consistent with the report from Ghana [14], further median delay in TB diagnosis in women in our study might be related to the seeking medical center differences between men and

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