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The Fever Response after Treatment of Tuberculosis: What is the Expected Time and What are the Risk Factors?

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Abstract

Background: The symptoms of pulmonary Tuberculosis include anorexia, weight loss, cough, night sweeting and fever. Fever is a common symptom and an efficient tool that is utilized for checking the response to anti-TB treatment.

Objectives: The main goals of this study are evaluating the time of fever stop and effective factors on fever response according to anti tuberculosis treatment.

Materials and methods: This study is a cross sectional study on tuberculosis (TB) patients hospitalized in the infectious diseases department of Imam Khomeini Complex Hospital (Tehran, Iran), from 1997 to 2006. We study the information related to 205 patients using the available database.

Results: The median of the patients' age is 40 years ranging from 15 to 88 and the average age is 45 years with standard deviation of 19.8. The average duration of fever response is 11.7 days with standard deviation of 7.5. No significant correlation was found among various factors such as: age, gender, different anti-tuberculosis regime, extra pulmonary or pulmonary TB, underlying disease, receiving immune-suppressing drugs, anemia, hyponatremia, history of drug addiction, and fever response followed by anti-TB treatment.

Conclusion: The time of fever stop is relatively long in our patients following anti-tuberculosis treatment. Due to similar prognosis between rapid and slow response in different patients, fever response should not be considered as a strict criterion for response to treatment and time of discharge.

Keywords: Pulmonary tuberculosis; Anti-tuberculosis treatment

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Introduction

Tuberculosis (TB) is one of the oldest diseases and today, it is one of the most common infectious diseases, especially in developing countries. Tuberculosis is the second cause of death after HIV in infectious diseases and in 1993, the World Health Organization (WHO) declared TB as a "global health emergency" [1]. According to the WHO reports presented in 2014, 9 million new cases of Tuberculosis (pulmonary and extra-pulmonary types) were detected worldwide [2]. The prevalence of Tuberculosis is 32 per 100,000 persons and its annual incidence is 21 per 100,000 individuals in Iran [3].

The symptoms of pulmonary Tuberculosis include anorexia, weight loss, cough, night sweeting and fever and these factors are usually used for estimation of severity, deterioration and level of response to treatment [4]. Fever is a common symptom and an efficient tool that is utilized for checking the response to anti-TB treatment. The time of fever stop can be attributed to the severity or deterioration of disease. Conversely, continuation of fever after treatment may be due to drug-resistant organisms and treatment failure; it is also used as an important index for evaluating the efficacy of different drug regimens [5]. This study is performed to assess the fever response in tuberculosis patients who received anti- TB treatment.

Materials and Methods

This cross sectional study was accomplished on 205 patients with Tuberculosis that admitted in infectious diseases department of

Imam Khomeini Complex Hospital, a tertiary care educational hospital in Tehran, Iran from 1997 to 2006. The inclusion criteria are definite diagnosis of pulmonary or extra-pulmonary TB, admission in hospital before starting anti-TB treatment, and recording the patient's temperature in vital sign sheet. The exclusion criteria are liver and renal failure, existence of any extra pulmonary focal infection that causes fever before starting anti-TB treatment, simultaneous treatment with corticosteroid and anti-TB, and using systemic anti-biotic one week before or during first two weeks of admission. A questionnaire is used for data gathering and the data are analyzed with SPSS software (ver. 15). This research was approved by ethics committee of Tehran University of Medical Sciences.

Results

205 patients were registered as tuberculosis in the TB registration system of the infectious diseases department. 46 patients were excluded due to not starting anti-TB treatment on this admission, 46 patients for not having fever on their admission time, six for not completing the diagnostic criteria record and one patient for not having temperature chart. Finally, 106 files are evaluated. Demographic and disease characterization of this study is shown in **Table 1**.

In evaluation of level of fever, 66 patients were febrile at arrival (body temperature >37.8 °C) and 66 patients were afebrile at arrival. Mean and median levels of body temperature of patients were 37.6 and 37 °C, respectively. 35% (37 patients) had a rapid response to treatment and were afebrile during the first 10 days and the fever was stopped in 70% (74 patients) 20 days after starting the treatment. 23.6% were febrile during admission despite anti-TB treatment.

We did not find any significant correlaton between fever response followed by anti-TB treatment and various independent variables including: age (P Value=0.51), gender (P Value=0.64), different anti-tuberculosis regimen (P Value=0.61), extra pulmonary or pulmonary TB (P Value=0.79), underlying disease (P Value=0.7), receiving immune-suppressing drugs (P Value=0.2), anemia (P Value=0.44), hyponatremia (P Value=0.41), history of drug addiction (P Value=0.36), duration of disease (P Value=0.63), level of fever at arrival (P Value=0.68), severity of lung involvement (P Value=0.1), and level of positivity of sputum smear (P Value=0.2). There was no significant difference in prognosis between patients who remained febrile despite receiving anti-TB treatment and those who were afebrile during two weeks after the treatment.

Table 1 Demographic and disease characterization of the patients.

Patients characteristics	Value
Sex	
Male	56 (52.8%)
Female	50 (47.2%)
Mean age (± SD)	45 (± 19.8)
TB type	
Pulmonary	98 (92.5%)
Extrapulmonary	7 (6.6%)
Mixed	1 (0.9%)
Drug Regimen	
Cat 1	94 (88.8%)
Other Regime	12 (11.3%)
Disease Duration❖	70.6 (5- 377) days
Cavitary lesions on CXR♦	23 (21.7%)
Underlying diseases	
Diabetes Mellitus	14 (13.2%)
HIV	26 (24.5%)
Others	58 (54.7%)
Immunosuppressive therapy	8 (7.5%)

❖ Disease Duration: Mean time of starting symptom through starting treatment; ♦ Missing data in 38 patients.

Discussion

In this study, the status of the stopping fever in patients with pulmonary and extra-pulmonary TB is discussed. We found that in spite of starting the treatment, 23.6% of total patients (106 individuals) were febrile during admission despite anti-TB treatment. 35% of patients (37 Individuals) had a rapid response to treatment and were afebrile during the first 10 days and the fever stopped in 70% of patients (74 Individuals) 20 days after starting the treatment.

General symptom like fever is an important factor in Tuberculosis treatment and it can be used for estimating the severity and deterioration of the disease. In addition, stopping fever after the treatment was identified as the response index to treatment. However, it is not still clear which factors are more effective on the time of fever response after treatment of Tuberculosis.

Different rates of fever response have been reported in different studies [4-10]. In a study performed in Madrid, median time in fever response after starting anti-TB treatment was four and six days in HIV- and HIV+ patients, respectively. Finally, 25% of patients were febrile two weeks after starting the treatment [6]. In another study on 597 patients in China, 22% of patients were afebrile three days after anti-TB therapy and in 93%, the fever response observed in two weeks [7]. In a study on 161 patients in United States, 89% of patients were afebrile in one week after treatment and 93% of patients were afebrile after two weeks [8]. Another study on 75 patients in Indiana, USA, showed that the average time of fever response was 16 days with 10 days median and 1 to 109 days range. In our study, about one third of patients were afebrile during the first week of treatment. The reason behind slow rate of fever response is not still clear. Male sex, old age, immune compromised situations including HIV, and infection with resistant organisms are possible factor responsible for fever response. We evaluated the relationship between time of fever response and different variables including demographic, disease characteristics, and laboratory indices; however, there were not any significant relationships.

In a study in Madrid, no especial factor such as HIV was found for describing or predicting the delay in fever response [6]. In another study in China, no significant factors such as sex, age, immune-compromised, history of TB, type of TB, extensive pulmonary involvement, cavitation and infection with resistant type of TB were found for justifying the delay in fever response [7]. Barnes et al. [8] found a strong correlation between duration of fever and anemia, hyponatremia, hypo albuminemia, alcohol consumption, and body temperature higher than 38.8 °C;

however, anti-TB regime was not effective in fever response. In Kiblawis et al. study, there were just two effective factors in delay of fever response: patients' temperature at arrival and progressive disease. They noticed that rifampin included regimen was very effective in fever response [9].

Despite considerable number of patients with persisting fever in this study, there was no significant difference in prognosis between these patients and those who were afebrile during two weeks after the treatment. Our study has some limitations. Since this study was accomplished on the patients' files in retrospective manner, there was probably some inaccuracy in recording the patients' body temperature. Besides, limitation of statistical population might exert a negative impact on evaluations despite long duration of investigations. In conclusion, the rate of fever response can be very variable in different populations. However, it is expected to be less than 20 days in more than 70% of patients. Due of the similar prognosis between patients with rapid and slow response to anti-TB treatment, it is rational to discharge the patients with good conditions despite no fever response.

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