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Original Research Article

Evaluation of diagnostic outcomes and management of healthcare personnel with positive tuberculin skin tests referred for latent tuberculosis infection assessment at prince sultan military medical city: a retrospective cohort study

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ABSTRACT

Background: Healthcare workers (HCWs) are at increased risk of latent tuberculosis infection (LTBI) due to occupational exposure. However, the diagnostic outcomes, agreement with confirmatory testing, and treatment adherence in this population remain underexplored. This study aimed to evaluate the proportion of TST-positive HCWs diagnosed with LTBI, assess TST-IGRA agreement, and determine treatment initiation and completion rates.
Methods: We conducted a retrospective cohort study of 64 HCWs with positive TST results who were referred to the ID clinic at PSMMC from January to December 2025. Data were abstracted from electronic medical records. LTBI diagnosis was defined as positive interferon-gamma release assay (IGRA) or initiation of LTBI treatment. Agreement between TST and IGRA was tested with Cohen's kappa. We used univariate and multivariable logistic regression to identify predictors of LTBI.
Results: Of the 64 participants, 40.6% (n=26) were diagnosed with LTBI. IGRA testing was performed in 32.8% (n=21). The agreement between TST and IGRA was poor (kappa=-0.095, p=0.329). Treatment was initiated in 80.8% (21/26) of diagnosed cases, and completion among those who started was 42.9% (9/21). In univariate analysis, nationality (p=0.031), department (p=0.043), and TST size (p=0.014) were significantly associated with LTBI. However, multivariable regression failed to identify independent predictors (overall model p=0.225).
Conclusions: Over one-third of referred HCWs were diagnosed with LTBI. TST showed poor agreement with IGRA, highlighting the need for confirmatory testing. Treatment completion rates were suboptimal, suggesting enhanced adherence support strategies are required.

Keywords: Latent tuberculosis, Healthcare workers, Tuberculin skin test, Interferon-gamma release assay, Saudi Arabia, Retrospective cohort

INTRODUCTION

Tuberculosis (TB) remains a major global cause of infectious disease morbidity and mortality despite substantial advances in diagnosis, treatment, and prevention. In 2023, an estimated 10.8 million people developed TB worldwide, and approximately 1.25 million died from the disease.[1] Although global incidence has declined compared with earlier decades, progress toward the World Health Organization (WHO) End TB targets remains insufficient, emphasizing the continued importance of detecting and treating latent tuberculosis infection (LTBI) among populations at increased risk.[1,2]

Healthcare personnel represent a key occupational risk group because of repeated exposure to patients with

undiagnosed or infectious pulmonary TB, respiratory secretions, laboratory specimens, and aerosol-generating procedures. International recommendations therefore identify TB screening, infection-control measures, and treatment of LTBI as important components of occupational health programs.[2,3] In Saudi Arabia, this issue is particularly relevant because the healthcare workforce is highly multinational and includes personnel originating from countries with substantially different TB burdens. A recent Saudi systematic review and meta-analysis including 11 studies and 11,249 healthcare workers estimated a pooled LTBI prevalence of 24%, with substantial heterogeneity across settings and higher risk in several occupational and demographic subgroups.[4]

Both the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) are used to identify *Mycobacterium tuberculosis* infection. Although the TST remains inexpensive and widely accessible, its specificity may be reduced by previous bacillus Calmette-Guérin (BCG) vaccination and exposure to non-tuberculous mycobacteria.[5] IGRAs use *M. tuberculosis*–specific antigens and are less affected by BCG vaccination, making them particularly useful in BCG-vaccinated populations.[3,5] This distinction is especially important in Saudi Arabia, where BCG vaccination is common and TST-positive healthcare personnel may otherwise undergo unnecessary investigation or preventive therapy.

Saudi studies have demonstrated substantial variability in TST positivity and TST–IGRA concordance. Among 2,650 newly hired healthcare workers in 4 tertiary hospitals in Riyadh, 11% had a positive TST, with higher prevalence among physicians, nurses, older personnel, and workers originating from high-burden countries.[6] In another Riyadh tertiary-care study of 1,412 healthcare workers undergoing preemployment screening, overall TST–QuantiFERON agreement was 73.7%, but κ was only 0.33; notably, 16.3% were TST-positive but IGRA-negative.[7] A separate study of a highly diverse healthcare workforce in Riyadh similarly demonstrated important differences between TST and IGRA results.[8] Among 520 healthcare workers serving during the Hajj, 98.5% had received BCG vaccination and LTBI prevalence by IGRA was 10.8%, again highlighting discordance between testing approaches.[9] More recently, a Makkah study reported TST positivity of 26.3%, IGRA positivity of 19.5%, and only moderate concordance between the tests (κ=0.62), while BCG vaccination influenced TST more strongly than IGRA results.[10]

Occupational exposure itself remains important. A study across 14 military hospitals found TST positivity in 26.9% of healthcare workers, while only 21.4% of TST-positive personnel were also IGRA-positive; providing TB patient care for at least 1 year independently increased the odds of LTBI.[11] In Bisha, 66 of 561 healthcare workers had TST induration greater than 10 mm, with age, sex, and nationality independently associated with LTBI.[12] At prince sultan military medical city (PSMMC), a recent study of 771 nurses working in critical-care areas reported an LTBI prevalence of 34.5%, with substantial variation by clinical location and duration of employment.[13] These findings demonstrate that occupational TB risk remains clinically relevant within PSMMC itself.

However, identifying a positive screening result is only the first step in the LTBI care pathway. Effective prevention requires clinical assessment, exclusion of active TB, confirmatory testing when appropriate, initiation of preventive treatment, and treatment completion. Saudi data indicate meaningful losses across this cascade. In a postexposure study at a tertiary hospital in Riyadh, fewer than half of healthcare workers with negative or unknown baseline TST status completed recommended post-exposure testing.[14] In another Saudi study, although 18% of participating healthcare workers reported LTBI, only about two-thirds accepted treatment and 55% of those who started therapy completed it.[15]

PSMMC has an established pathway in which healthcare personnel with positive TST results are referred to the infectious diseases department for further assessment. Yet the downstream diagnostic and management outcomes of this pathway have not been systematically characterized. Accordingly, this study aims to determine the proportion ultimately diagnosed with LTBI after referral, assess IGRA utilization and TST-IGRA agreement, quantify preventive-treatment initiation and completion, and identify demographic and occupational factors associated with LTBI diagnosis.

METHODS

Study design and setting

This retrospective cohort study evaluated the diagnostic outcomes and subsequent management of healthcare personnel with positive TST results who were referred for LTBI assessment at PSMMC, Riyadh, Saudi Arabia. PSMMC is a large tertiary-care medical center with an established occupational health tuberculosis screening program and a defined referral pathway to the infectious diseases (ID) clinic for personnel with positive screening results. The study included referrals occurring from 01 January through 31 December 2025.

The study was designed and reported in accordance with the strengthening the reporting of observational studies in epidemiology (STROBE) recommendations for cohort studies.[16] Because routinely collected electronic health information and clinical records constituted the primary data source, relevant principles from the reporting of studies conducted using observational routinely collected health data (RECORD) statement were also applied.[17]

STROBE recommends explicit reporting of eligibility criteria, variable definitions, data sources, potential sources of bias, study-size determination, missing-data handling, and statistical methods.[16,17]

Study population and participant selection

The source population comprised healthcare personnel working at PSMMC who underwent occupational tuberculosis screening. The study cohort included physicians, nurses, technicians, administrative personnel, and other healthcare workers with a documented positive TST who were subsequently referred to the ID clinic for LTBI assessment during the study period.

Eligible participants were healthcare personnel with a documented positive occupational-health TST and a corresponding ID clinic referral for LTBI evaluation between 01 January and 31 December 2025. Participants were excluded if active tuberculosis was documented at the time of referral, if they had previously completed treatment for LTBI, or if the available referral or electronic medical record contained insufficient information to establish eligibility or determine the primary study outcome. The reasons for exclusion were documented to permit transparent reporting of the participant flow in accordance with STROBE.[16]

Participants were followed through the available clinical record from the date of ID referral through determination of the LTBI diagnostic outcome and, for those prescribed preventive therapy, through the last documented treatment outcome. The final manuscript should specify the administrative end date for treatment follow-up if treatment completion extended beyond December 31, 2025.

Study size

A total-population sampling strategy was used; therefore, no random sampling was undertaken. All healthcare personnel meeting the eligibility criteria during the predefined study period were considered for inclusion. JAMA guidance indicates that a formal power calculation is generally unnecessary when the sample size of an observational study is fixed by an established source population, provided the method by which the study size was determined is clearly reported.[18] Sixty-eight potentially eligible participants were identified. Four participants had incomplete information for key demographic or clinical variables considered in regression analyses. Thus, descriptive analyses should retain all participants with available outcome data whenever possible, whereas complete-case multivariable analyses included 64 participants. The number of participants contributing to each analysis should be reported explicitly rather than describing 64 participants as the “final cohort” for every analysis.

Data sources and data collection

Data were retrospectively abstracted from occupational health screening records, ID clinic referral records, and the hospital electronic medical record using a standardized study-specific data abstraction form. To minimize abstraction variability, variables and coding categories were defined before analysis. Demographic variables included age, sex, nationality, and documented history of bacillus Calmette-Guérin (BCG) vaccination. Occupational variables included department or clinical unit and years of service. Clinical variables included documented comorbid conditions, including diabetes mellitus, hypertension, dyslipidemia, hypothyroidism, fatty liver disease, and other recorded chronic conditions.

Diagnostic variables included TST induration in millimeters and IGRA testing status and results, categorized as positive, negative, indeterminate, or not performed. Management variables included the prescribed tuberculosis preventive treatment regimen, treatment initiation, treatment completion, date of completion when available, and documented reasons for non-initiation or noncompletion. WHO guidance conceptualizes LTBI care as a cascade involving identification of at-risk individuals, exclusion of active TB disease, testing for TB infection, initiation of preventive therapy, adherence support, and treatment completion.[19,20]

Each participant was assigned a unique study identification number. Direct patient identifiers were excluded from the analytic dataset.

Outcome definitions

The primary outcome was the final classification of LTBI following ID clinic assessment. Ideally, LTBI should be defined from the clinician-documented final diagnosis after exclusion of active TB, supported by the available TST, IGRA, clinical assessment, and radiographic information. WHO and CDC guidance define TB infection in the absence of clinical evidence of active TB disease rather than on treatment initiation alone.[19,21]

If a clinician-recorded final LTBI diagnosis was not consistently available, the prespecified operational definition used in the database-positive IGRA or initiation of LTBI preventive therapy after exclusion of active TB- should be reported explicitly as an operational study classification, rather than presented as a universally accepted diagnostic definition. A sensitivity analysis restricted to participants with a positive IGRA would strengthen interpretation because treatment initiation may itself depend on the treating clinician's assessment of the TST and other clinical information.

Secondary outcomes included the proportion undergoing IGRA testing, the distribution of IGRA results among TST-positive personnel, initiation of preventive treatment among participants classified as having LTBI, and completion of the prescribed treatment regimen. Treatment completion was defined according to documentation in the ID or pharmacy record that the prescribed regimen had been completed. WHO currently recognizes TST and IGRA as accepted tests for TB

infection and emphasizes that active TB disease should be excluded before preventive treatment is initiated.[19,22]

Exposures and potential predictors

Candidate predictors of LTBI classification were selected a priori on the basis of clinical relevance and previously reported associations in Saudi healthcare-worker populations. These included age, sex, nationality, BCG vaccination history, years of service, TST induration size, occupational department or unit, and presence of comorbidity. Age, years of service, and TST induration were analyzed initially as continuous variables to avoid unnecessary loss of information. Sex was categorized as male or female; nationality as Saudi or non-Saudi; BCG status according to available documentation; and comorbidity status as presence of at least 1 recorded comorbidity versus none. Any additional categorization of continuous variables should be prespecified and the category boundaries reported, as recommended by STROBE.[16]

Assessment of bias

Several approaches were used to reduce potential bias inherent to retrospective EHR research. Selection bias was limited by using a total-population approach that included all eligible referrals during the predefined study period rather than a convenience sample. A structured abstraction form and prespecified variable definitions were used to reduce information and classification bias. Diagnostic and treatment variables were obtained from clinical records rather than participant recall. Nevertheless, because inclusion required a positive TST, the study estimates outcomes among TST-positive referred healthcare personnel and should not be interpreted as estimating LTBI prevalence among all PSMMC healthcare workers. Similarly, referral decisions and clinician treatment decisions may introduce selection and incorporation bias and should be considered when interpreting the operational LTBI classification.

Missing data

The extent of missingness was assessed for each study variable. Missing values were not coded as absence of an exposure or clinical characteristic. Descriptive analyses used available denominators, which should be reported for variables with missing observations.

Four participants had missing data for variables required for the regression analysis and were excluded only from the complete-case multivariable model. Characteristics of participants included and excluded from the regression analysis should be compared descriptively when feasible to assess the potential for complete-case selection bias. No statistical imputation was performed because of the small number of missing observations and limited sample size. STROBE and RECORD recommend transparent reporting of both the extent of missingness and the method used to address it.[16,17]

Statistical analysis

Statistical analyses were performed using IBM statistical package for the social sciences (SPSS) Statistics for windows, version 26.0 (IBM Corp). Continuous variables were summarized as mean (SD) when approximately normally distributed and median (IQR) when distributions were skewed. Categorical variables were summarized as number and percentage. Distributional characteristics of age, TST induration, and years of service were evaluated using graphical assessment and the Shapiro-Wilk test. Because formal normality tests can be sensitive to sample size, distributional shape and influential observations were considered together rather than relying solely on the normality-test p value.

The primary outcome was summarized as n/N (%) with a 95% CI. IGRA utilization and positive, negative, indeterminate, and unperformed test results were similarly summarized using absolute numbers, percentages, and appropriate denominators. Emphasis was placed on effect estimates and 95% CIs rather than interpretation based exclusively on statistical significance.[18]

TST and IGRA findings

Because eligibility for the cohort required a positive TST, all participants had the same TST classification. Consequently, a conventional 2×2 TST-positive/TST-negative by IGRA-positive/IGRA-negative table cannot be constructed, and Cohen κ is not an appropriate measure of agreement in this selected cohort because one of the 2 variables has essentially no variation. Therefore, the clinically interpretable analysis should report the proportion of TST-positive participants who were IGRA-positive, IGRA-negative, indeterminate, or not tested, together with 95% CIs. Discordance can be described as the proportion of TST-positive personnel with a negative IGRA. Cohen κ would only be appropriate if the underlying screened population included both TST-positive and TST-negative personnel with corresponding IGRA results. Although κ is widely used to assess agreement between categorical measures, its interpretation requires variation in both measurements.[23]

Unadjusted analyses

Associations between LTBI classification and categorical variables were evaluated using Pearson χ^2 tests when expected cell frequencies were adequate and fisher exact tests when sparse cells made χ^2 assumptions inappropriate. Continuous variables were compared between participants classified as LTBI-positive and LTBI-negative using the independent-samples t-test when distributional assumptions were reasonably satisfied or the Mann-Whitney U test otherwise. Unadjusted associations should

additionally be reported as effect estimates with 95% CIs wherever possible rather than only as p values.

Multivariable analysis

Multivariable logistic regression was originally planned to identify factors independently associated with LTBI classification. Candidate variables identified a priori included age, sex, nationality, BCG vaccination status, years of service, TST induration, and comorbidity status. Adjusted odds ratios (ORs) with 95% CIs should be reported. However, only 26 outcome events were available among 64 complete cases. Entering all 7 candidate predictors into an ordinary maximum-likelihood logistic regression model would yield fewer than 4 events per parameter and carries substantial risk of coefficient instability, inflated standard errors, separation, and overfitting.[24,25] Simulation work has shown that sparse event-to-parameter ratios can materially compromise conventional logistic regression estimates, although the traditional 10-events-per-variable rule should not be viewed as an absolute threshold.[24,25]

The preferable approach is therefore to use a parsimonious prespecified model containing only a small number of clinically essential predictors or, if all prespecified variables must be retained, a penalized likelihood method such as firth logistic regression. Variable selection based solely on univariate p values should be avoided. Model results should be regarded as exploratory because of the limited number of outcome events.

All hypothesis tests were 2-sided. P<0.05 was considered statistically significant, but interpretation emphasized magnitude and precision of effect estimates rather than statistical significance alone. No adjustment for multiple testing was applied; therefore, secondary and exploratory analyses should be interpreted as exploratory.[18]

Ethical considerations

The study was conducted in accordance with the principles of the declaration of Helsinki and was approved by the institutional review board of prince sultan military medical city. Because the study involved retrospective review of existing clinical records without direct participant contact or intervention, informed consent was waived by the approving institutional review board. All records were deidentified before analysis. No direct personal identifiers were retained in the analytic dataset. Study data were stored on password-protected institutional systems accessible only to authorized members of the research team.

RESULTS

A total of 64 healthcare workers with positive TST results who were referred for LTBI assessment were included in the final analysis after excluding 4 participants with incomplete data on key predictor variables. The baseline demographic and clinical characteristics of the study population are presented in Table 1. The mean age of the participants was 37.34±11.85 years (range: 18-69 years), and the majority were female (n=37, 57.8%). The cohort comprised 54.7% (n=35) non-Saudi nationals and 45.3% (n=29) Saudi nationals. In 34.4% (n=22), there was a history of BCG vaccination, but in 65.6% (n=42), vaccination status was unknown. Data on department/unit were available for 33 participants, with the most common categories being “others” (42.4%) and “critical and emergency care” (24.2%). Comorbidity data were available for 55 participants, of whom 23.6% (n=13) had at least one comorbidity, most commonly diabetes mellitus (n=8, 14.5%). Mean TST induration size was 13.86±3.64 mm, median of 13 mm (IQR: 4), and average years of service was 11.15±9.77 years of the 21 participants who had IGRA testing, 52.4% (n=11) were positive. Treatment for LTBI was prescribed to 21 participants, with the most common regimens being Rifampicin for 4 months (n=5, 23.8%) and INH plus pyridoxine (n=5, 23.8%). Treatment was initiated in 21 out of 60 participants (35.0%) with documented initiation status, and among the 12 participants with documented completion status, 9 (75.0%) completed their treatment.

Table 2 presents the agreement between the TST (using the standard ≥10 mm cut-off for healthcare workers) and the IGRA results among the 21 participants who underwent both tests. Among the 20 participants with a positive TST (≥10 mm), 10 (50.0%) were IGRA-positive, and 10 (50.0%) were IGRA-negative. Notably, one participant with a TST reading of <10 mm (specifically 0 mm) tested positive on IGRA. The overall agreement observed between the two tests was 47.6%. Cohen's kappa coefficient was -0.095 (p=0.329), indicating poor agreement. Furthermore, Fisher's exact test demonstrated no statistically significant association between TST category and IGRA result (p=1.000).

Table 3 displays the univariate analysis comparing the characteristics of participants with and without LTBI. Several factors were found to be significantly associated with LTBI diagnosis and are described in detail below. There was a significant association of LTBI with nationality. The proportion of LTBI among Saudi nationals was higher than non-Saudis (55.2% versus 28.6%, p=0.031). The department category was also significantly associated with LTBI diagnosis (p=0.043), with the highest proportions in the “surgical and procedural specialties” group (71.4%) and the “others” category (64.3%). By contrast, the “medical and specialty outpatient clinics” group had no diagnosed cases (0%). Median TST size was significantly larger in participants with a diagnosis of LTBI than in those without (16mm versus 13 mm; p=0.014). Also, as expected, IGRA results, treatment initiation, and treatment completion were all very significantly associated with LTBI diagnosis (all p<0.001), as these variables are part of the LTBI definition.

In contrast, no significant associations were found for other variables. The diagnosis of LTBI was not significantly associated with gender (p=0.295), with 48.1% of males and 35.1% of females diagnosed. BCG vaccination history also did not differ significantly (p=0.269). Among those with known BCG history, 50.0% were LTBI-positive compared with 35.7% of those with unknown status. Comorbidities did not significantly affect LTBI diagnosis (p=0.587); 53.8% of participants with comorbidities were diagnosed with LTBI compared to 45.2% of participants without comorbidities. Further, age (p=0.727) and years of service (p=0.736) did not differ significantly between LTBI-positive and LTBI-negative groups.

Table 1: Baseline demographic and clinical characteristics of the study population (n=64).

Characteristics	Category	N	Percentage (%)
Gender	Male	27	42.2
	Female	37	57.8
Nationality	Saudi	29	45.3
	Non-Saudi	35	54.7
BCG vaccination history	Yes	22	34.4
	Unknown	42	65.6
Department (n=33)	Critical and emergency care	8	24.2
	Surgical and procedural specialties	7	21.2
	Medical and specialty outpatient clinics	4	12.1
	Others	14	42.4
Comorbidities (n=55)*	Present	13	23.6
	None	42	76.4
	Diabetes mellitus	8	14.5
	Hypertension	2	3.6
	Dyslipidemia	2	3.6
	Others^	2	3.6
TST size (mmm)	TST positive (≥10 mm)	62	96.9
	TST negative (<10 mm)	2	3.1
IGRA result (n=21)	Positive	11	52.4
	Negative	10	47.6
LTBI treatment regimen (n=21)	Rifampicin	1	4.8
	Rifampicin 4 months	5	23.8
	Rifampicin 600 mg for 3 months	1	4.8
	Rifampicin 600 mg for 4 months	2	9.5
	INH 3 months	1	4.8
	INH 6 months	4	19
	INH 9 months	1	4.8
	INH + pyridoxine	5	23.8
	Pyrazinamide, ethambutol, INH AND rifampicin	1	4.8
Treatment initiated (n=60)	Yes	21	35
	No	39	65
Complete LTBI treatment (n=12)	Yes	9	75
	No	3	25
Continuous variables			
Age (years)	Mean±SD	37.34±11.85	
	Median (IQR)	35 (12)	
	Min-max	18-69	
TST size (mm)	Mean±SD	13.86±3.64	
	Median (IQR)	13 (4)	
	Min-max	0-22	
Years of service	Mean±SD	11.15±9.77	
	Median (IQR)	10 (11)	
	Min-max	0-35	

*Percentages for individual comorbidities are calculated based on the total participants with comorbidities (n=13). The sum of subcategory percentages exceeded 100% because one participant had overlapping conditions, ^ fatty liver (n=1) and hypothyroidism (n=1)

Table 2: Agreement between TST ≥10 mm and IGRA results.

Variable	IGRA positive, N (%)	IGRA negative, N (%)	Total	P value
TST positive (≥ 10 mm)	10 (50)	10 (50)	20	1.000
TST negative (< 10 mm)	1 (100)	0 (0)	1	
Total	11	10	21	

Fisher's exact test, observed agreement: 47.6%, Cohen's kappa (κ): -0.095 (p=0.329)

Table 3: Factors associated with LTBI diagnosis (n=64).

Characteristic	Category	LTBI positive (n=26), N (%)	LTBI negative (n=38), N (%)	P value
Gender	Male	13 (48.1)	14 (51.9)	0.295
	Female	13 (35.1)	24 (64.9)	
Nationality	Saudi	16 (55.2)	13 (44.8)	0.031
	Non-saudi	10 (28.6)	25 (71.4)	
BCG vaccination history	Yes	11 (50)	11 (50)	0.269
	Unknown	15 (35.7)	27 (64.3)	
Department	Critical and emergency care	2 (25)	6 (75)	0.043*
	Surgical and procedural specialties	5 (71.4)	2 (28.6)	
	Medical and specialty outpatient clinics	0 (0)	4 (100)	
	Others	9 (64.3)	5 (35.7)	
Comorbidities	Present	7 (53.8)	6 (46.2)	0.587
	None	19 (45.2)	23 (54.8)	
IGRA result	Positive	11 (100)	0 (0)	<0.001*
	Negative	0 (0)	10 (100)	
Treatment initiated	Yes	21 (100)	0 (0)	<0.001
	No	3 (7.7)	36 (92.3)	
Complete LTBI treatment	Yes	9 (100)	0 (0)	0.005*
	No	0 (0)	3 (100)	
Continuous variables				
Age (years)	Median (IQR)	36 (28)	35 (9)	0.727**
TST size (mm)	Median (IQR)	16 (5)	13 (4)	0.014**
Years of service	Median (IQR)	10 (21.5)	9 (6.5)	0.736**

Chi-square test, *Fisher's exact test, **Mann-Whitney test.

Table 4: Multivariable logistic regression model predicting LTBI diagnosis.

Predictor variable	Adjusted odds ratio (aOR)	95% confidence interval	P value
Age (per 1-year increase)	0.893	(0.666-1.196)	0.448
Gender (ref. female)	0.882	(0.254-3.061)	0.843
Nationality (ref. non-saudi)	7.312	(0.597-89.582)	0.120
BCG status (ref. unknown)	0.511	(0.033-7.810)	0.629
Years of service (per 1-year increase)	1.242	(0.853-1.808)	0.258
TST size (per 1-mm increase)	1.071	(0.912-1.259)	0.401
Comorbidity (ref. present)	1.507	(0.279-8.138)	0.634

Model fit statistics: complete case analysis (N=55, 26 positive, 29 negative). Overall model: χ^2=9.403, df=7, p=0.225 (Omnibus test). Nagelkerke R^2=0.210. Hosmer-Lemeshow test: p=not significant (indicating adequate model fit)

Table 4 presents the results of the multivariable logistic regression model constructed to identify independent predictors of LTBI diagnosis after adjusting for potential confounders, including age, gender, nationality, BCG status, years of service, TST size, and comorbidity presence. A complete case analysis was employed, yielding a final sample of 55 participants (26 LTBI-positive and 29 LTBI-negative) for this model. The overall model was not statistically significant (χ^2=9.403, df=7, p=0.225) and explained only 21% of the variance in LTBI diagnosis (Nagelkerke R^2=0.210). The Hosmer-Lemeshow test indicated adequate model fit (p=not significant). None of the individual predictors achieved statistical significance (all p>0.05). Although not significant, nationality was the strongest predictor, with Saudi healthcare workers having substantially higher odds of LTBI diagnosis than non-Saudis (aOR=7.312, 95% CI: 0.597-89.582, p=0.120). Similarly, TST size showed a

modest, non-significant association (aOR=1.071, 95% CI: 0.912-1.259, p=0.401), while all other variables showed no meaningful associations with LTBI diagnosis in the adjusted model.

DISCUSSION

This retrospective cohort study evaluated the diagnostic outcomes and management of 64 healthcare workers with a positive tuberculin skin test (TST) who were referred to PSMMC for evaluation of LTBI. The main findings showed that 40.6% of the referred healthcare workers had LTBI and there was poor agreement between TST and IGRA. Treatment initiation was recorded for 35% of participants, but only 42.9% of those who initiated treatment completed it. Univariate analysis identified nationality, department, and TST size as significant factors associated with LTBI diagnosis; however, multivariable regression failed to identify any independent predictors, possibly due to limited statistical power.

The primary outcome of this study showed that LTBI was diagnosed based on the positive IGRA result or treatment initiation in 40.6% (26/64) of TST-positive health care workers under assessment. This proportion is much higher than the 24% prevalence reported by Almohaya et al among healthcare workers using the QuantiFERON-TB gold plus assay.[19] It is notably higher than the 23.1% prevalence reported by Goweda among healthcare students and medical doctors.[31] However, this is comparable to the prevalence of 42% reported in the study of healthcare workers in Bangladesh by Islam et al, although this population had higher endemic TB rates.[32]

The higher proportion we observed likely reflects the referral nature of the study population, all of whom had already screened positive on TST; they represent a selected high-risk group rather than a general screening population. Conversely, Al Shahrani reported that only 66 of 561 healthcare workers (11.8%) had a TST reading of ≥10 mm at King Abdullah Hospital in Bisha, suggesting that our cohort represents a subset of the wider healthcare worker population with positive screening results.[30]

Importantly, this study demonstrated poor concordance between TST and IGRA. There was worse than chance agreement, with an observed agreement of 47.6% and Cohen's kappa of -0.095 (p=0.329). This is in line with the findings of Anwar et al who reported poor agreement between TST and the QuantiFERON-TB gold in-tube test (kappa=0.028) in Egyptian health care workers.[33] Keshavarz et al also reported moderate agreement (kappa=0.72) in BCG-vaccinated individuals, which is better than our results, but still suggests that TST and IGRA are not interchangeable.[34]

Our study finds poor agreement, which may be attributed to several factors. Firstly, the high prevalence of BCG vaccination in Saudi Arabia (universal vaccination at birth) causes false-positive TST reactions due to cross-reactivity with non-tuberculous mycobacteria.[28] Secondly, 60.3% of our cohort were non-Saudi citizens from countries endemic for TB, which adds to variability in TST interpretation. Thirdly, the TST is known to have variability in both administration and interpretation among operators, whereas the IGRA provides more objective results.[35]

In one participant with a TST reading of 0 mm, the IGRA was positive, adding to the possibility of TST-missed latent infection. This is consistent with the finding by Dorman et al who found 6-9 times higher IGRA conversion rates than TST conversion rates among health care workers.[36] Given the poor agreement between TST and IGRA, our results strongly support the WHO and CDC recommendation to use IGRA as a confirmatory test for TST-positive individuals, especially in BCG-vaccinated and multicultural populations.

Among 26 patients with LTBI, 21 (80.8%) initiated preventive therapy. The overall initiation rate was 35.0% (21/60) for the entire cohort with initiation status. This is similar to the 33% treatment rate in a Canadian cohort of health care workers and students reported by Xu and Schwartzman.[14] Only 42.9% (9/21) of patients who initiated therapy completed it, which is much lower than the 79% treatment completion rate found by Xu and Schwartzman.[37]

Several factors could be responsible for the suboptimal completion rate observed in our study. Reasons documented for not completing included patient refusal ("did not want, refuse"), loss to follow-up ("did not attend clinic"), and clinical deferral ("delay after transplant"). These results are consistent with the findings of Xu and Schwartzman, who reported that the main reasons for treatment discontinuation were loss to follow-up and abdominal discomfort.[37] The relatively low completion rate highlights the need for improved adherence support strategies, such as patient education, closer follow-up and perhaps the use of shorter, more tolerable regimens such as the 3-month isoniazid-rifapentine (3HP) regimen.

Factors related to LTBI diagnosis

Nationality was significantly associated with LTBI diagnosis in univariate analysis (p=0.031). LTBI was higher among Saudi nationals than among non-Saudis (55.2% versus 28.6%). This finding is contrary to the findings of Kofi et al, who found higher rates of TST positivity among international contract workers (6.7%) than those on local contracts (3.1%) at PSMMC.[38] In a similar study, Al Shahrani found a strong association between nationality and the risk of infection in a multivariate analysis.[30] The higher proportion of LTBI among Saudi nationals in our study may reflect the universal BCG vaccination policy in Saudi Arabia, which can cause false-positive TST results not confirmed by IGRA, and the fact that Saudi HCWs may have longer

cumulative occupational exposure than more recently hired expatriate staff.

Department category was significantly associated with LTBI diagnosis (p=0.043), with the highest proportions in the "surgical and procedural specialties" (71.4%) and "others" (64.3%) groups. No diagnosed cases were found in the "medical and specialty outpatient clinics" group. This finding is consistent with Islam et al, who found that TST positivity was significantly higher among staff assigned to medicine wards (aOR=3.65) and gynecology/obstetrics wards (aOR=2.46) compared with administrative staff.[9] Differences between departments may reflect differences in patient exposure, aerosol-generating procedures, and compliance with infection control practices.

Median TST size in participants diagnosed with LTBI was significantly larger (16 mm) than in those without (13 mm) (p=0.014). This finding is consistent with the general understanding that larger induration sizes are more likely to represent true infection.[3] In univariate analysis, the association between larger TST size and LTBI diagnosis persisted, but not in the multivariable model, possibly due to the small sample size and limited statistical power.

Univariate analysis revealed no significant associations between gender, history of BCG vaccination, presence of comorbidity, age, and years of service and the diagnosis of LTBI. Interestingly, no association was found with BCG vaccination history, while Almohaya et al reported that lack of BCG vaccination at birth was a significant independent predictor of LTBI (aOR=3.08).[19] However, a large proportion of participants in our study had unknown BCG status (65.6%), which may have masked any true association.

In the multivariable logistic regression model, no independent predictors of LTBI diagnosis were statistically significant. The overall model was not significant ($\chi2$=9.403, df=7, p=0.225) and explained only 21% of the variance (Nagelkerke R2=0.210). Although not significant, nationality was the strongest predictor, with Saudi healthcare workers having greater odds of LTBI than non-Saudis (aOR=7.312, 95% CI: 0.597-89.582, p=0.120). But the very wide confidence interval indicates substantial uncertainty, likely due to the small sample size.

Most likely, the reason for not identifying independent predictors in the multivariable model is limited statistical power. There were only 55 complete cases, and 7 predictors were entered into the model, so the study was underpowered to detect small effect sizes. Future research with a larger sample size is warranted to validate the possible role of nationality and other factors as independent predictors of LTBI in this population. This is in line with the results of Dobler et al, who stressed that, in low-incidence settings, the risk of occupational tuberculosis infection is very low. Large sample sizes are needed to identify relevant associations.[35]

Strengths

There are several strengths to this study. To the best of our knowledge, this is one of the few studies that comprehensively evaluates the diagnostic outcomes and management of TST-positive healthcare workers referred for LTBI assessment at a major tertiary care hospital in Saudi Arabia. The study was conducted on a diverse population of healthcare workers from different nationalities and departments; therefore, the findings are more generalizable. A structured data abstraction form was utilized, and both univariate and multivariable analyses were performed, providing a rigorous analytical framework.

Limitations

However, some limitations must be acknowledged. First, the small sample size (N=64) limited the statistical power, especially for the multivariable regression analysis, which may have failed to identify true associations due to a type II error. Second, the retrospective nature of the study relied on the accuracy and completeness of medical records and data on some variables (e.g., department, comorbidities), which were missing for a large proportion of the participants. Third, BCG vaccination status was unknown for 65.6% of participants, limiting our ability to assess the true effect of BCG vaccination on the diagnosis of LTBI. Fourth, only 32.8% of participants were tested with IGRA, which may have introduced selection bias. Finally, the single-center design may limit generalizability of findings to other health care settings.

CONCLUSION

In this retrospective cohort study, we found that more than one-third (40.6%) of TST-positive healthcare workers referred for LTBI evaluation were diagnosed with LTBI at PSMMC. Agreement between TST and IGRA was poor, indicating that IGRA can be used as a confirmatory test in BCG-vaccinated and multi-ethnic populations. Treatment initiation was documented in 80.8% of diagnosed patients, and among those who initiated therapy, only 42.9% completed treatment, suggesting a need for improved adherence support strategies. In univariate analysis, nationality, department, and TST size were significant factors associated with LTBI. However, independent predictors of LTBI could not be confirmed in multivariable regression due to limited statistical power. Further large-scale studies are needed to confirm these findings and to optimize the LTBI screening and management protocols for healthcare workers in Saudi Arabia.

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