

Comparative Analysis of Tuberculosis Patterns in Migrant and Local Communities Across Türkiye

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ABSTRACT

Objective: This study investigates changes in tuberculosis incidence among migrant and local populations in the Kayseri and Adana regions of central and southern Türkiye, compared to the pre-migration period.

Materials and Methods: This multicenter retrospective study analyzed data from patients hospitalized for tuberculosis at three regional tertiary care hospitals from May 2011 to April 2024. The study identified whether patients were migrants or non-migrants, assessed their immunosuppressive status, drug resistance, and the sites of tuberculosis involvement.

Results: The study included 280 participants, comprising 55 migrants and 225 non-migrants. Among migrants, males (92.7%) represented a significantly higher proportion compared to non-migrants ($p < 0.001$). Immunosuppression was also more prevalent in migrants ($p < 0.001$). The cavitation rate in pulmonary tuberculosis was 50.9% in migrants and 28.9% in non-migrants ($p = 0.002$). Migrants also exhibited a higher incidence of positive tuberculosis (TB) cultures. The rates of drug resistance were similar between the two groups, showing no increase from the pre-migration data. However, the frequency of drug resistance testing was lower than the national average. Multiple logistic regression analysis indicated that an immunosuppressive condition significantly increased the risk of mortality (odds ratio [OR]=3.681).

Conclusion: The study highlights a higher prevalence of immunosuppression and cavitation in pulmonary TB among migrants. Tuberculosis cases among refugees have increased significantly since 2011, although drug resistance rates have not. Areas with more widespread drug resistance testing requires further studies.

Keywords: Cavitory, migration, public health, Syrian refugees, tuberculosis.



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INTRODUCTION

The Syrian civil conflict, which escalated in 2011, has led to an unprecedented migration crisis, with millions seeking refuge in neighboring countries, including Türkiye. Türkiye has become the leading global recipient of refugees through its humanitarian efforts directed towards Syrians.



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Despite Türkiye's efforts to provide preventive health services and vaccination programs in refugee camps, the high number of refugees living outside the camps and the inadequate vaccination coverage within the camps contribute to an increased prevalence of infectious diseases. Among these challenges, the resurgence and transmission dynamics of tuberculosis (TB) have emerged as a critical concern.

Previous studies have documented the association between migration and the spread of infectious diseases, including TB.¹ However, the specific impact of the Syrian refugee crisis on TB's demographic and racial distribution, as well as on the development of drug resistance in Türkiye, remains inadequately explored.

This multicenter study aims to examine the changes in organ involvement, drug resistance, and mortality rates of tuberculosis cases in the Kayseri and Adana regions of Türkiye following the large-scale Syrian migration compared to the pre-migration period. The findings aspire to contribute to the body of knowledge concerning the intersection of migration and infectious diseases, thereby offering insights into the challenges and strategies for tuberculosis control arising from large-scale human migrations.

MATERIALS AND METHODS

The multicenter study was conducted in accordance with the Declaration of Helsinki and was approved by the Erciyes University Faculty of Medicine Clinical Research Ethics Committee [Decision number: 2024/212; Date: 27/03/2024]. This cross-sectional study retrospectively examined patients hospitalized for tuberculosis in three centers in the Kayseri and Adana regions between May 2011 and April 2024. The inclusion criteria were adults aged 18 years and older who had positive cultures for *Mycobacterium tuberculosis*, were smear-positive, exhibited pathologically confirmed caseous granulomatous inflammatory lesions after excluding other causes, responded to treatment, and/or clinically compatible patients who tested positive for TB polymerase chain reaction (TB-PCR). Exclusion criteria included patients with granulomatous inflammatory lesions caused by conditions other than tuberculosis, non-tuberculous mycobacteria, patients whose data could not be accessed, and those for whom TB was not considered based on advanced diagnostic tests. Additionally, since the data pertained to inpatient cases, tuberculosis cases treated on an outpatient basis were omitted.

The collected data included demographic information such as age, gender, and racial situation; clinical data including medical history, presence of immunosuppression like chronic kidney disease (CKD), Human Immunodeficiency Virus (HIV)

KEY MESSAGES

- **Increased Immunosuppression and Cavitory Disease in Migrants:** Migrants exhibit a significantly higher prevalence of immunosuppression and cavitory pulmonary tuberculosis compared to non-migrants.
- **Stable Drug Resistance Rates Despite Increased Tuberculosis (TB) Cases:** While tuberculosis cases among refugees have risen significantly since 2011, drug resistance rates have remained stable, emphasizing the effectiveness of current TB treatment protocols and the necessity for continued surveillance.
- **Higher Mortality Risk Associated with Immunosuppression:** Immunosuppression condition independently increases the risk of mortality.

status, and organs affected by tuberculosis; and outcome measures like the presence of cavities in pulmonary TB, TB culture results, drug resistance profiles, length of hospital stay, discharge outcomes, and mortality.

Statistical analysis was performed using the R software. Descriptive statistics summarized the demographic and clinical characteristics of the participants. Continuous variables were expressed as mean \pm standard deviation or median (range), and categorical variables as frequencies and percentages. Differences between immigrants and non-immigrants were analyzed using t-tests for continuous variables and chi-square tests for categorical variables. The p-values were calculated to determine statistical significance. To determine the independent risk factors associated with mortality among individuals with tuberculosis, we conducted a logistic regression analysis. Both univariate and multiple logistic regression models were employed to identify significant predictors of death.

Initially, univariate analyses were performed to calculate odds ratios (OR) and 95% confidence intervals (CI) for each variable. Variables included anti-tumor necrosis factor (anti-TNF) usage, immunosuppression condition, cancer status, and central nervous system involvement. Variables with a p-value less than 0.05 in the univariate analysis were considered for inclusion in the multiple analysis model.

Subsequently, a multiple logistic regression analysis was conducted to adjust for potential confounding factors and to assess the independent effects of the variables on mortality. Analyses were stratified by migration status to evaluate differences in TB manifestations, drug resistance, and hospital outcomes.

Table 1. Demographic and clinical profiles of participants stratified by migration status

Variables	Total (n=280)	Immigrant (n=55)	Non-Immigrant (n=225)	p
Gender (female)	100 (35.7%)	4 (7.3%)	96 (42.7%)	< 0.001
Age, Median (min–max) (year)	54 (16–88)	48 (16–83)	54.5 (16–88)	0.095
Any immunosuppressive condition, n (%)	93 (33.2%)	36 (65.5%)	57 (25.3%)	< 0.001
Chemotherapy (CT) status, n (%)	7 (2.5%)	1 (1.8%)	6 (2.7%)	0.718
Diabetes mellitus (DM), n (%)	36 (12.9%)	7 (12.7%)	29 (12.9%)	0.965
Chronic kidney disease (CKD), n (%)	14 (5.0%)	0 (0.0%)	14 (6.2%)	0.058
Presence of Cancer, n (%)	20 (7.2%)	3 (5.5%)	17 (7.6%)	0.582
Anti-TNF usage, n (%)	12 (4.3%)	1 (1.8%)	11 (4.9%)	0.313
HIV status, n (%)				0.001
Present	1 (0.4%)	1 (1.8%)	0 (0.0%)	
Absent	240 (85.7%)	54 (98.2%)	186 (82.5%)	
Unknown	39 (13.9%)	0 (0.0%)	39 (17.3%)	
Other risk factors, n (%)	4 (1.4%)	0 (0.0%)	4 (1.8%)	0.323

CT: Chemotherapy; Anti-TNF: Anti-tumor necrosis factor; HIV: Human immunodeficiency virus. The term 'Other Risk Factors' refers to other unspecified conditions that weaken the immune system, such as steroid use and malnutrition.

RESULTS

The study comprehensively examined the demographic and clinical attributes of participants categorized by migration status, involving 55 immigrants and 225 non-immigrants.

The median age was distinctly lower in the immigrant group at 48 years (range 16–83) compared to the non-immigrant group, which had a median age of 54 years (range 16–88) ($p=0.095$). The gender distribution revealed a significantly higher percentage of males in the immigrant group (92.7%) than in the non-immigrant group (57.3%, $p<0.001$) (Table 1).

In terms of immunosuppression, a notably higher prevalence was observed in immigrants (65.5%) compared to non-immigrants (25.3%) ($p<0.001$). All immigrants were free from chronic kidney disease (CKD), while 6.2% of non-immigrants had CKD ($p=0.058$). The status of Human Immunodeficiency Virus (HIV) was significantly different between the groups, with 1.8% of immigrants testing positive compared to none in the non-immigrant cohort ($p=0.001$) (Table 1).

Tuberculosis Manifestations and Outcomes

Immigrants showed a significantly higher incidence of cavity presence in pulmonary TB at 50.9%, compared to 28.9% in non-immigrants ($p=0.002$). The culture results for TB also differed significantly, with 78.2% of immigrants showing positive cultures, in contrast to 52.9% in non-immigrants ($p=0.001$) (Table 2).

Drug resistance testing was conducted on 127 patients (45.4%), revealing five patients had isolated isoniazid (INH) resistance. Combined INH and rifampicin (RIF) resistance was found in only one patient. There were no differences in drug resistance between the migrant and non-migrant groups.

The median length of hospital stay was slightly lower for immigrants at two days (range 0–34) compared to 5 days (range 0–75) for non-immigrants, though this was not statistically significant ($p=0.540$). Discharge rates were high across both groups, with 98.1% of immigrants and 95.1% of non-immigrants being discharged, reflecting no significant difference ($p=0.333$) (Table 2).

Regression Analysis

In the univariate logistic regression analysis, various variables were examined for their association with mortality in individuals with TB (Table 3). The results showed that anti-TNF usage was not significantly associated with mortality [$p=0.450$, OR=2.300 (95% CI, 0.265–19.969)]. In contrast, an immunosuppression (IS) condition significantly increased the risk of death [$p=0.024$, OR=4.167 (95% CI, 1.206–14.392)]. Cancer status did not have a significant association with mortality [$p=0.999$, OR=0 (95% CI, 0.000-not applicable, NA)]. Central nervous system (CNS) involvement emerged as a significant protective factor [$p=0.034$, OR=0.047 (95% CI, 0.003–0.799)].

In the multiple logistic regression analysis, the independent effects of the variables on mortality were further evaluated. The use of anti-TNF showed no significant independent effect on mortality

Table 2. Tuberculosis characteristics and outcomes stratified by migration status

Variables	Total (n=280)	Immigrant (n=55)	Non-Immigrant (n=225)	p
TB-PCR result, n (%)				0.461
Positive	27 (9.6%)	5 (9.1%)	22 (9.8%)	
Not tested	126 (45%)	21 (38.2%)	105 (46.7%)	
Positive culture result, n (%)	162 (57.9%)	43 (78.2%)	119 (52.9%)	0.001
Positive ARB result, n (%)	119 (42.5%)	23 (41.8%)	96 (42.7%)	0.909
Cavity presence, n (%)	93 (33.2%)	28 (50.9%)	65 (28.9%)	0.002
Pulmonary involvement, n (%)	242 (86.4%)	52 (94.5%)	190 (84.4%)	0.050
Tuberculous empyema, n (%)	2 (0.7%)	0 (0.0%)	2 (0.9%)	0.483
Tuberculous pleurisy, n (%)	29 (10.4%)	6 (10.9%)	23 (10.2%)	0.881
Intrathoracic lymphadenitis, n (%)	49 (17.5%)	14 (25.5%)	35 (15.6%)	0.083
Extrathoracic lymphadenitis, n (%)	8 (2.9%)	2 (3.7%)	6 (2.7%)	0.690
Tuberculous meningitis, n (%)	1 (0.4%)	0 (0.0%)	1 (0.4%)	0.620
CNS involvement, n (%)	3 (1.1%)	0 (0.0%)	3 (1.3%)	0.389
Peritoneal/GIS involvement, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Genitourinary involvement, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Extrapulmonary skeletal involvement, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Vertebral involvement, n (%)	1 (0.4%)	0 (0.0%)	1 (0.4%)	0.620
Pericardial involvement, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	NA
Rifampicin (RIF) resistance, n (%)	1 (0.8)	0 (0.0%)	1 (0.9%)	0.677
Isoniazid (INH) resistance, n (%)	5 (3.9%)	2 (210.5%)	3 (2.7%)	0.104
Combined RIF and INH resistance, n (%)	1 (0.8)	0 (0.0%)	1 (0.9%)	0.655
Pre-XDR-TB status, n (%)				0.974
Absent	142 (50.7%)	28 (50.9%)	114 (50.7%)	
Not tested	138 (49.3%)	27 (49.1%)	111 (49.3%)	
XDR-TB status, n (%)				0.974
Absent	142 (50.7%)	28 (50.9%)	114 (50.7%)	
Not Tested	138 (49.3%)	27 (49.1%)	111 (49.3%)	
Length of hospital stay median (min–max) (day)	4 (0–75)	2 (0–34)	5 (0–75)	0.540
Outcome (discharged, etc.), n (%)				0.333
Examined	12 (4.3%)	1 (1.9%)	11 (4.9%)	
Discharged	266 (95.7%)	52 (98.1%)	214 (95.1%)	

TB-PCR: Tuberculosis polymerase chain reaction; ARB: Acid-fast bacilli; GIS: Gastrointestinal; CNS: Central nervous system; Pre-XDR-TB: Extensively drug-resistant tuberculosis; XDR-TB: Extensively drug-resistant tuberculosis; NA: Not applicable.

(p=0.601, OR=1.817, 95% CI: 0.194–17.011). Immunosuppression condition remained a significant independent risk factor for death, with a p-value of 0.047 and an OR=3.681 (95% CI, 1.017–3.327). Central nervous system involvement was found to have a p-value of 0.064 and an odds ratio of 0.059 (95% CI, 0.003–1.185%), indicating a potential protective trend, although it was not statistically significant in the multiple model (Table 3).

DISCUSSION

The study highlights the ongoing public health challenge posed by tuberculosis in Türkiye, especially among migrant populations. This study, conducted in the southern regions of Türkiye following the intense migration from Syria, observed that cavitory disease was more frequently found, particularly among male migrants. A review of data from Türkiye between

Table 3. Univariate and multiple logistic regression model determining independent risk factors for death among individuals with tuberculosis (TB)

Variable	Univariate analysis			Multiple analysis		
	p	OR	95% CI	p	OR	95% CI
Anti-tumor necrosis factor (anti-TNF) usage	0.450	2.300	0.265–19.969	0.601	1.817	0.194–17.011
IS condition	0.024	4.167	1.206–14.392	0.047	3.681	1.017–3.327
Cancer status	0.999	0	0.000–NA	–	–	–
CNS involvement	0.034	0.047	0.003–0.799	0.064	0.059	0.003–1.185

OR: Odds ratio; CI: Confidence interval; CNS: Central nervous system; IS: Immunosuppression; NA: Not applicable.

2011 and 2020 indicates a significant increase in the number of refugees diagnosed with tuberculosis,² but no significant increase in drug resistance.

Tuberculosis remains a major public health issue globally, including in Türkiye. In 2019, it was estimated that 10 million people were affected by tuberculosis worldwide, with 1.2 million TB-related deaths.³ Individuals with laryngeal involvement, cavitory lesions, and acid-fast bacilli (AFB) positive results have a higher risk of transmission. Controlling tuberculosis involves promptly screening and providing prophylactic treatment to individuals with infectious cases.

Türkiye, which hosts the largest number of Syrian refugees, has faced unique public health challenges, particularly regarding TB control and prevention. Since 2011, there has been a substantial increase in the number of tuberculosis cases among Syrians.⁴ The number of Syrian cases, which was zero in 2011, reached 595 in 2018 in Türkiye. Poor hygiene conditions, homelessness, and refugee status due to wars have led to an increase in many infectious diseases, including tuberculosis.⁵ The interaction between population movement and TB epidemiology is complex, influenced by factors such as living conditions, access to healthcare, and the prevalence of drug-resistant TB strains among the refugee population. Although the literature recommends conducting tuberculin skin tests (TST) and chest X-ray screenings for latent tuberculosis infection (LTBI) for migrants, when necessary, analyses of the cost-effectiveness of these screening programs reveal that the impact of current screening programs is low while the costs are high. A study conducted in the Urfa region of Türkiye found that tuberculosis was transmitted to more individuals through refugees who entered the country due to the war.⁶

The most recent data from 2020 indicates that males comprised 57.2% of tuberculosis cases in Türkiye.² In 2022, 55% of individuals diagnosed with tuberculosis worldwide were men, and 33% were women.² In our study, the total percentage

of male participants was 64.3%. Among the non-immigrant group, the rate of males was similar to the national data at 57.3%, whereas in the immigrant group, 92.7% were male. This may be due to a lack of access to healthcare services and the fact that men migrating from regions with a high prevalence may have been previously infected or may be carriers of latent tuberculosis.

Additionally, stress, inadequate nutrition, and psychosocial pressures could further compromise their resistance to tuberculosis. Furthermore, the necessity for migrant men to work in low-wage, strenuous, and unhealthy jobs could increase the spread and impact of the disease. The study also showed that sexually transmitted infections are more prevalent among immigrant men.⁷ This may be related to the high prevalence of men who have sex with men within the immigrant male population, although present in only one HIV positive (+) case in our study.

When examined in terms of organ involvement, our study found that consistent with the literature, the lungs were most affected (86.4%). Following this, intrathoracic lymph node involvement (17.5%) and tuberculosis pleurisy (10.4%) were the most common. According to our country's 2020 data, the most common extrapulmonary site of involvement is the extrathoracic lymph nodes (32.6%).² This is followed by pleural (22.3%) and intrathoracic lymph node (9.4%) involvement.

One of the most observed clinical characteristics of TB is pulmonary cavitation. This accounts for over 40% of adults with pulmonary TB at the time of diagnosis.⁸ Also, cavitation is responsible for a higher bacterial load in sputum, poor clinical outcomes, and easier transmission of infection.⁹ Additionally, treatment failure and relapse rates are higher in patients with cavitory disease.¹⁰ A study conducted in China reported that diabetes and multidrug resistance are risk factors for cavitation.¹¹ In our study, despite the lack of significant differences in chemotherapy, anti-TNF agent use, and diabetes

mellitus, cavitory lesions were significantly more common in the immigrant group ($p=0.002$). This may be due to the higher prevalence of immunosuppressive conditions, HIV, and chronic kidney disease among immigrants. Additionally, the high virulence of the Mycobacterium and poor living conditions could have affected immunity, increasing the risk of cavitory infection. This underscores the potential for high transmission rates in this patient group and indicates the need for stricter implementation of prevention protocols. In our study, the culture positivity rate was significantly higher among migrants ($p=0.001$). This can be explained by the higher prevalence of pulmonary cavitory disease in this population.

Following the migration, 5% of the multidrug-resistant tuberculosis (MDR-TB) cases in Türkiye in 2016 were of Syrian origin. In subsequent years, this rate decreased due to health policies.¹² In 2019, there were approximately 0.5 million cases of drug-resistant tuberculosis, of which 78% were resistant to multiple TB drugs. The problem of multidrug resistance TB, defined as simultaneous resistance to at least rifampicin and INH, the two most effective first-line anti-TB drugs, complicates the management of TB.¹² In our study, the percentage of patients who underwent drug susceptibility testing was 45.4%. According to data from the Turkish Ministry of Health, the average rate reported over the last nine years is approximately 64%. The lower testing rate in our study could be attributed to the high cost of these tests. Also, in patients who underwent drug susceptibility testing, the rate of INH resistance was 1.8%, with no significant difference between migrant and non-migrant individuals. According to the Ministry of Health's 2011 and 2020 data, the rate of isolated INH resistance was reported to be higher at 5.2%. The lower rate observed in our study may be attributed to fewer drug susceptibility tests performed. Despite this, our study found the MDR-TB rate to be 0.4%, consistent with the Ministry of Health data. Despite fewer drug susceptibility tests being performed, the similarity of this finding suggests that the actual combined resistance rate may be higher. In the hospitals participating in our study, no pre-extensively drug-resistant TB (Pre-XDR-TB) cases were detected. In contrast, the Ministry of Health data shows a significant decrease in MDR among migrants and non-migrants over the past ten years. One reason for the absence of MDR in our study may be that only hospitalized patients were screened. Another reason could be that patients with Pre-XDR-TB detected on an outpatient basis were referred to specialized centers for treatment.

Central nervous system tuberculosis is a fatal condition caused by the hematogenous spread of Mycobacterium tuberculosis from primary sites across the blood-brain barrier,¹³ leading to cerebral pathology and granulomatous inflammation at the base of the meninges. In tuberculosis with CNS involvement,

mortality rates can be around 20%, while complications can reach up to 50%.^{14,15} In a study including 116 cases of tuberculosis with CNS involvement, it was found that CNS involvement increased mortality by a factor of 5.69.¹⁶ According to the country's general data, CNS involvement increased from 2.7% in 2009 to 4.3% in 2020. In our study, the rate of CNS involvement was 1.5%, and no difference was observed between migrants and non-migrants. In our study, although univariate analysis found CNS involvement to be associated with mortality, no significant association was observed in the multiple analysis ($p=0.059$). This may be due to the limited sample size, and a specific region. However, nationwide data show a significant increase in CNS involvement compared to the pre-migration period, indicating a rise in military disease due to increased migration.²

Tuberculosis is also a significant infection in immunocompromised patients due to its increased morbidity and mortality. The clinical presentation and severity of tuberculosis in immunocompromised patients vary according to the degree of immunosuppression. The increasing use of immunosuppressive drugs, HIV infection, and transplants in these patient groups necessitate latent TB screening and prophylaxis for early disease recognition and prevention. In a large cohort study conducted among pre-2015 immigrants in Canada, it was observed that the risk of respiratory disease mortality nearly tripled in any given year. However, the relationship between immunosuppression and mortality was not examined.¹⁷ Ethnicity, cavities, and drug resistance were not associated with mortality. In contrast, the presence of severe immunosuppression due to HIV was found to increase mortality in tuberculosis by 3.48 times.¹⁸ In our study, although the presence of immunosuppression was found to have a significant impact on mortality, CNS involvement was not statistically significant and should be further supported by larger cohorts with an expanded patient population.

Our study has certain limitations. The most significant limitations are the limited number of patients and the fact that the study was conducted using records from only three tertiary healthcare institutions. Also, survival analysis could not be performed due to the lack of data on the causes of death and the duration from diagnosis to death.

CONCLUSION

This study, conducted in the southern and inner region Türkiye following the Syrian migration, observed a higher prevalence of cavitory disease among male migrants. While tuberculosis cases among refugees have significantly increased since 2011, drug resistance rates have not risen. Further studies are needed where drug resistance tests are conducted more extensively.

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