Prevalence of Latent Tuberculosis in Saudi Arabia: A Systematic Review

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Abstract

This systematic review aims to provide a comprehensive synthesis of studies conducted in the Kingdom of Saudi Arabia (KSA) that have investigated the prevalence and characteristics of latent tuberculosis infection (LTBI) within various populations. Seven studies were identified and analyzed, encompassing diverse populations, methodologies, and diagnostic tools. The review highlights the variability in LTBI prevalence estimates, particularly among healthcare workers, and underscores the challenges in diagnostic concordance between tuberculin skin test (TST) and interferon gamma release assays (IGRA). Demographic factors such as age, occupation, and nationality were found to influence LTBI prevalence. The findings emphasize the importance of tailored interventions for high-risk groups and standardized diagnostic approaches. This review contributes valuable insights into the complexity of LTBI within KSA and informs future public health strategies.

Introduction

Tuberculosis (TB), caused by Mycobacterium tuberculosis, remains a major global public health concern, affecting millions of individuals and posing a significant burden on healthcare systems worldwide [1, 2]. Despite the progress made in TB control and treatment, the disease's prevalence and its latent form—latent tuberculosis infection (LTBI)—continue to challenge healthcare systems, particularly in high-burden countries [3-6].

Tuberculosis ranks among the leading causes of morbidity and mortality worldwide, with an estimated 10 million new cases and 1.4 million deaths reported in 2019 alone [1]. The disease is transmitted through airborne droplets, primarily affecting the respiratory system, although it can manifest in various forms, including pulmonary and extrapulmonary presentations [3, 7]. While active TB cases require prompt diagnosis and treatment to limit transmission and improve patient outcomes, an equally critical facet of TB control is understanding and addressing its latent form—LTBI [7].

LTBI refers to a state in which an individual is infected with M. tuberculosis but remains asymptomatic and non-infectious [8]. However, the bacteria can reactivate, leading to active TB disease, particularly in individuals with compromised immune systems. Given that approximately one-quarter of the global population is estimated to harbor LTBI, it presents a substantial reservoir for potential TB outbreaks and a significant challenge for TB control efforts [8-11]. Saudi Arabia, while positioned as a prosperous nation with advanced healthcare infrastructure, is not immune to the complexities of TB and its latent form.

Study Aim

This systematic review aims to provide a comprehensive understanding of the prevalence and characteristics of LTBI within the Kingdom of Saudi Arabia (KSA), taking into account diverse population groups and epidemiological contexts.

Rationale and Objectives of the Systematic Review

This systematic review seeks to address the existing gaps in the understanding of LTBI prevalence and characteristics within the context of Saudi Arabia. By synthesizing findings from studies that have investigated LTBI prevalence across various populations, the review aims to provide a comprehensive overview of the disease's burden and distribution. The systematic synthesis of available data will contribute to refining TB control measures by identifying high-risk groups, enhancing diagnostic strategies, and informing targeted interventions.

Methodology

Search Strategy: A comprehensive literature search was conducted across multiple electronic databases, including PubMed, Embase, and Scopus. The search terms encompassed variations of "latent tuberculosis infection," "prevalence," "Saudi Arabia," and related synonyms. The search was limited to studies published from 1990 to the present to ensure contemporary relevance.

Study Selection: The screening process involved a two-step approach. Initially, titles and abstracts were screened for relevance and eligibility, followed by a full-text review of selected articles. Inclusion criteria encompassed studies conducted in KSA, investigating

LTBI prevalence, and providing relevant data on study characteristics, population demographics, diagnostic tools, and findings. Exclusion criteria included studies conducted outside KSA or focusing solely on active tuberculosis cases.

Data Extraction: Data from the included studies were extracted systematically. The extracted information included study title, year, city, population type, population number, study design, assessment methods, diagnostic tools used, and key findings related to LTBI prevalence and associated factors. Discrepancies were resolved through consensus among reviewers.

Quality Assessment: The quality of the included studies was assessed using appropriate tools depending on study designs, such as the Newcastle-Ottawa Scale for observational studies. Quality assessment focused on study methodology, sampling, participant recruitment, and outcome measurement.

Data Synthesis: Due to the heterogeneity of study populations, methodologies, and diagnostic tools, a narrative synthesis approach was employed. The results were organized according to study characteristics, and key findings were summarized in a tabular format.

Results

Search Results

The initial literature search yielded a total of 421 articles across various electronic databases. After removing duplicates, 238 unique records remained for title and abstract screening. Subsequently, 170 articles were excluded based on title and abstract assessment. The full-text review was conducted on 65 articles. During this phase, 58 articles were further excluded due to reasons such as irrelevant focus, inappropriate study design, and lack of relevant data. Ultimately, a total of 7 articles were considered eligible and included in the systematic review.

The included studies covered a range of populations, study designs, and geographic locations within the Kingdom of Saudi Arabia. The characteristics and key findings of these studies are summarized in Table 1.

The systematic review's findings are presented based on the synthesized data from the 7 included studies, offering a comprehensive insight into the prevalence and characteristics of latent tuberculosis infection in Saudi Arabia. The following sections detail the analysis and discussion of these findings, contributing to a deeper understanding of LTBI's epidemiology within the Saudi context.
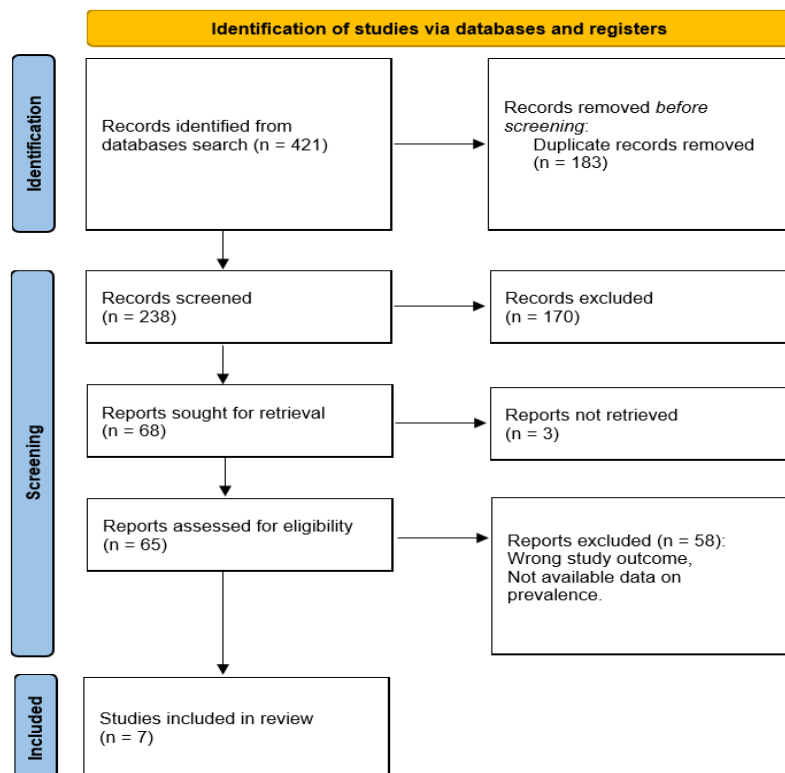
Figure 1: PRISMA Flow Diagram for the Search Process.

Qualitative Data Synthesis

The review encompassed a comprehensive analysis of seven distinct studies conducted within the Kingdom of Saudi Arabia (KSA), each contributing valuable insights into the prevalence and characteristics of latent tuberculosis infection (LTBI) among various populations.

Table 1: Characters of the included studies.

Study	Year	City	Population type	Population number	Study design	Assessment	Diagnostic Tool	Findings
Bukhary et al., 2018 [12]	2018	Multiple	Healthcare workers	520	Cross-sectional prospective	Hajj pilgrimage	IGRA and TST	The overall prevalence of LTBI was 10.8%. Agreement between QFT-GIT and TST was poor (kappa = 0.02). LTBI prevalence associated with longer employment, higher in physicians, and HCWs working in chest hospitals.
Balkhy et al., 2017 [13]	2017	Riyadh	Population-based	1369	Cross-sectional study	Primary healthcare centers	TST and QFT-GIT	Overall prevalence of LTBI was 9.3% using TST and 9.1% using QFT-GIT. ARTI was 0.36% using TST and 0.35% using QFT-GIT.
El-Helaly et al., 2014 [14]	2014	Riyadh	Healthcare workers	1412	Retrospective cross-sectional	Tertiary-care hospital	TST and QFT-G	Overall agreement between TST and QFT-G was 73.7%. Concordance associated with young age, female gender, Saudi-born

								nationals, and early career.
Hassan and Diab, 2014 [15]	2014	Dammam	Laboratory personnel	134	Cross-sectional study	Routine diagnostic laboratories	QFT-GIT	Prevalence of positive QFT-GIT results among laboratory personnel was 19.4%. Positive results associated with age ≥ 30 years, employment >10 years, and non-Saudi nationality.
Abbas et al., 2010 [16]	2010	Riyadh	Healthcare workers	2650	Survey	Tertiary care hospitals	TST	Overall LTBI prevalence was 11%. Highest positive rates among physicians (14.9%) and nurses (12.9%). Positive rates highest in age group ≥ 50 years (32.6%) and among HCWs from sub-Saharan countries (61.1%).
Al Khoufi, 2021 [17]	2021	Al Ahsa	Patients with IHD	98	Cross-sectional study	N/A	QFT	LTBI prevalence among IHD patients was 19.3%. LTBI significantly associated with coronary artery atherosclerosis.
Hibah et al.,	2015	Muhayil	Healthcare workers	N/A	Cross-sectional study	Muhayil National Hospital	TST	LTBI prevalence among HCWs

2015 [18]								was 22.5%. Highest prevalence in age group $\geq$ 50 years (26.3%) and nurses (28.7%). Lowest prevalence among physicians (16.5%) and HCWs from Saudi Arabia and Yemen (16.5%).

Bukhary et al., 2018: In their cross-sectional prospective study involving healthcare workers (HCWs) during the Hajj pilgrimage, Bukhary et al. found a prevalence of LTBI of 10.8%. They assessed LTBI using interferon gamma release assays (IGRA) and the tuberculin skin test (TST). The study emphasized poor agreement between IGRA and TST results, with a kappa coefficient of 0.02. The prevalence of LTBI was associated with longer employment duration, higher rates among physicians, and HCWs working in chest hospitals [12].

Balkhy et al., 2017: A population-based cross-sectional study conducted by Balkhy et al. investigated the prevalence of LTBI in Saudi Arabia. Their study included 1369 participants from various sociodemographic groups. The overall prevalence of LTBI was reported to be 9.3% using TST and 9.1% using IGRA (QuantiFERON TB Gold in tube - QFT-GIT). Stratified analyses showed variable prevalence rates across different sociodemographic groups, except for marital status. Additionally, the annual risk of tuberculosis infection (ARTI) was estimated to be 0.36% using TST and 0.35% using QFT-GIT [13].

El-Helaly et al., 2014: In a retrospective cross-sectional study, El-Helaly et al. evaluated the agreement between TST and QFT-G among healthcare workers. The study involved 1412 participants and revealed an overall agreement of 73.7% between the two tests. Concordance was associated with factors such as young age, female gender, Saudi-born nationality, and early career. The study underscored the need for further investigations

before recommending QFT-G as a pre-employment screening test for LTBI [14].

Hassan and Diab, 2014: Focusing on laboratory personnel, Hassan and Diab conducted a cross-sectional study to assess LTBI prevalence using QFT-GIT. Their study revealed a 19.4% prevalence of positive QFT-GIT results among laboratory personnel. Significant associations were observed between positive results and age $\geq$ 30 years, employment duration >10 years, and non-Saudi nationality. The study highlighted the importance of effective institutional tuberculosis infection control plans and regular screening for LTBI among laboratory personnel [15].

Abbas et al., 2010: Abbas et al. conducted a survey to identify the prevalence of LTBI among healthcare workers newly hired in Riyadh's major tertiary care hospitals. Among the 2650 participants, the overall prevalence of LTBI was reported as 11% using TST. Notably, physicians (14.9%) and nurses (12.9%) exhibited the highest positive rates, while certain factors, including age, job category, and country of origin, influenced the prevalence rates [16].

Al Khoufi, 2021: Al Khoufi's cross-sectional study aimed to assess the prevalence of LTBI among patients with ischemic heart disease (IHD) and its association with coronary artery atherosclerosis. Out of the 98 patients with previously diagnosed IHD, 19.3% were found to have LTBI using QFT-GIT. An interesting finding was the significant association between LTBI and coronary artery atherosclerosis, suggesting a potential relationship between long-term cell-mediated

immunity activation and atherosclerosis development [17].

Hibah et al., 2015: Hibah et al. conducted a cross-sectional study involving healthcare workers at Muhayil National Hospital. Among the 208 participants who underwent the tuberculin skin test (TST), the prevalence of LTBI was 22.5%. This prevalence varied across different demographic groups, with nurses exhibiting the highest prevalence (28.7%). The study emphasized the high prevalence of LTBI among healthcare workers and the influence of factors such as age, job category, and country of citizenship [18].

Overall, the studies included in this systematic review collectively contribute to an enhanced understanding of the prevalence of latent tuberculosis infection within the Kingdom of Saudi Arabia. While disparities in prevalence rates were observed across different populations, the prevalence of LTBI among healthcare workers and specific demographic groups remained a consistent concern. Additionally, the poor agreement between diagnostic tests emphasizes the complexity of accurately assessing LTBI, warranting further investigation into the development of effective screening strategies within the Saudi Arabian context.

Discussion

Tuberculosis (TB) remains a significant global health challenge, with latent tuberculosis infection (LTBI) representing a critical aspect of its epidemiology. The Kingdom of Saudi Arabia (KSA) has not been exempt from this concern, and a thorough understanding of the prevalence and characteristics of LTBI within its population is essential for effective public health interventions. This systematic review synthesized findings from seven diverse studies conducted in KSA, shedding light on the complex landscape of LTBI prevalence and its associated factors.

The variations in LTBI prevalence reported across the studies highlight the heterogeneous nature of this condition within different populations. The prevalence estimates ranged from 9.1% to 22.5%, reflecting the diversity of the sampled groups and the unique risk profiles they may have. This divergence underscores the importance of considering population-specific characteristics, such as occupation, age, and nationality, when assessing LTBI prevalence. Notably, healthcare workers emerged as a consistently high-risk group, with prevalence rates ranging from 10.8% to 22.5%. This finding is in line with the occupational exposure

inherent in healthcare settings, where close contact with TB patients can lead to an increased risk of infection. The higher prevalence rates observed among physicians and nurses compared to other healthcare workers further emphasize the necessity for targeted interventions within this subgroup.

The utilization of different diagnostic tools—namely, the tuberculin skin test (TST) and interferon gamma release assays (IGRA), such as QuantiFERON-TB Gold In-Tube (QFT-GIT)—contributed to the diversity in reported LTBI prevalence rates. Discrepancies between TST and QFT-GIT results were evident, as seen in the study by Bukhary et al. (2018), where poor agreement was observed (kappa = 0.02) [12]. This discrepancy might arise from differences in immune response assessment, varying sensitivities, and the influence of prior Bacillus Calmette–Guerin (BCG) vaccination. The challenge of accurately diagnosing LTBI is evident, as the choice of diagnostic tool can significantly impact prevalence estimates, complicating comparisons across studies.

Another critical consideration is the potential impact of demographic factors on LTBI prevalence. The studies collectively demonstrate the influence of factors such as age, job category, and nationality on LTBI prevalence rates. For instance, the study by Abbas et al. (2010) highlighted a higher prevalence of LTBI among older healthcare workers and those from sub-Saharan countries [16]. This emphasizes the importance of tailored interventions that account for the unique risk profiles of different subpopulations. Furthermore, the association between LTBI and coronary artery atherosclerosis reported by Al Khoufi (2021) raises intriguing questions about the potential links between immune responses to TB and cardiovascular diseases, underscoring the need for multidisciplinary research to explore these associations further [17].

The findings of this systematic review bear several implications for public health policy and practice. Firstly, the consistently high prevalence of LTBI among healthcare workers warrants targeted screening programs and preventive measures within this group. Implementing regular screening and offering chemoprophylaxis to those identified with LTBI could play a pivotal role in reducing disease transmission and ensuring the health of this essential workforce. Secondly, the variability in prevalence estimates based on diagnostic tools highlights the need for standardized approaches to LTBI assessment. Future research should focus on elucidating the factors contributing to

diagnostic discordance and identifying strategies to enhance diagnostic accuracy.

Despite the insights gained from this review, certain limitations warrant consideration. The heterogeneity in study designs, settings, and methodologies across the included studies may introduce inherent biases and reduce comparability. Additionally, some studies lacked specific details regarding certain demographic characteristics, potentially limiting the generalizability of their findings.

Conclusion

In conclusion, this systematic review provides a comprehensive overview of the prevalence and characteristics of latent tuberculosis infection within the Kingdom of Saudi Arabia. The collective findings underscore the significance of healthcare workers as a high-risk group, the challenges in diagnostic concordance, and the influence of demographic factors on LTBI prevalence. These insights carry important implications for public health strategies, emphasizing the need for targeted interventions, standardized diagnostic approaches, and further research to unravel the complex associations between LTBI and related health outcomes.

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