Treatment outcomes of smear-positive pulmonary tuberculosis patients: A retrospective cross-sectional study in Ilam, Iran

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Abstract

Introduction: The control of tuberculosis (TB) has shown significant progress, however this disease continues to present difficulties for public health in Iran. The aim of this study was to analyze the treatment outcomes among smear-positive pulmonary tuberculosis (SPPTB) patients in Ilam province, Iran, from 2016-2024 and to identify demographic and clinical factors linked with successful treatment outcome.

Materials and Methods: In this study outcomes were categorized based on World Health Organization (WHO) standards and success was considered as cured or treatment completed. Descriptive statistics, chi-square and Fisher exact tests, crude and adjusted odds ratios (ORs) using logistic regression analysis with 95% confidence interval (CI) were obtained by the use of SPSS software version 22 with significance at $p<0.05$.

Results: A total of 120 patients had a mean symptom-to-diagnosis interval 69.63±77.47 days and diagnosis-to-treatment interval of 4.18±9.56 days. The annual number of SPPTB cases ranged from 23 (during 2016–2017) to eight (during 2020–2021), and the mean incidence was 2.47 per 100,000 population. The odds of successful treatment outcome were significantly higher in patients with body mass index (BMI) 18.5–24.9 kg/m² (OR=3.16; 95% CI:1.02–9.77) compared to other categories.

Conclusion: The treatment success rate was 80.2%, which is comparatively lower than the benchmark established by WHO. Factors such as BMI were significantly associated with the study results, whereas other factors such as age, gender, hospitalization, and area of residence did not show a significant association with the results.

Keywords: Epidemiology, *Mycobacterium tuberculosis*, Smear-positive pulmonary tuberculosis, Treatment success, Treatment outcomes

1. Introduction

Tuberculosis (TB) is an infectious and contagious disease that represents significant public health challenge worldwide, continuously threating human health [1-3]. The WHO reported 7.5 million new cases of TB in its 2023 publication, contributing to an estimated total of over 10 million cases globally. Moreover, around 410,000 individuals are estimated to have multidrug-resistant TB (MDR-TB) or show resistance to rifampicin. Given these circumstances, the WHO is urging immediate action to combat and eradicate the global TB epidemic [4]. Diagnostic methods for TB include direct smear microscopy, culture, TB fluorochrome staining, interferon-gamma release assays (IGRA), molecular testing, tuberculin skin tests (PPD), and chest radiography. Certain forms of TB can be detected through urine tests, analysis of pleural or abdominal fluid, and biopsies of lymph nodes and other lesions [5]. Currently, TB diagnosis primarily relies on direct observation of sputum smears, which is a straightforward method. However, culture is more sensitive and definitive, allowing for phenotypic drug susceptibility testing. While smear is the gold standard for TB diagnosis, its effectiveness depends on the tester's expertise and the quality of the sputum sample tested. TB diagnosis by smear microscopy smear has a minimum detection limit (LOD) of 5,000 to 10,000 bacilli per milliliter (CFU/ml) of sputum result in missed cases and false positives [6-8]. Timely and precise diagnosis of smear-positive pulmonary TB is crucial, particularly as sputum smear microscopy remains the main diagnostic method in developing countries [9, 10], where approximately 95% of TB cases and 98% of TB-related deaths occur [11]. Negative smear cases, which account for approximately 17% of TB cases, can transmit the disease. Each pulmonary TB patient with a negative smear can infect up to two individuals within a year; therefore, identifying these patients is as urgent as identifying those with positive smears. The smear method detects only about 50% of active TB cases [12]. Among molecular tests, commercial Polymerase chain reaction (PCR)-based methods provide rapid identification of TB and enable drug susceptibility testing for first- and second-line treatments shortly after sample collection. These tests are highly sensitive and specific, making them essential diagnostic tools for both pulmonary and extrapulmonary TB. The objective for 2025 is to guarantee that all reported TB patients receive an initial rapid diagnostic test. However, as of 2022, only 47% of the patients had undergone such testing, with significant variations in usage across different countries [4]. Since sputum direct smear method remains the primary diagnostic method for TB in developing countries, this retrospective cross-sectional study aimed to examine patients with positive smear results for pulmonary TB in Ilam Province, Iran, from 2016 to 2024.

2. Materials and Methods

The present retrospective cross-sectional study used the National TB Registry System (NTBRS) data from the TB and Leprosy Department of the Ministry of Health, Treatment, and Medical Education of the Islamic Republic of Iran to assess treatment results for smear-positive pulmonary tuberculosis (SPPTB) patients in Ilam province, Iran from March 20, 2016 to March 19, 2024. Ilam province; located in western region of Iran, shares a 425-kilometer-long border with Iraq and covers an area of approximately 20,133 km2. The straight-line distance from Ilam to Tehran (capital city of Iran) is approximately 511 km. According to census conducted by the Iran Statistics Center the average population of this province during the period from March 2016 to March 2024 was 608,030 which includes both urban and rural population groups [13]. All registered patients meeting the inclusion criteria: a confirmed diagnosis of sputum smear-positive pulmonary TB and residency in Ilam province; were considered, resulting in a total of 120 patients. As per national guidelines, a diagnosis of sputum smear-positive TB was established if a patient met at least one of the following criteria: (a) at least two sputum smears positive on microscopy; (b) one positive sputum smear supported by a positive sputum culture; or (c) one positive sputum smear in conjunction with chest radiographic findings consistent with pulmonary TB [14]. A standardized checklist extracted the data which included essential demographic and clinical information such as gender, age, education level, area of residence, marital status, body mass index (BMI), referral center, time intervals from symptom onset to diagnosis and from diagnosis to treatment initiation, history of contact with a TB patient, HIV status and imprisonment history, hospitalization during treatment and degree of smear positivity prior to treatment. The sputum smear microscopy grading system criteria classified results as follows: "scanty" corresponded to 1–9 acid fast bacilli (AFB) per 100 oil-immersion fields, "grade 1+" represented 10–99 AFB per 100 oil-immersion fields, "grade 2+" indicated 1–10 AFB per oil-immersion field (check 50 fields), and "grade 3+" showed >10 AFB per oil-immersion field (check 20 fields) [15]. Patients were classified following WHO definitions: "new patients" and "previously treated patients", with the latter further subcategorized into "relapse patients", "treatment after absence", and "other previously treated patients" (Table 1). Treatment outcomes were also defined as defined in the WHO guidelines: "cured", "treatment completed", "treatment failed", "died", "lost to follow-up", "not evaluated", and "treatment success". In addition, "patients still undergoing treatment" were defined as those who had not yet completed their treatment course (Table 2) [16]. The research defines "treatment success" as the combination of cured patients and those who completed their treatment (as shown in Table 2), while all other results, including "treatment failure", "death", "lost to follow-up", and "not evaluated", fall under "unsuccessful treatment".

Table 1. Classification based on history of previous TB treatment (patient registration group) according to WHO's framework.

Patient registration group	Definition
New patients	A TB patient who has never been treated for TB or has taken anti-TB drugs for less than 1 month.
Previously treated patients	A TB patient who has received 1 month or more of anti-TB drugs in the past.
Relapse patients	A TB patient who has previously been treated for TB, was declared cured or treatment completed at the end of his/her most recent course of treatment, and is now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by reinfection).
Treatment after absence	A TB patient who has previously been treated for TB and was declared lost to follow-up at the end of his/her most recent course of treatment.

Other previously treated patients	A TB patient who has previously been treated for TB but whose outcome after his/her most recent course of treatment is unknown or undocumented.

Table 2. Treatment outcomes for TB patients according to WHO's framework.

Outcome	Definition
Cured	A pulmonary TB patient with bacteriologically 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.
Treatment completed	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.
Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Died	A TB patient who dies for any reason before starting or during the course of treatment.
Lost to follow-up	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	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.
Treatment success	The sum of cured and treatment completed.

2.1. Statistical analysis

The main outcome was treatment success, and the analysis of treatment outcomes excluded patients who continued their treatment (9 patients). The subcategories of previously treated patients were aggregated into a single category. The data analysis included descriptive statistics, which presented categorical variables through frequency tables and percentages, and continuous variables through mean and standard deviation. The analysis used Chi-square and Fisher exact tests to study the relationships between variables and treatment results. The analysis used logistic regression to evaluate the effects of predictors on treatment outcomes by presenting crude and adjusted odds ratios (OR) with 95% confidence intervals (95% CI). All statistical tests were conducted using SPSS software, version 22 (IBM Corp., Armonk, NY, USA). The research established a significance threshold of 0.05.

3. Results

The study followed 120 SPPTB patients throughout eight years in Ilam province, Iran. The mean age of these patients was 55.35 (SD ± 19.20) years, the male population made up 61.7% of the total. The majority of patients (65.8%) lived in urban areas, 49.2% had a history of hospitalization during the treatment period and 1.7% were prisoners. The detailed distribution of demographic and clinical characteristics is presented in Table 3 and shows no statistically significant differences between the factors ($P > 0.05$). The average time interval between the onset of TB symptoms and diagnosis was 69.63 ± 77.47 days, while the mean interval between diagnosis and initiation of treatment was 4.18 ± 9.56 days.

Table 3. Distribution of demographic and clinical characteristics of SPPTB patients.

Variable	Total frequency (%)	Patients still undergoing treatment	Treatment Outcomes		P-value
			Successful	Unsuccessful	
			No. (%)	No. (%)	
Gender					0.123
Male	74 (61.7)	4	53 (75.7)	17 (24.3)	
Female	46 (38.3)	5	36 (87.8)	5 (12.2)	
Age (year)					0.197
<30	15 (12.5)	0	14 (93.3)	1 (6.7)	
31-60	52 (43.3)	5	39 (83.0)	8 (17.0)	
>61	53 (44.2)	4	36 (73.5)	13 (26.5)	
Education					0.586

Illiterate	51 (42.5)	5	34 (73.9)	12 (26.1)	
Elementary School	22 (18.3)	3	15 (78.9)	4 (21.1)	
Middle School	14 (11.7)	0	12 (85.7)	2 (14.3)	
High School and Religious sciences (formal religious/seminary education)	22 (18.3)	0	20 (90.9)	2 (9.1)	
Higher education (associate degree to doctorate)	11 (9.2)	1	8 (80.0)	2 (20.0)	
Residence Area					0.736
Rural	41 (34.2)	4	29 (78.4)	8 (21.6)	
Urban	79 (65.8)	5	60 (81.1)	14 (18.9)	
Prisoner					0.359
Yes	2 (1.7)	0	1 (50.0)	1 (50.0)	
No	118 (98.3)	9	88 (80.7)	21 (19.3)	
Marital Status					0.944
Married	75 (62.5)	6	55 (79.7)	14 (20.3)	
Single	25 (20.8)	1	20 (83.3)	4 (16.7)	
Divorced and widowed	20 (16.7)	2	14 (77.8)	4 (22.2)	
BMI (kg/m^2)					0.316
<18.5	39 (32.5)	1	27 (71.1)	11 (28.9)	
18.5-24.9	60 (50.0)	5	47 (85.4)	8 (14.6)	
25-29.9	16 (13.3)	2	12 (85.7)	2 (14.3)	
>30	5 (4.2)	1	3 (75.0)	1 (25.0)	
Referral Center					0.053
Health network system (Subordinate hospitalizing units)	65 (54.2)	6	43 (72.5)	16 (27.0)	
Health network system (Subordinate outpatient units)	26 (21.7)	1	20 (80.0)	5 (20.0)	
Office - private clinic	15 (12.5)	1	14 (100.0)	0 (0.0)	
Self-introduce	1 (0.8)	0	1 (100.0)	0 (0.0)	
Prison	2 (1.6)	0	1 (50.0)	1 (50.0)	
Others	11 (9.2)	1	10 (100.0)	0 (0.0)	
Contact History with TB Patient					0.788
Yes	8 (6.7)	0	7 (87.5)	1 (12.5)	
No	87 (72.5)	9	63 (80.8)	15 (19.2)	
Unknown	25 (20.8)	0	19 (76.0)	6 (24.0)	
Degree of Smear Positivity Before Treatment					0.927
Scanty	8 (6.7)	1	6 (85.7)	1 (14.3)	
1+	26 (21.7)	2	18 (75.0)	6 (25.0)	
2+	24 (20.0)	0	20 (83.3)	4 (16.7)	
3+	62 (51.6)	6	45 (80.4)	11 (19.6)	
Group of Disease Record					0.138
New	112 (93.3)	8	85 (81.7)	19 (18.3)	
Previously treated	8 (6.7)	1	4 (57.1)	3 (42.9)	
HIV Infection					0.347
Yes	0 (0.0)	0	0 (0.0)	0 (0.0)	
No	101 (84.2)	8	76 (81.7)	17 (18.3)	
Unknown	19 (15.8)	1	13 (72.2)	5 (27.8)	
Hospitalization History					0.537
Yes	59 (49.2)	5	42 (77.8)	12 (22.2)	
No	61 (50.8)	4	47 (82.5)	10 (17.5)	

The annual number of SPPTB cases fluctuated throughout the study period from 23 cases in 2016–2017 to 8 cases in 2020–2021 before rising to 14 cases in 2023–2024 (Figure 1). During the study period 120 SPPTB cases were included, yielding a mean weighted population-based incidence rate for SPPTB of 2.47 per 100,000 population.

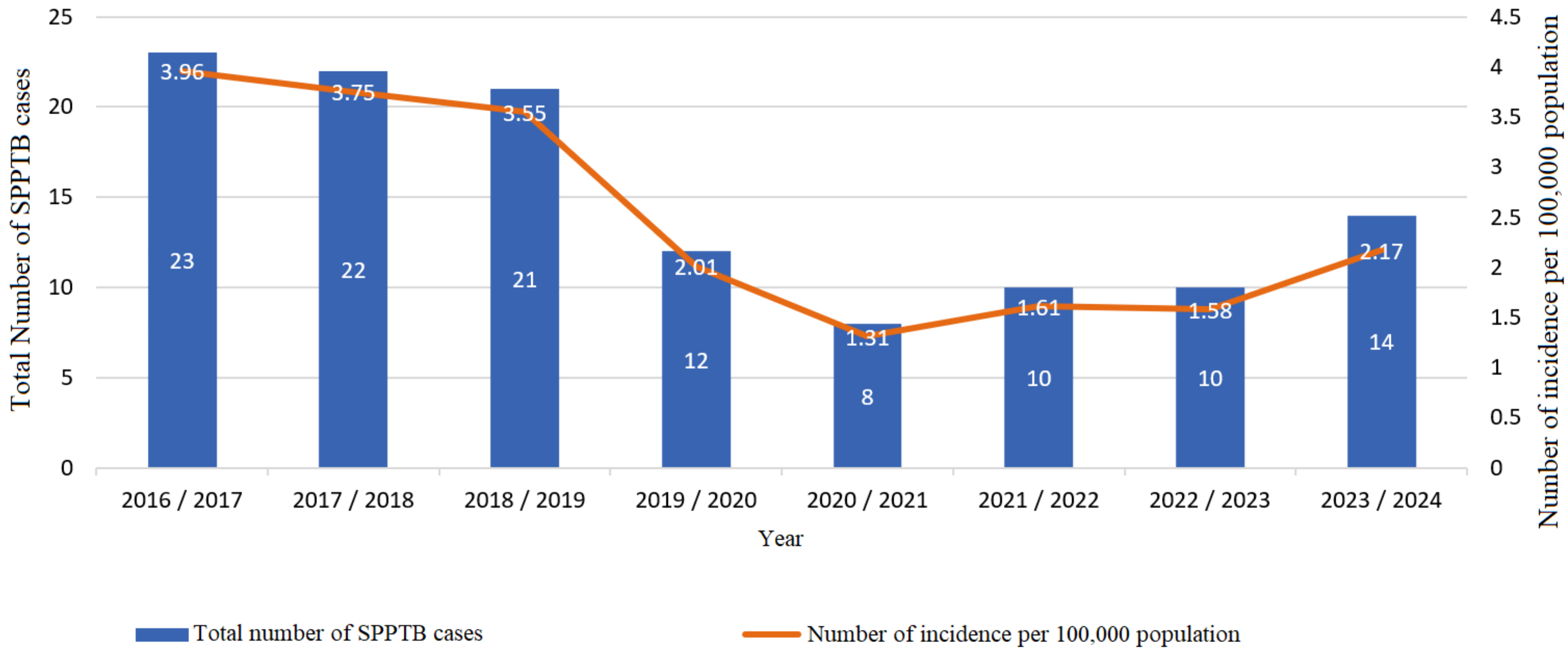

Figure 1. Annual distribution of registered SPPTB cases in Ilam province, Iran (2016–2024).

According to the registration status of patients, 93.3% (112 cases) were new cases, 4.2% (five cases) were relapse cases, for treatment after absence it was 0.8% (one case) and other previously treated patients were seen in 1.7% of cases (two cases) recorded during the study period (Table 4).

Table 4. Classification of disease records among SPPTB patients based on WHO definitions.

Group of Disease Record	Frequency	Percentage (%)
New	112	93.3
Relapse	5	4.2
Treatment after absence	1	0.8
Others	2	1.7
Total	120	100.0

At the time of assessment, nine patients were still being treated. According to the treatment outcome results of the patients, 75 cases (67.6%) were cured, and the completion rate was 12.6% (14 cases) which demonstrate an overall 80.2% successful treatment outcome rate. Death was occurred in 13.5% (15 cases) and loss to follow-up for 3.6% (four cases), whereas only 2.7% experienced failure of treatment (three cases) which display a 19.8% unsuccessful treatment rate altogether (Table 5).

Table 5. Treatment outcomes of SPPTB patients.

Treatment Outcome	Frequency	Percentage (%)
Successful treatment		80.2
Cured	75	67.6
Treatment completed	14	12.6
Unsuccessful treatment		19.8
Death	15	13.5
Lost to follow-up	4	3.6
Treatment failed	3	2.7
Total	111	100.0

The average rate of those with definitive outcomes who were successfully treated (cured or treatment completed) was 80.2% during the study period. No association with treatment success between age, sex, area of residence, marital status, and history of hospitalization or degree of smear positivity was found in logistic regression analysis. However, after adjusting for potential confounders, having a BMI of 18.5–24.9 kg/m2 was significantly associated with higher odds of treatment success (OR = 3.16, 95% CI: 1.02–9.77). Other variables did not exhibit a statistically significant relationship with treatment success in the adjusted model (Table 6).

Table 6. Logistic regression analysis of factors potentially associated with treatment success among SPPTB patients (* P-value < 0.05).

Variables	Crude Model			Adjusted Model		
	OR	95% CI	P-value	OR	95% CI	P-value
Gender						
Female	1.00	-	-	1.00	-	-
Male	0.433	(0.15, 1.28)	0.130	0.34	(0.10, 1.21)	0.095
Age (year)						
<60	1.00	-	-	1.00	-	-
>61	0.47	(0.18, 1.22)	0.119	0.42	(0.12, 1.42)	0.162
Hospitalization History						
No	1.00	-	-	1.00	-	-
Yes	0.75	(0.29, 1.90)	0.537	0.74	(0.26, 2.07)	0.560
Degree of Smear Positivity Before Treatment						
Scanty	1.00	-	-	1.00	-	-
1+	0.50	(0.05, 5.04)	0.556	0.24	(0.02, 3.28)	0.286
2+	0.83	(0.08, 8.95)	0.880	0.54	(0.04, 8.07)	0.651
3+	0.68	(0.07, 6.26)	0.735	0.38	(0.03, 4.67)	0.446
BMI (kg/m^2)						
<18.5	1.00	-	-	1.00	-	-
18.5-24.9	2.34	(0.84, 6.54)	0.104	3.16	(1.02, 9.77)	**0.046***
25-29.9	2.44	(0.47, 12.77)	0.289	2.10	(0.32, 13.88)	0.443
>30	1.22	(0.11, 13.07)	0.868	0.71	(0.05, 9.76)	0.797
Marital Status						
Single	1.00	-	-	1.00	-	-
Married	0.79	(0.23, 2.67)	0.699	1.20	(0.26, 5.62)	0.817
Divorced and widowed	0.70	(0.15, 3.28)	0.651	0.73	(0.10, 5.27)	0.759
Residence Area						
Urban	1.00	-	-	1.00	-	-
Rural	0.85	(0.32, 2.24)	0.736	0.81	(0.27, 2.42)	0.699

4. Discussion

This study aimed to evaluate the treatment outcomes of SPPTB patients over an 8-year time period and showed that the overall treatment success rate was 80.2%, which is marginally lower than the WHO's target of 85% [17]. In our study, the estimated mean number of incidences in Ilam province was 2.47 cases per 100,000 populations. In addition, significant changes were observed, from 3.96 cases per 100,000 population in 2016–2017 to 1.31 in 2020–2021 and then rising to 2.17 in 2023–2024. The decline in the number of TB cases during 2020–2021 was likely driven by the combined effects of the COVID-19 pandemic, quarantine regulations, and disruptions in healthcare services in Iran. As a result of these measures the contact between people were dramatically decreased. Meysamie et al., in Sistan and Baluchestan province (a location with highest SPPTB rates in Iran), reported that incidence of SPPTB in 100,000 persons was 18.96, 21.78, 24.42, and 22.88, respectively in 2005, 2006, 2007 and 2008, which was notably higher than our study [18]. A comprehensive analysis by Moosazadeh et al., between 2005-2015 in Iran, 34,012 smear positive TB cases were recorded and the mean of smear positive TB monthly incidence was 404.9 (SD=54.7). This study provided valuable insights about patterns of SPPTB [19]. Another study by Pourostadi et al., 329 TB-confirmed patients were evaluated, which 254 cases (77.2%) were identified as smear positive and 75 (22.8%) were negative. This study indicate that about one-quarter of TB cases in the northwest of Iran are smear- negative which is troublesome for diagnosis and treatment [20]. Rastegar et al., reported that the highest proportion of SPPTB were over 64 years old (35.3%), and the prevalence was higher among males (54.6%) compared to females (45.4%) [6]. In the present study, the average time interval between the onset of TB symptoms and diagnosis was 69.63 ± 77.47 days, while the mean interval between diagnosis and initiation of treatment was 4.18 ± 9.56 days. This data provides valuable insights into the healthcare systems response and can be useful for evaluating diagnosis processes, assessing treatment access and informing policymaking. Our average time interval between the onset of TB symptoms and diagnosis is relatively longer than the 58 days reported in China [10], and the 36 days reported in Portugal [7]. This indicates that the diagnostic delay in Ilam province remains a concern, and suggests for improving early detection measures. The results demonstrated no notable relationship between gender and age factors with treatment outcomes which contrasts with the findings reported in previous research [21-23]. In addition, the unsuccessful treatment was more likely among males compared to females. The higher proportion of unsuccessful treatment outcome in males could be associated with their high-risk behaviors, such as elevated rates of tobacco use and alcohol or other substance abuse, along with higher burden of co-morbid conditions such as diabetes or chronic kidney disease, that complicate the standard drug regimen. In addition, there was no notable association between location of residence and treatment outcome. There are some reasons that explain this phenomenon, including a health insurance coverage system in Iran, and the introduction of family physicians in rural area which might help to enhance patient diagnosis and treatment outcomes. In our study, TB patients who had a BMI ranging from 18.5 to 24.9 kg/m2 during the treatment period were more likely to have successful treatment in adjusted model. This result is consistent with recent pooled evidence by Li et al., showing that undernutrition at treatment initiation is a strong predictor of mortality in TB patients. According to their meta-analysis, low BMI ($<18.5\ kg/m^2$) was associated with markedly increased mortality, while adjusted analyses suggested that higher BMI is associated with reduced mortality [24]. The impairment of cell-mediated immunity, worsening of drug tolerance and comorbidity risk can be the reasons behind this result [25].

5. Conclusion

In our study, the treatment success rate was recorded 80.2%, slightly lower than the benchmark established by the WHO. Multiple key factors were recognized as playing a role in less-than-ideal outcome, particularly gender, hospitalization history, age, and residence area. These factors must be considered when creating strategies to improve the effectiveness of TB treatment. Moreover, additional epidemiological studies are crucial to identify the fundamental factors affecting treatment effectiveness. These initiatives are vital for minimizing the likelihood of drug-resistant TB, decreasing complications and deaths related to the disease, and reducing the period of infection.

6. Limitations

Several limitations of this study should be recognized. Our analysis was based on registry data; therefore, we could not directly examine certain patient-level variables, such as HIV status, history of hospitalization, and the degree of smear positivity before treatment.

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7. Authors' contributions

A.P and A.GH conceived and designed the study, led data collection and curation, performed primary data processing, drafted the manuscript, and coordinated project activities. K.NG performed the formal statistical analyses, prepared tables and figures, and reviewed analytical results. M.YM, N.M and S.K supervised the study, contributed to study design and interpretation of results, and critically revised the manuscript for intellectual content; they serve as co-corresponding authors. R.F assisted with data collection, case verification, and manuscript revision. F.S supported data acquisition and contributed to manuscript editing.

8. Ethics

This study was approved by the Ilam University of Medical Sciences Research Ethics Committee (IR.MEDILAM.REC.1401.249). All procedures were conducted in accordance with the Declaration of Helsinki. Patient consent was waived due to the retrospective nature of the study and anonymized registry data.

9. Funding

No Funding.

10. Conflict of Interest

The authors have no competing interests to declare.

11. Data Availability

The data supporting the results of this study can be obtained from the corresponding author upon reasonable request. Mohammad Yazdanmanesh had unrestricted access to all study data and accepts full responsibility for the integrity of the data and the accuracy of the analyses.

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