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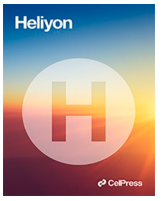

Research article

Prevalence, treatment outcomes and determinants of TB/HIV coinfection: A 4-year retrospective review of national tuberculosis registry in a country in a MENA region

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ABSTRACT

Background: The co-occurrence of tuberculosis (TB) and AIDS (HIV) has emerged as a significant public health challenge. This study investigated the epidemiological factors and treatment outcomes of TB in individuals based on their HIV status in Iran.

Methods: The current study was a descriptive-analytical cross-sectional study that focused on new patients diagnosed with TB in Iran between 2018 and 2021. Patients' data were sourced from the National Tuberculosis Registry database of Iran. A multiple logistic regression model was used to investigate the relationship between the most important influencing factors and TB/HIV coinfection.

Results: Over a 4-year period, a study was conducted on 25,011 new TB patients out of 30,762 registered in the national database. TB and HIV were coinfected in 672 cases (2.68%). The highest number of coinfection cases were found in patients with smear-negative pulmonary tuberculosis (249 patients, 37.05%) and extrapulmonary tuberculosis (123 patients, 18.19%). TB patients with coinfection had a median TB treatment duration of three months longer than others. The success rate of TB treatment was lower in patients with coinfection (437 patients, 65.02%) than in non-coinfection patients (20,302 patients, 83.41%). Treatment success probability in smear-positive pulmonary tuberculosis patients with and without coinfection was lower than other types of TB. Logistic regression analysis showed that having a TB risk factor was the strongest predictor of coinfection, with an odds ratio of 29.73 (95% CI: 22.05–40.07), followed by having an HIV risk factor with an odds ratio of 17.52 (95% CI: 13.68–22.45).

Conclusions: The findings of this research offer significant insights into the potential causes of HIV coinfection in individuals with TB, which could be used to inform the development of policies and strategies aimed at enhancing the identification and treatment of TB patients who are at risk of TB/HIV coinfection and to promote optimal health status for patients with TB.

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1. Introduction

HIV and TB are two lethal infectious diseases that are interconnected [1], in such a way that the co-occurrence of both results in a significant public health challenge [2]. The prevalence of TB is rising rapidly in regions with high HIV rates, posing a new obstacle to TB control [3]. Various studies have demonstrated the harmful interactions between HIV and TB, which negatively impact population health [4]. For instance, research conducted in Africa revealed that the HIV and TB epidemics are intertwined [5], while a study in Ethiopia uncovered a two-way relationship between these two diseases [6]. The detrimental and reciprocal effects of HIV and TB are evident at both individual and population levels, particularly in sub-Saharan African nations [7].

The coinfection of TB and HIV is mutually beneficial for both pathogens and results in the acceleration of both diseases [8,9]. People who are infected with both TB and HIV are at a high risk of mortality due to the reciprocal relationship between these two infections [10]. HIV can increase the risk of developing active TB up to 30 times [11], lead to atypical clinical manifestations of TB, complicate diagnosis and treatment, and ultimately affect the prognosis of TB disease [8]. In contrast, TB slows down the recovery of $CD4^+$ T lymphocytes [12], increases viral replication [13], and accelerates the progression of AIDS and death in HIV patients by 6–8 times [7]. The World Health Organization's latest report shows that approximately 10.6 million people were diagnosed with TB in 2021, resulting in 1.6 million deaths due to the disease, including 187,000 TB-related deaths among those with HIV [14]. In 2019, global estimates revealed that over one-third of people with HIV were concurrently suffering from tuberculosis, and about 8% of people with TB were HIV positive [15].

Overall, Tuberculosis is known to be the most prevalent opportunistic infection in HIV-positive people [11]. It is the primary cause of mortality in these patients [16], and responsible for one-third of all HIV-related deaths [17]. In some studies, it has been found that up to 40% of HIV patients who passed away had also TB [18]. Despite the slow progression of TB at the individual level, its inherent slow dynamics can have significant long-term consequences on the population level. Therefore, it is essential to develop mathematical models that can help estimate future trends and create a better understanding of the long-term outcomes of TB [19].

The primary objective of the End TB Strategy is to reduce TB deaths by 90% and TB incidence by 80% by 2030, compared to 2015 [20,21]. However, since TB is still a leading cause of death in people with HIV, and HIV is the most significant risk factor for latent TB infection progression to active disease [22,23], failing to control the double burden of TB and HIV would not only make it impossible to achieve the aforementioned goals but also jeopardize the elimination of TB by 2050 [24]. Therefore, it is crucial to study patients with coinfection and enhance health programs for controlling both diseases [25]. However, patients with TB and HIV coinfection have not received adequate attention [6].

The Global Burden of Disease Study 2019 revealed that tuberculosis has re-emerged as the most important disease associated with HIV in Iran. Despite a decrease in the burden of other major infectious diseases such as malaria, measles, and diphtheria over the past 30 years, the number of people infected with HIV has increased significantly. This has caused a halt in the decreasing trend of tuberculosis in this country since the mid-2000s [26]. Timely diagnosis and treatment of patients with TB/HIV coinfection is beneficial for these patients [10]. Identifying the key factors affecting the co-occurrence of both will create the basis for the timely identification and treatment of these patients. Therefore, this study was conducted to investigate the epidemiological factors and treatment outcomes of people with TB based on their HIV status in Iran. Moreover, the findings of the present study would also provide appropriate solutions for public policy and planning in this field.

2. Methods

2.1. Study design and source of data

This study was a cross-sectional study that focused on patients diagnosed with tuberculosis in Iran between 2018 and 2021. The information about all the identified tuberculosis patients across the country from March 21, 2018, to March 20, 2021, was obtained from the Tuberculosis and Leprosy Department of the Ministry of Health, Treatment, and Medical Education of the Islamic Republic of Iran.

The National Tuberculosis Registry database consolidates data of all TB patients receiving care at Primary Health Care Centers (PHC) nationwide. Trained staff in PHCs, electronically recorded and routinely reviewed patient information, encompassing diverse epidemiological factors, results of paraclinical tests, and treatment outcomes. In addition, the information recorded in this database is regularly monitored and evaluated by experienced experts.

Drawing from previous research, pivotal factors influencing TB/HIV coinfection were identified from the database. Statistical experts were consulted to deploy optimal statistical methodologies for thorough data analysis.

2.2. Study population

To be eligible for the study, patients had to be diagnosed with either pulmonary tuberculosis (PTB) or extrapulmonary tuberculosis (EPTB) within four years. PTB patients were divided into two groups: those with positive sputum smear (SPPTB) and those with negative sputum smear (SNPTB), as defined by the World Health Organization guidelines [27]. SPPTB patients had at least two positive sputum smears or one positive sputum smear with clinical symptoms and chest radiograph consistent with tuberculosis, while SNPTB patients had negative sputum smears with clinical and radiographic symptoms and their diagnosis of tuberculosis was confirmed by a specialist doctor. Extrapulmonary tuberculosis (EPTB) patients were diagnosed with tuberculosis by their physician based on bacteriological, radiological, histological tests, and other complementary methods, depending on the affected organ. Patients who were

registered as "misdiagnosed," those undergoing retreatment due to recurrence or absence, and those with unclear diagnoses of HIV or TB or missing information about their epidemiological factors and treatment outcomes were excluded from the study.

The study included 30,762 individuals diagnosed with TB based on the inclusion criteria. However, after applying the exclusion criteria, only 25,011 new patients with a confirmed diagnosis of TB were analyzed (see Fig. 1). It is important to mention that if the HIV test result is positive in the final sample of TB patients, these patients are considered to have TB/HIV coinfection.

2.3. Study parameters

This study investigated various epidemiological factors, including nationality (Iranian and non-Iranian), place of residence (urban and rural), marital status (single, married, divorced/widowed), prison history, weight, and age at the time of tuberculosis diagnosis, and delay in diagnosis of tuberculosis (the interval between the onset of TB symptoms and its diagnosis is classified as less than one month, between one and three months, or more than three months). Additionally, the type of tuberculosis (SNPTB, SPPTB, and EPTB) and the status of TB and HIV risk factors were also analyzed. This study classified marital status into three groups: singles, who have never been married; married individuals, who currently have a spouse; and the divorced/widowed group, which includes people who were previously married but are currently living alone due to divorce or death of their spouse. The study also categorized SPPTB

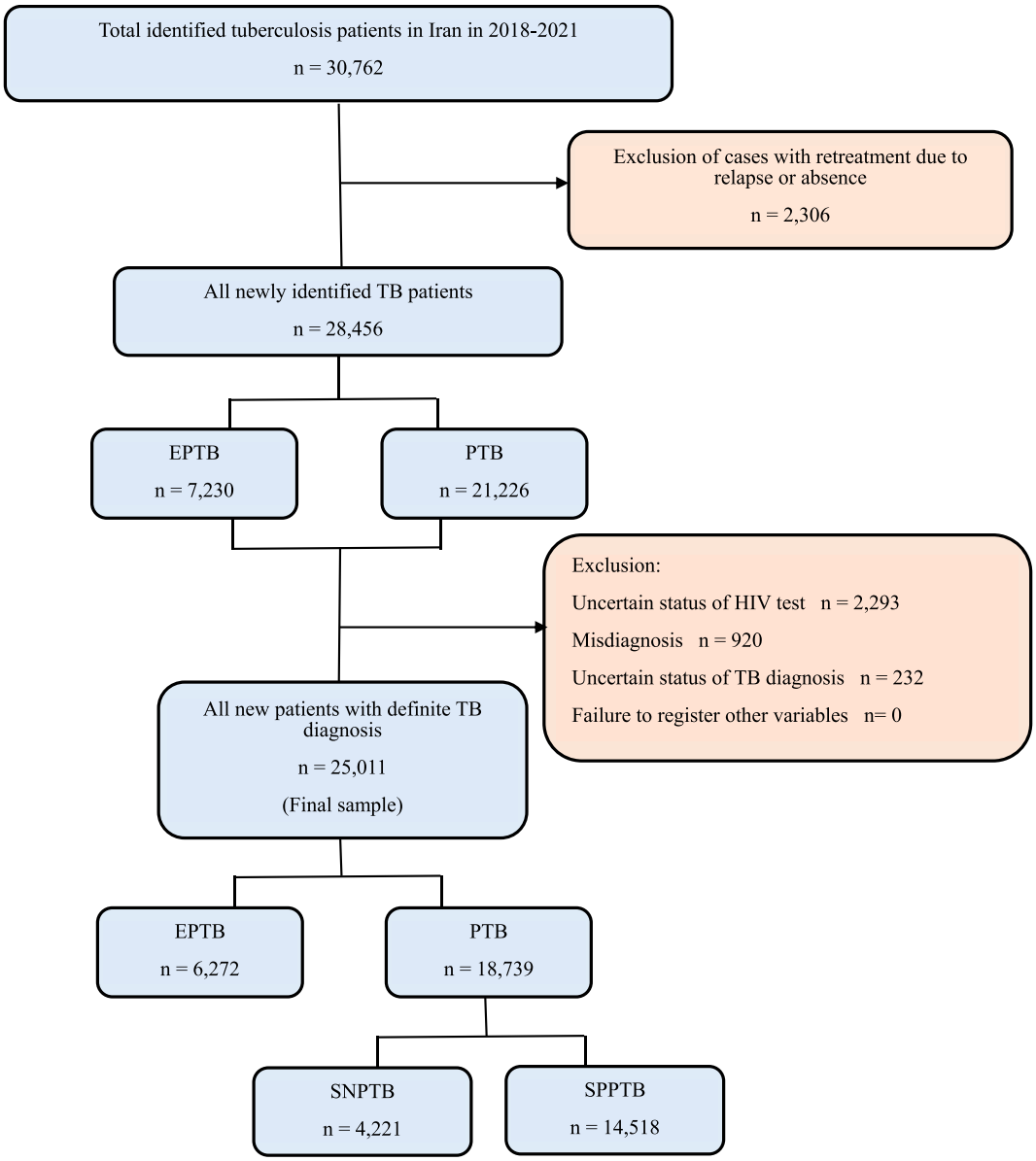

Fig. 1. Enrollment of TB patients for this study.

patients based on the number of acid-fast bacilli observed in their sputum smear, using the World Health Organization's classification into groups 1–9 bacilli in 100 microscopic fields, +1 (10–99 bacilli in 100 microscopic fields), +2 (1–10 bacilli per microscopic field), and +3 (more than 10 bacilli per microscopic field) [28].

The study analyzed available information about TB and HIV risk factors on confirmed TB patients in the database and identified 14 cases of TB and 9 cases of HIV. For each patient, at least one of the risk factors was positive, was considered a risk factor for the disease. Table 1 provides detailed information on these risk factors.

The study examined the therapeutic outcomes of tuberculosis treatment and analyzed them according to the type of tuberculosis diagnosis (SPPTB, SNPTB, and EPTB) in both HIV-positive and negative subgroups. The treatment results were divided into four groups: cured, completion of treatment, treatment failure, and other outcomes (such as death, absence from treatment, or transfer), as defined by the World Health Organization guidelines [27], in Table 2. It is important to note that, according to the national guidelines for tuberculosis control in Iran, the "cured" treatment result is not applicable to SNPTB and EPTB patients because it is not possible to monitor the treatment outcome based on sputum smear in these patients [29].

2.4. Statistical analysis

The patients' identity information was removed, and the data was entered into IBM SPSS version.26 software for analysis. The epidemiological factors and treatment outcomes of all TB patients and HIV-positive and negative subgroups were analyzed at a significance level of 0.05.

This study also investigated the duration of tuberculosis treatment required for complete recovery of the disease. The researchers estimated this duration using a Kaplan-Meier diagram of the survival probabilities for both HIV-positive and HIV-negative groups. In addition to providing descriptive and analytical statistics, the study evaluated the role of underlying factors in TB/HIV coinfection using a multiple logistic regression model. A criterion of P value < 0.25 was used in the multiple logistic regression model to determine which underlying variables to include. The study also analyzed changes in the frequency of TB/HIV coinfection over a four-year period based on the type of tuberculosis diagnosis.

Ethical approval

This study was approved by the Biomedical Research Ethics Committee part of Mashhad University of Medical Sciences (Ethical approval code IR.MUMS.MEDICAL.REC.1401.683), and research was performed following relevant regulations with anonymized data.

3. Results

The Tuberculosis and Leprosy Department of the Ministry of Health, Treatment, and Medical Education of Iran registered 30,762 individuals diagnosed with tuberculosis between 2018 and 2021. Of these individuals, 25,011 new patients with a definite diagnosis were registered based on the inclusion and exclusion criteria and were included in the study. Among the patients, 672 (2.68%) had TB/HIV coinfection, while 24,339 (97.31%) had a negative HIV test.

3.1. Characteristics of patients with TB

Table 3 displays the socio-demographic characteristics of all patients, as well as those specifically with TB/HIV coinfection.

Among the new patients with a definite diagnosis of tuberculosis included in the study, TB/HIV coinfection was more prevalent in men than in women. Specifically, 570 men (4.20%) had TB/HIV coinfection, while only 102 women (0.90%) had it. This difference in TB/HIV coinfection between men and women was statistically significant (P-value$<$0.001).

The study found that the average age at the time of tuberculosis diagnosis was 40.66 $\pm$ 10.55 years for patients with TB/HIV

Table 1
Risk factors related to TB and HIV disease.

TB risk factors	HIV risk factors
HIV infection	Prison history
Tuberculosis infection in the last 2 years	History of the prisoner's wife
Injection addiction/amphetamine compounds	History of injection addiction
Diabetes mellitus	Spouse's history of injecting drug addiction
Silicosis disease	History of risky sexual behavior
Prolonged treatment with corticosteroids	History of sexually risky behavior of the spouse
Taking immunosuppressive drugs	History of receiving blood and blood products
Head and neck cancer	Birth of an HIV-infected mother
Blood and reticuloendothelial malignant diseases	Having an infected spouse
Chronic renal failure	
Gastrectomy or intestinal bypass	
Chronic malabsorption syndromes	
Low body weight (at least 10% less than the desired amount)	
CXR findings suggestive of old tuberculosis in an untreated individual	

Table 2
Treatment outcomes of tuberculosis disease.

The outcome of tuberculosis treatment		Definitions
Success in treatment	**Cured**	A patient with SPPTB whose sputum test was negative at the end of treatment and at least the result of her/his previous sputum test (which was done for the purpose of monitoring during treatment) was also declared negative.
	Completion of treatment	A patient who has received the full course of anti-tuberculosis treatment, but does not have classification criteria in the cured and treatment failure groups (for example, there is no information about the performance or result of her/his sputum test at the end of the treatment).
Failure in treatment	**Treatment failure**	A patient with SPPTB whose direct sputum test is still positive five months (or more) after the start of treatment or becomes positive again within the same period after becoming negative, or a patient with SNPTB whose direct sputum test at the end of the second month of treatment tested positive or a patient who is diagnosed with treatment-resistant tuberculosis at any time during the treatment.
	Deceased	A patient who dies for any reason during the anti-tuberculosis treatment.
	Absence of treatment	A patient whose treatment has been interrupted for 2 consecutive months or more.
	Transferred	A patient who was transferred to another registration and reporting unit (city) after starting the treatment and there is no information about the result of her/his treatment.

Table 3
Baseline characteristics of the diagnosed new TB patients in Iran between 2018 and 2021[a].

Sociodemographic characteristics	Total	TB/HIV Coinfection		P-value[b]
		NO	YES	
Number of patients with TB	25,011 (100.00)	24,339 (100.00)	672 (100.00)	
Age (Years)	49.9422.65	50.2022.84	40.6610.55	<0.001[c]
Weight (Kg)	57.8117.88	57.8617.93	56.1015.60	0.004[c]
Gender				
Female	11,420 (45.65)	11,318 (46.50)	102 (15.17)	<0.001[d]
Male	13,591 (54.34)	13,021 (53.50)	570 (84.82)	
Age grouping of the patients				
<15 y	929 (3.71)	920 (3.78)	9 (1.33)	<0.001[d]
15-35 y	6484 (25.92)	6303 (25.90)	181 (26.77)	
35-63 y	9795 (39.16)	9334 (38.35)	461 (68.19)	
>63 y	7803 (31.19)	7782 (31.97)	21 (3.10)	
Marital status				
Single	5318 (21.26)	5021 (20.63)	297 (43.93)	<0.001[d]
Married	15,757 (63.00)	15,500 (63.69)	257 (38.01)	
Divorced/Widowed	3936 (15.73)	3818 (15.68)	118 (17.45)	
Type of disease				
Smear negative PTB	4221 (16.87)	3972 (16.31)	249 (37.05)	<0.001[d]
1-9 basil	1811 (7.24)	1738 (7.14)	73 (10.86)	
1+	4615 (18.45)	4508 (18.52)	107 (15.92)	
2+	2909 (11.63)	2864 (11.76)	45 (6.69)	
3+	5183 (20.72)	5108 (20.98)	75 (11.16)	
EPTB	6272 (24.84)	6149 (27.72)	123 (18.19)	
Delayed diagnosis (month)				
<1	6919 (27.66)	6682 (27.45)	273 (40.38)	<0.001[d]
1–3	10,409 (41.61)	10,128 (41.61)	281 (41.56)	
>3	7683 (30.71)	7529 (30.93)	154 (22.78)	
Location				
Urban	17,526 (70.07)	16,949 (69.63)	577 (85.86)	<0.001[d]
Rural	7485 (29.92)	7390 (30.36)	95 (14.13)	
Nationality				
Non-Iranian	4571 (18.27)	4554 (18.71)	17 (2.52)	<0.001[d]
Iranian	20,440 (81.72)	19,785 (81.28)	655 (97.47)	
Prison condition				
No	24,346 (97.34)	23,755 (97.60)	591 (87.94)	<0.001[d]
Yes	665 (2.65)	584 (2.39)	81 (12.05)	
Having HIV risk factors				
No	22,029 (88.11)	21,912 (90.05)	117 (17.45)	<0.001[d]
Yes	2982 (11.88)	2427 (9.94)	555 (82.54)	
Having TB risk factors				
No	19,433 (77.69)	19,373 (79.59)	60 (8.92)	<0.001[d]
Yes	5578 (22.30)	4966 (20.40)	612 (91.07)	

[a] Values are reported as Mean SD or frequency (percent).
[b] Significant at the level of 0.05.
[c] Student t-test.
[d] Chi-square test.

coinfection, while it was 50.20 ± 22.84 years for other TB patients. This age difference was statistically significant (P-value<0.001).

Moreover, the results revealed that TB/HIV coinfection was significantly associated with age groups (P-value<0.001). The highest frequency of coinfection was observed in the age group of 35–63 years, while the lowest frequency was observed in the age group of less than 15 years.

Additionally, the results of the present study showed that patients who had both TB and HIV infections had a lower weight at the time of TB diagnosis compared to patients who only had TB. On average, the weight of patients with TB/HIV coinfection was 56.10 ± 15.60 kg, while the weight of other TB patients was 57.86 ± 17.93 kg. This difference was statistically significant (P-value<0.04).

It was also found that TB/HIV coinfection was more frequent in single patients (5.60%), followed by divorced/widowed patients (3.00%) and married patients (1.60%) among all new TB patients. There was a statistically significant relationship between marital status and TB/HIV coinfection (P-value<0.001).

Moreover, considering the type of TB diagnosis, the findings revealed that there was a significant difference in the type of TB diagnosis (SPPTB, SNPTB, and EPTB) among patients with TB/HIV coinfection (P-value<0.001). The majority of patients with co-infection were in the SNPTB group, followed by the EPTB group.

Regarding the duration of TB diagnosis delay, the current study showed that there was a significant difference in the duration of TB diagnosis delay among patients with TB/HIV coinfection (P-value<0.001). Most patients with coinfection experienced a delay of one to three months before being diagnosed with tuberculosis.

Additionally, the prevalence of TB/HIV coinfection was higher among patients living in urban areas (3.30%) compared to those living in rural areas (1.30%). There was a statistically significant relationship between residence and coinfection (P-value<0.001).

According to the results, among the TB patients included in the analysis, 3.20% of Iranian patients and 0.40% of non-Iranian patients had HIV coinfection. This difference was statistically significant in terms of nationality (P-value<0.001).

In addition, the study found that 12.20% of TB patients with a history of prison had HIV coinfection, while only 2.40% of TB patients without a prison history had coinfection. The prevalence of TB/HIV coinfection was higher among patients with a prison history, and this difference was statistically significant (P-value<0.001).

The study also examined tuberculosis patients based on their HIV risk factor status and found that TB/HIV coinfection was reported in 18.60% of patients with an HIV risk factor, compared to only 0.50% of patients without an HIV risk factor. This difference was statistically significant (P-value<0.001). Furthermore, based on the TB risk factor status, the study found that 11.00% of patients with the TB risk factor had TB/HIV coinfection, while only 0.30% of patients without the TB risk factor had coinfection. This difference was also statistically significant (P-value<0.001).

Trends in TB/HIV coinfection from 2018 to 2021.

The trend of the frequency of TB patients diagnosed with TB/HIV coinfection in a 4-year period by the type of TB diagnosis is shown in Fig. 2.

3.2. Treatment outcome of TB patients

Table 4 presents the results of tuberculosis treatment for all new tuberculosis patients and by type of tuberculosis diagnosis. The statistics show that the success rate of TB treatment (i.e., the total number of patients who were cured or completed the treatment course) was 65.02% (437 patients) for those with TB/HIV coinfection and 83.41% (20,302 patients) for those without coinfection. Therefore, patients with TB/HIV coinfection had a lower treatment success rate compared to other TB patients. The results were similar when examining the treatment outcomes by type of diagnosed tuberculosis. However, patients with smear-positive pulmonary tuberculosis had a lower probability of treatment success (i.e., 62.66% for those with HIV infection and 82.08% for those without HIV

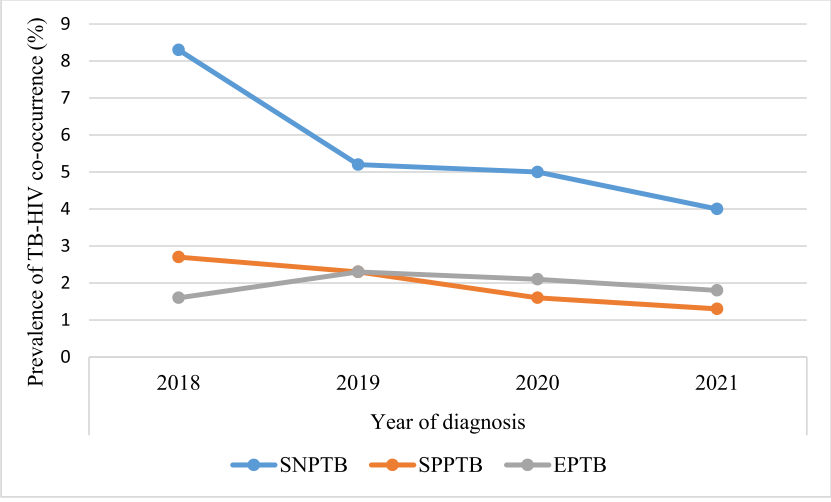

Fig. 2. The temporal trend of the prevalence of TB/HIV coinfection in a 4-year period by the type of TB diagnosed..

infection) compared to other types of tuberculosis. The observed difference in TB treatment outcomes for patients with TB/HIV co-infection was statistically significant for all TB patients and separately for SNPTB, SPPTB, and EPTB (P-value<0.001).

The study found that patients coinfected with TB and HIV had a longer duration of treatment until complete recovery from TB compared to other TB patients. The average time of treatment for coinfection was 11 months with a 95% confidence interval of 10.07–11.92 (95% CI: 10.07–11.92), while it was 8 months with a 95% confidence interval of 7.92–8.07 (95% CI: 7.92–8.07) for other patients. The Log-rank test showed a significant difference in survival rates between patients with and without TB/HIV coinfection (P-value<0.001). Fig. 3 shows the Kaplan-Meyer diagram related to the duration of treatment until complete recovery of tuberculosis based on TB/HIV coinfection. The diagram indicates that the probability of non-recovery in patients with TB/HIV coinfection is higher than in other TB patients (P-value<0.05).

3.3. Associations of TB/HIV coinfection by patient characteristics

The study analyzed the role of underlying factors in TB/HIV coinfection by using a multiple logistic regression model and considering the inclusion of background variables with a p-value less than 0.25. Table 5 displays the details of this analysis.

Results from the multiple LR model revealed that age, gender, marital status (married vs. single), delayed diagnosis, prison, nationality, location, type of disease, having TB risk factors, and HIV risk factors had a significant association with the co-occurrence of TB/HIV (P-value<0.05). However, other variables had not a statistically significant association with the co-occurrence of TB-HIV (P-value>0.05). Therefore, by adjusting the effect of other variables in the model, the odds of co-occurrence of TB/HIV in males was 1.65 times more than in females and this difference is statistically significant (P-value<0.05). Also, by controlling the effect of other variables in the model, having HIV and TB risk factors is positively associated with co-occurrence of TB/HIV and the odds of it in individuals who had HIV and TB risk factors were 17.52 and 29.73 times than in patients without HIV and TB risk factors, respectively (P-value>0.05). As well as by adjusting the effect of other variables, per each unit increase in age, the odds of co-occurrence of TB/HIV declined by 3 percent (P-value<0.05) (Table 5). Receiver operating characteristic (ROC) curves were used to assess the ability of the multiple LR model to predict having co-occurrence of TB/HIV. The Area under the ROC curve (AUC = 0.9574) of the final multiple LR model indicates the well-predictive power of the final model (Fig. 4).

4. Discussion

The study analyzed data from the national tuberculosis database in Iran from 2018 to 2021 and identified 25,011 new tuberculosis patients with a definite diagnosis. Among these patients, 672 (2.68%) tested positive for HIV and had TB/HIV coinfection, while the rest of the patients had negative HIV test results. Meanwhile, other studies investigating TB/HIV coinfection have reported different rates of infection, such as a study in Nigeria that reported a 22.50% coinfection rate among TB patients over 5 years [30], or a study in Kenya, conducted by Wekunda et al. that reported a 35.00% coinfection rate [31]. Another study conducted on HIV/AIDS patients over 18 years of age in Turkey found that 5.30% of these patients had active tuberculosis at the same time [32], while a study in China, done by Wang et al. that examined only EPTB patients reported a 7.00% coinfection rate [33], compared to 2.00% in the present study. The

Table 4
Treatment results of definitive TB patients based on the type of TB diagnosis and HIV test status in the period of 2018–2021.

Type of disease	Treatment outcome	TB patient	TB/HIV Coinfection		P-value[a]
			No	Yes	
SNPTB	Cured	0 (0.00)	0 (0.00)	0 (0.00)	<0.001[b]
	Completed treatment	3473 (82.25)	3307 (83.25)	166 (66.66)	
	Treatment failure	30 (0.71)	29 (0.73)	1 (0.40)	
	Other	718 (17.01)	636 (16.01)	82 (32.93)	
		4221 (100.00)	3972 (100.00)	249 (100.00)	
SPPTB	Cured	10,602 (73.02)	10,446 (73.47)	156 (52.00)	<0.001[b]
	Completed treatment	1257 (8.65)	1225 (8.61)	32 (10.66)	
	Treatment failure	350 (2.41)	343 (2.41)	7 (2.33)	
	Other	2309 (15.90)	2204 (15.50)	105 (35.00)	
		14,518 (100.00)	14,218 (100.00)	300 (100.00)	
EPTB	Cured	0 (0.00)	0 (0.00)	0 (0.00)	<0.001[b]
	Completed treatment	5407 (86.20)	5324 (86.58)	83 (67.47)	
	Treatment failure	1 (0.00)	1 (0.00)	0 (0.00)	
	Other	864 (13.80)	824 (13.40)	40 (32.52)	
		6272 (100.00)	6149 (100.00)	123 (100.00)	
Total	Cured	10,602 (42.38)	10,446 (42.91)	156 (23.21)	<0.001[c]
	Completed treatment	10,137 (40.53)	9856 (40.49)	281 (41.81)	
	Treatment failure	381 (1.52)	373 (1.53)	8 (1.19)	
	Other	3891 (15.55)	3664 (15.05)	227 (33.77)	
		25,011 (100.00)	24,339 (100.00)	672 (100.00)	

[a] Significant at the level of 0.05.
[b] Fisher Freeman-Halton asymptotic test.
[c] Chi-square test.

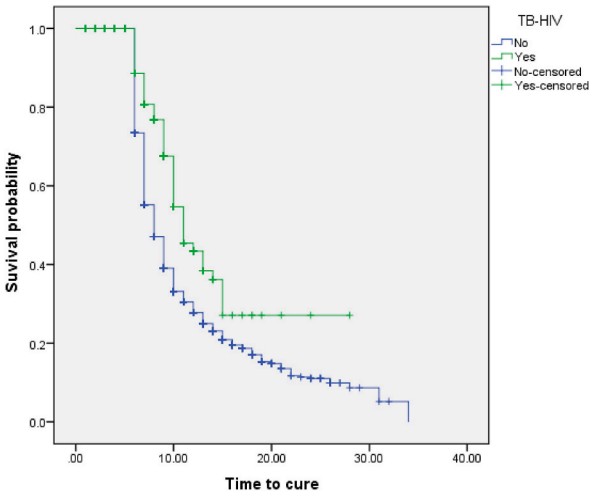

Fig. 3. Estimated survival curves using Kaplan-Mayer for TB/HIV co-occurrence..

Table 5
Investigating the factors associated with co-occurrence of TB/HIV using a multiple logistic regression model.

Variables (reference)		OR (95% CI)[a]	P-value[b]
Age		0.97 (0.96, 0.98)	<0.001
Weight		1.000 (0.994, 1.006)	0.97
Gender (female)	Male	1.65 (1.25, 2.17)	<0.001
Marital status (single)	Married	0.64 (0.50, 0.82)	<0.001
	Widowed/Divorced	1.16 (0.84, 1.59)	0.35
Delayed diagnosis (<1 month)	1–3 months	0.71 (0.56, 0.89)	0.004
	>3 months	0.58 (0.44, 0.75)	<0.001
Prison (no)	Yes	0.71 (0.51, 0.98)	0.03
Nationality (Non-Iranian)	Iranian	3.08 (1.79, 5.27)	<0.001
Location (urban)	Rural	0.49 (0.38, 0.65)	<0.001
Type of disease (SNPTB)	SPPTB	0.21 (0.17, 0.27)	<0.001
	EPTB	0.48 (0.36, 0.64)	<0.001
Having HIV risk factors (no)	Yes	17.52 (13.68, 22.45)	<0.001
Having TB risk factors (no)	Yes	29.73 (22.05, 40.07)	<0.001

[a] OR=Odds Ratio.
[b] Significant at the level of 0.05.

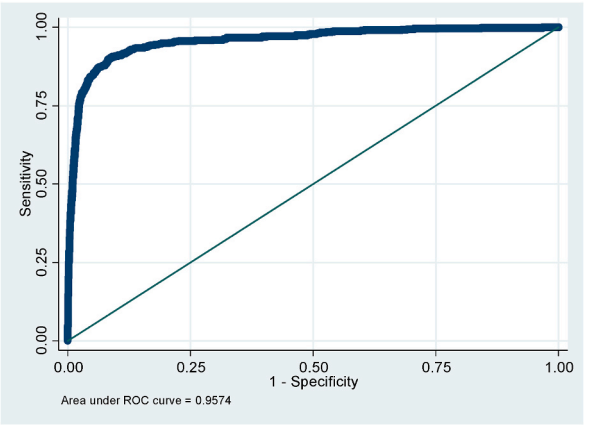

Fig. 4. Evaluating the predictive power of the final multiple LR model using the ROC curve..

differences in these results may be due to variations in population groups in different geographical areas, periods, and inclusion and exclusion criteria used in different studies.

The results of the present study revealed that patients diagnosed with TB/HIV coinfection were on average 9.54 years younger than other patients. This finding is consistent with the results of a study by Suwanpimolkul et al. Moreover, the average age of HIV-positive patients when starting antiretroviral treatment in coinfection with TB was reported to be lower than other patients without coinfection [34], which may suggest that the presence of one disease accelerates the progression of another disease.

The study found that the age group with the highest frequency of TB/HIV coinfection was 35–63 years, while the age group with the lowest frequency was less than 15 years. However, other studies have reported different age groups with the highest number of co-infection, such as the age group of 40–50 years in a study by Tiewsoh et al. [35], and the age group of 40–49 years in a recent study in Ghana. In contrast, the lowest frequency was reported for the age group of 50–59 years in Ghana [36], which differs from the present study where the lowest frequency was observed in the less than 15 years age group. However, a study by Cavalin et al. [37], reported results that are consistent with the present study, with the lowest number of coinfection observed in the age group of less than 19 years. The differences in these results may be due to variations in the classification of age groups used in different studies.

In this study, it was found that men had the highest proportion (84.82%) of TB/HIV coinfection, which is consistent with the findings of other studies [15,38–40]. However, a study conducted in South Africa by Mahtab et al. reported that coinfection was more prevalent in women than in men [41]. A similar result was also observed in a study on active tuberculosis in HIV-positive patients in Nigeria [42]. The variation in gender differences may be due to differences in geographical regions among the studies.

Patients diagnosed with TB/HIV coinfection had lower weight compared to other TB patients, which is in line with the findings of another study that investigated the occurrence of active tuberculosis among HIV-infected patients [34]. This may suggest that the presence of both TB and HIV exacerbates the progression of these diseases.

The present study found that the highest number of TB/HIV coinfection was observed in single patients, which is consistent with the findings of a study conducted by Jalal et al. in Malaysia [40]. However, in studies by Audu et al. in Nigeria [42], and Zerdali et al. in Turkey [32], the highest incidence of active TB among HIV-positive patients was reported in married individuals. The difference in results may be due to variations in geographical and cultural differences among the studied samples, as well as differences in the definition of marital status classification mentioned in these studies.

The results of this study showed that SNPTB patients had the highest proportion (37.05%) of TB/HIV coinfection, followed by EPTB patients with 18.19%. However, in several other studies, TB/HIV coinfection was found to be more common in PTB patients [32,41], and even this result was repeated in a study examining HIV patients as well [35]. However, in these studies, PTB patients were not categorized based on the positive or negative result of sputum smear. In contrast, the present study investigated the PTB patients based on sputum smear results. Some studies that investigated PTB based on sputum smear results, unlike the present study, found that the highest proportion of TB/HIV coinfection was related to SPPTB, followed by SNPTB [36,43]. In line with the findings of the present study in another study, although TB/HIV coinfection was more prevalent in SPPTB patients, there was no difference in the frequency of coinfection between SNPTB and EPTB patients [44]. These studies had a longer timeframe than the present study and different exclusion criteria, which can justify the differences in the results.

In this study, patients with TB/HIV coinfection were diagnosed with tuberculosis with a delay of 1–3 months, which is consistent with the findings of Kraef et al. who reported a delay of more than one month [45]. In Mohammadi et al.'s study, which aimed to investigate the risk factors for late diagnosis of HIV disease, coinfection with TB was identified as one of the most significant factors in predicting late diagnosis of HIV [46]. One possible explanation for this is the atypical clinical manifestations of these two diseases in the presence of each other.

Based on the findings of the current study, the prevalence of TB/HIV coinfection was higher among TB patients residing in urban areas, which is consistent with the results reported in previous studies by Akanbi et al. [47], and Tola et al. [44]. Additionally, Lelisho et al. conducted a study on TB coinfection among HIV-positive individuals and found that coinfection was more common among those living in urban areas [6], which could be attributed to the high population density and increased likelihood of risky behaviors, particularly in the outskirts of cities. Another study conducted in Malaysia with different residence classifications found that the highest rate of TB/HIV coinfection was observed in areas with medium or high-cost housing options such as apartments, condominiums, terrace houses, and bungalows [15].

According to the present findings, TB patients who were incarcerated had a higher likelihood of having TB/HIV coinfection, which is in line with the results of a review study that investigated HIV-infected prisoners. The review study found that HIV-infected prisoners are at a heightened risk of acquiring tuberculosis [48]. The elevated prevalence of TB/HIV coinfection among incarcerated patients could be attributed to prolonged and close contact between prisoners, overcrowding in prisons, and a higher likelihood of engaging in risky behaviors, such as drug injection, within this population group.

The current study reported a 65.02% success rate in TB treatment for patients with TB/HIV coinfection, which is lower than the 83.41% success rate observed in TB patients without coinfection. The analysis based on the type of diagnosed tuberculosis revealed lower success rates in patients with coinfection across all groups. Similar results were reported in the study by Bonsu et al. [35], where the success rate of TB treatment in patients with coinfection was lower. In a study conducted in hospitals and clinics, only 27.90% of patients with TB/HIV coinfection achieved complete success in TB treatment [40]. The difference in results compared to the present study can be attributed to the successful implementation of the Directly Observed Treatment Short-course (DOTS) plan by Iran's healthcare system, resulting in an increased success rate in TB treatment. Another study reported a 76.40% success rate in TB treatment for patients with coinfection [49], which may be due to the hospital-based sampling in this study. The present study found that patients with SPPTB and coinfection had a higher probability of unsuccessful TB treatment compared to other coinfected patients. However, in contrast to these findings, the study by Yang et al. reported a higher probability of unsuccessful TB treatment in HIV coinfection

patients with EPTB compared to PTB patients [39]. It should be noted that in that study, unlike the present study, PTB patients were not analyzed based on smear type.

This study found that patients coinfected with TB and HIV took longer to recover from TB, with an average treatment duration of 11 months compared to 8 months for other TB patients. However, other studies have reported different average durations, such as 8.30 months in Teng et al.'s study [50], and 6–12 months in another study for 48.10% of patients [15], but these studies did not compare TB/HIV coinfected patients to other TB patients. Hayibor et al.'s study reported a treatment duration of more than 6 months for both HIV-positive and HIV-negative groups, while the two groups did not differ from each other [43], which contradicts the findings of the present study. The difference in results may be due to differences in how treatment duration was classified in the Hayibor et al. study (less than 6 months and more than 6 months).

The present study had several strengths, including a large sample size, multi-year trend analysis, and the use of data from the Ministry of Health and Medicine, which has improved the accuracy and completeness of the data. However, one of the limitations of the study was its cross-sectional design, which did not allow for the investigation of causal relationships.

5. Conclusion

There are emerging concerns about a potential upsurge in TB/HIV coinfection in many resource-limited settings, such as Iran. The findings of the present indicated that various factors such as gender, marital status, nationality, region of residence, age at diagnosis, type of diagnosed tuberculosis, delay in diagnosis, and having TB or HIV risk factors have a significant role in TB/HIV coinfection. These results provide a basis for further planning to improve the identification and treatment of patients at risk of TB/HIV coinfection. Based on these findings, it is recommended that the healthcare system adapt its TB care program to high-risk groups based on the above variables. It is also suggested that HIV screening be conducted regularly for TB patients at higher risk of TB/HIV coinfection. Considering the goal set in the 3rd global Sustainable Development Goal of promoting healthy lives and well-being for all by 2030, and the End TB Strategy to reduce TB deaths and TB incidence by 2030, applying such measures in the care programs of TB patients through faster identification and treatment of HIV in them will provide the basis for improving the health status of these patients in the future.

Submission statement

All authors declare that this manuscript was submitted solely to this journal, and the work described therein is original research that has not been published previously and is not under consideration for publication elsewhere in whole or in part.

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Ethics statement

We confirm that this study was conducted in accordance with established ethical guidelines. This study was approved by the Biomedical Research Ethics Committee part of Mashhad University of Medical Sciences (approval number: IR.MUMS.MEDICAL.REC.1401.683). All the data were de-identified and provided by the National Tuberculosis Registry database of Iran. Therefore, identifiable individuals were not involved in the current study.

Data availability statement

The study's ownership is held jointly by the Mashhad University of Medical Sciences and the Ministry of Health, Treatment, and Medical Education of Iran. The authors do not have permission to share data. Therefore, the data related to the present study has not been placed in a publicly available repository. If the license is obtained, access to the raw data can be granted in the form of an Excel file.

CRediT authorship contribution statement

Seyedeh Vajiheh Kazemian: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Mohammadtaghi Shakeri:** Writing – review & editing, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Conceptualization. **Eisa Nazar:** Writing – review & editing, Visualization, Validation, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation. **Mahshid Nasehi:** Visualization, Validation, Supervision, Software, Project administration, Investigation, Data curation. **Saeid Sharafi:** Visualization, Validation, Supervision, Software, Project administration, Investigation, Data curation. **Maliheh Dadgarmoghaddam:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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