Treatment outcome of new smear positive pulmonary tuberculosis patients in Hamadan, Iran: A registry-based cross-sectional study


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KEYWORDS
Tuberculosis; Treatment outcome; Cross-sectional study; Iran

Abstract
Objectives: Treatment outcome of Tuberculosis (TB), as a key determinant to evaluate the effectiveness of TB control program, remains a public health challenge in many developed and developing countries. This study aimed to assess treatment outcomes of new smear-positive pulmonary tuberculosis (PTB).

Methods: This retrospective cross-sectional study was conducted on 510 registered new PTB patients in Hamadan province, Iran during 2005–13. The data were extracted from the National TB Program (NTP). The main outcome was treatment success. The results of evaluation of the associated factors with successful treatment were presented as Odds Ratios (OR), and bootstrap method was used to obtain 95% Confidence Interval (95% CI). All statistical analysis was performed at 0.05 significant levels using the Stata 12 (Stata Corp, College Station, TX, USA).

Results: Overall, successful treatment outcome was 83.1%, and 9.4% of the patients died during the study period. In univariate logistic regression, only hospitalization history was associated with successful treatment. The factors of age, sex, co-morbidities, smoking, and residence status were not significantly associated with successful treatment.

Conclusion: The successful treatment rate of smear-positive PTB in Hamadan province was 83.1%. The factors associated with successful treatment were hospitalization history and age. The data and results of this study can be used to improve the control program and its outcomes.

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Introduction

Tuberculosis (TB) is a public health problem and the leading cause of death with an annual incidence rate of about 8.6 million cases. Additionally, 1.3 million people have been estimated to die due to the disease every year [1]. The burden of TB is the highest in Asia (59%) and Africa (26%) [2]. Besides, the case fatality rate has exceeded 50% in some African countries where HIV infection rates are high [3]. In Iran, the incidence rate of TB was 14.4 per 100,000 people in 2012 and about 50% of them was smear-positive pulmonary tuberculosis (PTB) [4].

In TB control program, it is important to achieve and sustain acceptable levels of treatment success among all TB patients. Therefore, treatment success is measured by a standardized process of treatment outcome monitoring [5]. In fact, treatment “success” has been measured by the number of patients being “cured” and those having their “treatment completed” [6]. Successful treatment of PTB has obvious benefits to both individual patients and the community. Hence, it can have an immediate impact on TB prevalence and mortality rates. On the other hand, a 95% reduction in TB-related deaths and a 90% reduction in TB incidence rate are the overall target of the strategy to end the global TB epidemic by 2035 [7].

The treatment success rate among all new TB cases was 86% globally [7]. This proportion varied from 75% in the European Region to 92% in the Western Pacific Region among the six World Health Organization (WHO) regions [7]. A systematic review in European Union countries also showed that treatment success rate varied from 60% to 87% [8]. Some factors, such as high prevalence of HIV/AIDS, high prevalence of drug resistance, poor quality of medical services, and aging, affect the treatment success [9,10].

Monitoring and assessing the treatment outcome of TB is essential in order to evaluate the effectiveness of interventions. Therefore, this study aims to assess the treatment outcomes of all PTB patients over a 9-year period by reviewing the registered cases in Hamadan province, Iran. This will enable us to ascertain the effectiveness of our treatment program and determine the risk factors of unsuccessful treatment outcome and longer treatment duration.

Methods

This cross-sectional study was performed on TB patients in Hamadan province, Iran using the surveillance database. All the registered smear-positive TB patients in all parts of the province (510 patients) from 2005 to 2013 were included in the study. The inclusion criteria of the study were (a) being a new case of TB and (b) living in Hamadan province. For diagnosis of sputum smear-positive TB, a case must meet one of the following criteria: (a) two positive sputum smears by microscopy, (b) one positive sputum smear and one positive sputum culture, and (c) one positive sputum smear with typical pathology of active TB on chest X-ray [11].

Conclusion: Treatment success rate in our study was 83.1%, which is slightly lower than the success target set by World Health Organization (WHO). Key determinants of poor treatment success rate, such as male gender, and not having hospitalization history during the treatment period, should be considered in efforts aimed to improve the treatment outcome in the management of TB.

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<table>
<thead>
<tr>
<th>Table 1</th>
<th>Treatment outcomes for new PTB patients according to WHO’s guideline [12].</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome</strong></td>
<td><strong>Definition</strong></td>
</tr>
<tr>
<td>Cured</td>
<td>A pulmonary TB patient with bacteriological confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion</td>
</tr>
<tr>
<td>Treatment completed</td>
<td>A TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable</td>
</tr>
<tr>
<td>Treatment failed</td>
<td>A TB patient whose sputum smear or culture is positive at month 5 or later during treatment</td>
</tr>
<tr>
<td>Died</td>
<td>A TB patient who dies for any reason before starting or during the course of treatment</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more</td>
</tr>
<tr>
<td>Not evaluated</td>
<td>A TB patient for whom no treatment outcome is assigned. This includes cases “transferred out” to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit</td>
</tr>
<tr>
<td>Treatment success</td>
<td>The sum of cured and treatment completed</td>
</tr>
</tbody>
</table>

PTB: positive pulmonary tuberculosis.
died, loss to follow up, or not evaluated) were categorized as unsuccessful treatment.

For data analysis, descriptive statistics, including frequency tables and percentage, were used to describe the study variables. In addition, chi-square test was used to compare the study groups. To determine the effect of predictors on treatment success, crude and adjusted Odds Ratios (OR) with 95% Confidence Interval (95% CI) were reported using logistic regression. In this study, bootstrap technique with 1000 replications was used to obtain 95% CI. In adjusted model, each predictor was entered into the model together with age, weight, and delayed diagnosis. To assess the effect of age, only weight and delayed diagnosis were entered into the model. All the analytical operations were performed using the Stata software, version 12 (Stata Corp, College Station, TX, USA) and $P < 0.05$ was considered to be statistically significant.

Results

During the study period (2005–13), a total of 510 PTB patients were included in the study. The mean age of the study patients was 36.8 (SD ± 21.4) years, 52.2% were male, and 39.6% lived in rural areas. In addition, hospitalization history during the treatment period was present in 52.7% of the patients and 2.7% were HIV-positive. Distribution of the demographic characteristics of the new PTB patients is shown in Table 2.

Overall, the mean treatment success of all the registered PTB patients was 83.1% during 2005–13. The summary of the treatment outcomes of all the new PTB patients during 2005–13 is presented in Table 3.

### Table 2: Distribution of the demographic characteristics of the new PTB patients in Hamadan province, Iran from 2005 to 2013.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Successful</th>
<th></th>
<th>Unsuccessful</th>
<th></th>
<th>Total</th>
<th></th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>215</td>
<td>80.8</td>
<td>51</td>
<td>19.2</td>
<td>266</td>
<td>0.146</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>209</td>
<td>85.7</td>
<td>35</td>
<td>14.3</td>
<td>244</td>
<td></td>
</tr>
<tr>
<td>Age group (year)</td>
<td>&lt; 30</td>
<td>75</td>
<td>87.2</td>
<td>11</td>
<td>12.8</td>
<td>86</td>
<td>0.211</td>
</tr>
<tr>
<td></td>
<td>31–60</td>
<td>136</td>
<td>85.5</td>
<td>23</td>
<td>14.5</td>
<td>159</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 61</td>
<td>213</td>
<td>80.4</td>
<td>52</td>
<td>19.6</td>
<td>265</td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td>Urban</td>
<td>258</td>
<td>83.8</td>
<td>50</td>
<td>16.2</td>
<td>308</td>
<td>0.639</td>
</tr>
<tr>
<td></td>
<td>Rural</td>
<td>166</td>
<td>82.2</td>
<td>36</td>
<td>17.8</td>
<td>202</td>
<td></td>
</tr>
<tr>
<td>Having HIV risk factors</td>
<td>No</td>
<td>390</td>
<td>83.9</td>
<td>75</td>
<td>16.1</td>
<td>465</td>
<td>0.155</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>34</td>
<td>75.5</td>
<td>11</td>
<td>24.5</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Having TB risk factors</td>
<td>No</td>
<td>351</td>
<td>83.9</td>
<td>67</td>
<td>16.1</td>
<td>418</td>
<td>0.248</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>73</td>
<td>79.4</td>
<td>19</td>
<td>20.6</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>HIV status</td>
<td>No</td>
<td>414</td>
<td>83.5</td>
<td>82</td>
<td>16.5</td>
<td>496</td>
<td>0.235</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>10</td>
<td>71.4</td>
<td>4</td>
<td>28.6</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

In univariate logistic regression, only hospitalization history during the treatment period was associated with successful treatment (OR = 2.02, 95% CI: 1.25, 3.24). After adjustment for the possible confounding factors, such as age, weight, and delayed diagnosis (Table 4), successful treatment was found to be significantly associated with male gender (OR = 0.54, 95% CI: 0.31, 0.84), having HIV risk factors (OR = 0.36, 95% CI: 0.15, 0.84), and having hospitalization history during the treatment period (OR = 1.89, 95% CI: 1.15, 3.12). The association between successful treatment and age, location, HIV status, and having TB risk factors was not significant (Table 4).

Discussion

This study aimed to assess the treatment outcomes of PTB patients over a 9-year period and revealed the overall treatment success rate to be 83.1%, which is slightly lower than the WHO’s target of 85% [1]. The proportion of treatment success in this study was also lower than that reported in the previous studies in different parts of Iran [2,13]. However, it was higher compared to the proportion reported in other countries [5,6]. This difference might be explained by several different factors, such as the study sample size, the proportion of variables including rural residency, old age, and male gender, the study period, HIV status of TB patients, and the quality of health services. As a result, the factors associated with poor treatment outcome are likely to be different among the world countries and also within a country. Over 90% treatment success rate by 2025 is one of the main goals of Iran’s Ministry of Health and Medical Education (MOHME) [14]. Accordingly, information about the factors associated with treatment outcome may help policymakers to ensure a successful TB control program and also to achieve the target of treatment success.

In the present study, the results of univariate logistic regression indicated no significant relationship between gender and treatment outcome. However, after controlling for weight, age, and delayed diagnosis, the results demonstrated that unsuccessful treatment was more likely among males compared to females. The higher proportion of unsuccessful treatment outcome in males might be related to their high-risk behaviors, such as substance and alcohol abuse, and more infection with HIV. In this regard, the results showed 92.8% HIV co-infection among male patients. A study in Iran also revealed that sex was independently associated with TB/HIV co-infection [15]. Although we have no information about substance and alcohol abuse, Jakubowiak et al. [16] and Johnstone et al. [4] found that alcohol consumption was related to an increased risk of treatment failure. Our finding was in agreement with those of other studies [3–5], indicating a direct
association between male gender and risk of unsuccessful treatment outcome. However, some studies have shown no variation by sex in the treatment outcome [11]. Other possible reasons for this gender disparity might be social, environmental, and health-related factors [17,18] which might be the causes of the high prevalence rate of multidrug-resistant TB (MDR-TB) among men [19].

We also found the prevalence rate of HIV co-infection of 2.7% among the TB patients. Besides, no significant relationship was observed between HIV co-infection and treatment outcome. This might be due to the small sample of TB patients with HIV co-infection. On the other hand, previous studies have found that HIV co-infection was an independent predictor of unsuccessful treatment outcome [20,21]. The prevalence of TB/HIV co-infection varied among countries; 23.5% in China [22], 42% in Southern Africa [23], 30% in Brazil [24], and 2.4% in Iran [25]. Although the prevalence rate of HIV co-infection in our study was slightly higher than the national average [25,26], it was very low compared to other regions. This finding might be justified by individuals’ low demand for HIV testing [27]. On the other hand, the results of adjusted logistic regression disclosed that having HIV risk factors, such as unprotected sex, was a predictor of unsuccessful treatment.

Age is an important factor in TB and its related outcomes [11,18,28,29]. Based on both univariate and adjusted logistic regression in the current study, no significant association was found between age and treatment outcome. This is inconsistent with the findings of other studies in Asia [11], USA [28], and Africa [30]. The higher rate of unsuccessful treatment observed among elderly patients may be due to complication with other diseases like diabetes mellitus, hypertension, and cardiovascular diseases or some high-risk behaviors, such as smoking and alcohol abuse, in this age group. Accordingly, assessment and recording of co-morbidities and high-risk behaviors might help physicians and health workers improve the treatment outcome in the management of TB.

In our study, the TB patients with hospitalization history during the treatment period were approximately 2 times more likely to have successful treatment in both univariate and adjusted models. We found no similar studies in this regard for comparison of the results. The directly observed treatment of short course (DOTS) strategy as a cost-effective strategy done by healthcare workers could justify this finding.

There was no significant association between place of residency and treatment outcome. There are some reasons justifying this phenomenon including a high coverage of health insurance system in Iran even in rural areas, implementation of DOTS strategy and implementation of family physician in rural area which might help to improve the diagnosis and treatment outcome of the patients. There are conflicting results in this regard. For example, a study conducted in Pakistan revealed that poor outcome of TB treatment was associated with living in rural areas [31]. Another study in Ethiopia reported that the treatment success was higher in rural areas [32].

Our study had some limitations. We used registry-based data for analysis. Accordingly, we could not directly investigate the TB patients’ information about some variables, such as HIV status, HIV risk factors, and hospitalization history. This might have caused information bias, leading to underestimation of the variables’ statuses.

**Conclusion**

The treatment success rate in our study was 83.1%, which is slightly lower than the success target set by WHO. The key determinants of poor treatment success rate, such as male gender, and not having hospitalization history during the
treatment period, should be considered in efforts aimed to improve the treatment outcome in the management of TB. Moreover, future epidemiological studies are required to identify the key factors associated with treatment success to prevent TB resistance to treatment and decrease morbidity, mortality, and period of infection.

**Authors’ contributions**

Conception and design: SK, AMH, HS; acquisition of data: AZ, SoK; analysis and interpretation of data: SK, SR, JH, EG; drafting of the manuscript: SK, SR, AMH, HS; critical revision of the manuscript for important intellectual content: JH, EG. All authors revised and approved the manuscript.

**Conflict of interest**

The authors declare that there is no conflict of interest.

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**References**


