Annals of Occupational and
Environmental Medicine AOEM

Review

Tuberculosis infection status and risk factors among health workers: an updated systematic review

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Abbreviations
AFB: acid fast bacilli; aOR: adjusted odds ratio;
ARTI: annual rate of tuberculosis infection;
BCG: Bacillus Calmette-Guerin; BMI: body
mass index; CI: confidence interval; CXR:
chest X-ray; GIT: QuantiFERON-TB Gold-
In-Tube; HIV: human immunodeficiency
virus; HR: hazard ratio; HW: health worker;
IGRA: interferon-gamma release assay; IRR:
Incidence rate ratio; LTBI: latent tuberculosis

ABSTRACT

Tuberculosis (TB) infection is a common occupational risk for health workers (HWs) and poses a threat to the patients under their care and to other HWs. Hence, the development of a prevention strategy is crucial. We conducted a study to understand the status and risk factors of TB infection among HWs. The existing literature was searched for all published reports from 1 August 2010 to 31 December 2018, related to TB among HWs according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The inclusion criteria were: (1) study participants working in a health care facility; (2) TB cases diagnosed by medical professionals; (3) original research articles; and (4) English reports in a peer-reviewed journal. We finally included 61 studies from 642 articles searched initially. The TB infection rate in HWs was higher than that of the general population. Based on 39 studies, the prevalence of TB in HWs (tuberculin skin test positive) was 29.94%. In contrast, the global burden of latent TB infection was 23.0% (95% uncertainty interval: 20.4%–26.4%) in 2014. The risk factors of TB among HWs were aging, long duration of employment, nursing professionals, lack of Bacillus Calmette-Guerin vaccination, and low body mass index. HWs have an increased risk for TB infection, which can cause secondary infections in patients or other HWs. An effective prevention strategy must be developed to enable early diagnosis and prompt treatment.

Keywords: Tuberculosis; Healthcare workers; Health care providers; Healthcare support workers; Cross infection

BACKGROUND

Health workers (HWs) are routinely exposed to infected blood and body fluids at their workplaces. One third of the world population has been infected by tuberculosis (TB), including the latent TB infection (LTBI), and the highest risk of TB transmission has been reported in HWs [1,2]. HWs are frequently exposed to patients with undiagnosed or untreated TB at work [3]. A HW infected with TB can act as a carrier and poses a threat to other patients or fellow HWs. Thus, TB infection of HWs at work is a major concern not only in the domain of occupational health but also in public health. Despite the large number of studies on TB infection among HWs, there is a lack of clarity regarding its prevalence in different countries and its risk factors in occupational settings.

Authors contributions
Conceptualization: Kang SK; Formal analysis: Lee S; Investigation: Lee S, Lee W; Methodology: Lee W, Lee S; Validation: Kang SK, Lee W; Writing - original draft: Lee S, Lee W, Kang SK; Writing - review &editing: Lee S, Lee W, Kang SK.

Baussano et al. [4] conducted an in-depth review of the research on the TB status among HWs. From January 2005 to July 2010, forty-three eligible studies were included. These accounted for 1,176 cases of LTBI among HWs with 49,576 person-years of follow-up and for 1,942 TB cases with > 1,010,047 person-years of follow-up. Cases of LTBI and TB among HWs were reported in 25 and 18 studies, respectively. Since then, the literature on the TB status among HWs has reported a significant increase. Thus, we conducted an updated systematic literature review for TB infection among HWs from August 2010. The aim of this review was to comprehensively and critically assess the literature regarding the intercontinental prevalence, risk factors, and the type of TB among HWs, and to gain a better understanding of TB among HWs for guiding the future research.

METHODS

Main goal and search strategy
This study systematically reviewed the TB infection status and risk factors for HWs, providing the academic evidence and a strategy to prevent HWs from TB. The main problem in the current review study was TB exposure to HWs. The TB infection status and risk factors were compared with the general population or non-HWs, outcomes were demonstrated with prevalence, incidence, or odds ratio (OR).

A systematic search was conducted on the databases of PubMed and Google Scholar for all published reports on TB among HWs according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines. The search term used was: "TB" OR "tuberculosis" OR "LTBI" OR "latent tuberculosis infection" AND work* OR occupation* OR industry* OR employee*. All the relevant published articles from 1 August 2010 to 31 December 2018 were identified, as the previous review had already included the 43 studies pertaining to TB among HWs published from 1 January 2005 to 31 July 2010 [4].

Inclusion and exclusion criteria
We included all studies that satisfied the following criteria: (1) study participants working in a health care facility; (2) TB patients diagnosed by medical professionals; (3) original research articles; and (4) English reports in a peer-reviewed journal.

Studies were excluded if they were: (1) reviews, notes, case reports, commentaries, or editorials; (2) non-human focused researches; (3) articles describing only guidance of clinical treatment or other similar study designs.

Selection and organization
After the search, the duplicates were removed. The titles and abstracts of the remaining articles were then screened, based on the inclusion and exclusion criteria. Thereafter, the screened articles were checked for eligibility by reviewing a random sample of the included and excluded studies. Full text screening was also performed to assess the articles against the inclusion criteria to complete the process of selection and organization. A flow chart of the process is demonstrated in **Fig. 1**. Finally, the selected articles were organized based on them pertaining to the following two aspects; (1) the status (prevalence or incidence) of TB among HWs; and (2) the risk factors of TB among HWs.
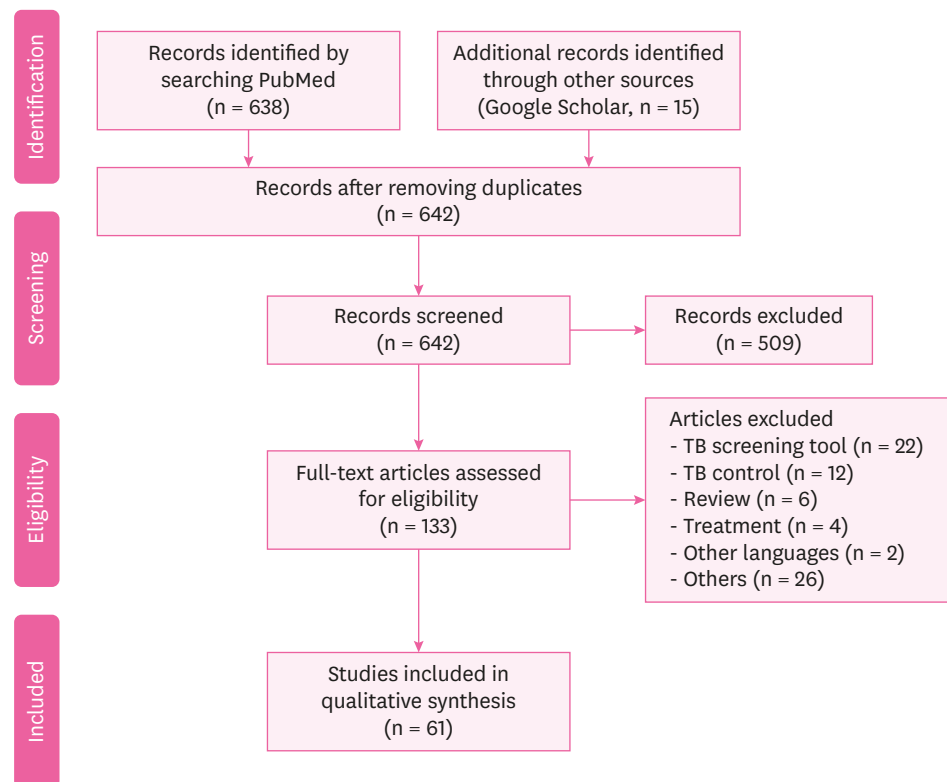
Fig. 1. The preferred reporting items for systematic reviews and meta-analyses flow diagram.

RESULTS AND DISCUSSION

We identified a total of 638 potentially relevant citations from the PubMed data base, and 15 from the other sources (Google Scholar). The article screening and selection were conducted by three authors. Five hundreds and nine articles were excluded by the initial screening because the quality and scope of these studies did not fit those of the current study. Finally, 61 studies were included by excluding 72 studies. The included studies were divided into two categories based on them pertaining to either the status of TB among HWs or the risk factors of TB among HWs. **Fig. 1** demonstrated the article selection flow.

The detailed description of the studies included in each type is as follows. The proportions and numbers of the major studies according to the geographic locations were: America 5%; Europe 23%; Asia 49%; and Africa 23%. The test methods used for the diagnosis of TB included interferon-gamma releasing assay (IGRA), 12%; tuberculin skin test (TST), 23%; survey questionnaire, 13%; and others/multiple tests, 50%. The test methods in the latter category included acid fast bacilli (AFB) stains, chest X-ray (CXR), genotyping data, and several studies used TST and IGRA together.

Both TST and QuantiFERON-TB Gold-In-Tube (QFT-GIT) are immunoassay tests used to determine whether the TB infection is latent or active. TST is considered positive if the skin over the injected portion is swollen (> 10 mm) within 48–72 hours after injecting it with *Mycobacterium tuberculosis* purified protein derivative. QFT-GIT is a cytokine release test, and interferon-gamma is higher than a certain level in patients with TB infection (including LTBI and active TB).

The status of TB among HWs

Table 1 showed the TB infection status among HWs. Based on the results of 39 studies, 29.94% of the HWs were found to be positive for TB. We compared the prevalence by the geographical location, gender, and screening test. Most of the European countries, except Italy, had about 30% positive cases. In Italy, 6.1% (TST positive) of the cases were positive in 2017 [5] compared to 4.3% in 2014 [6]. Infection rates in the other countries and the corresponding years were as follows, 27% (UK, 2017) [7]; 55.3% (Norway, 2013) [8]; QuantiFERON-TB (QFT) positive: 3.4%, TST positive: 55.3% (≥ 6 mm), 13.7% (≥ 15 mm), TST, QFT both positive: 4.7% (Georgia, 2013) [9]; 20.6% (Germany, 2011) [10]; 24.0% (Germany, 2010) [11]; and 16.2%

Table 1. Summary of published studies meeting inclusion criteria for the TB among HWs

Number	Author	Publication year	Country	Study design	Participants	Tuberculosis assessment	Prevalence or incidence
1	Chen et al. [16]	2019	China	Cross-sectional study	487	Questionnaire and IGRA for TB	IGRA positive: 33.9%
2	Nichimura et al. [51]	2018	Japan	Prospective cohort study	328	IGRA for TB	HW: 0.149/100 person-years Nursing student: 0.0825/100 person-years
3	Bukhary et al. [52]	2018	Saudi Arabia	Cross-sectional study	520	IGRA for TB	QFT-GIT positive: 56/520 (10.8%)
4	Henderson et al. [7]	2017	UK	Cross-sectional study	587	IGRA for TB	IGRA positive: 27%
5	Shrestha et al. [22]	2017	Nepal	Cross-sectional study	560	Self-administered questionnaire and CXR	Direct contact with patients: 76.8% Cough > 2 weeks: 10.4% Chest radiography: 20.0%
6	Lacerda et al. [25]	2017	Brazil	Cross-sectional study	708	Questionnaire and IGRA	LTBI prevalence: 27% (n = 196; 95% CI: 24%–31%)
7	Lacerda et al. [25]	2017	Brazil	Cross-sectional study	218	TST	TST positive: 39.4% (95% CI: 32.9–45.9) and 54.1% (95% CI: 47.4–60.7)
8	Yoon et al. [32]	2017	Korea	Cross-sectional study	902	TST, IGRA	TB patient care ≥ 1 year or more: 19.5% (176/902) TST positive: 26.9% (243/902) LTBI: 5.8% (52/902)
9	Janagond et al. [24]	2017	India	Prospective cohort study	206	Questionnaires, TST	TST positive: 36.8% (76/206)
10	Napoli et al. [5]	2017	Italy	Cross-sectional study	2,290	QFT, TST	TST positive: 141 (6.1%) QFT positive: 16.4%
11	Gehanno et al. [40]	2017	France	Retrospective study	233,389	Questionnaires	Nurse, health care assistants: 5.7/100,000 Administrative staff: 1.27/100,000
12	Pan et al. [13]	2015	Taiwan	Matched cohort study	44	AFB staining	Smear positive: 26.8% (11/41) Culture proven: 70.7% (29/41) Pathologically diagnosed: 9.8% (4/41) Clinically diagnosed: 24.4% (10/41)
13	He et al. [17]	2015	China	Longitudinal study	880	TST, QFT	TST positive: 11.4% QFT-GIT: 19.1% (OR: 142.62, 95% CI: 1.39–4.97) BCG scar: OR: 0.53, 95% CI: 0.28–1.00
14	Adams et al. [33]	2015	South Africa	Prospective cohort study	764	TST, QFT, CXR	TST positive: 38% QFT-GIT positive: 13%–22%
15	Hung et al. [14]	2015	Taiwan	Prospective cross-sectional study	193	QFT-G, TST	TST positive: 88.8% QFT-GIT positive: 14.5% Multivariable logistic regression: only the QFT-G test was associated with age (35 years or greater) (adjusted OR: 2.53, p = 0.03)
16	Chen et al. [31]	2014	China	Retrospective study	996	Sputum smear	TB: females > males (58.0% > 42.0%) TB positive: males > females (88.5% > 83.4%, p = 0.031)
17	Garcell et al. [34]	2014	Qatar	Cross-sectional study	202	TST, QFT-G	TST positive: 6.9% QFT-G positive: 3.0% TB positive is older than negative (44.5 vs. 38.9 years) More experience as HWs (21.7 vs. 16.8 years) Direct contact with Tb patients (83.3% vs. 25%)

Table 1. (Continued) Summary of published studies meeting inclusion criteria for the TB among HWs

Number	Author	Publication year	Country	Study design	Participants	Tuberculosis assessment	Prevalence or incidence
18	Szep et al. [27]	2014	USA	Cross-sectional study	95	TST	TST positive: 4.2% or 6.87 per 1,000 person weeks (95% CI: 1.87–17.60).
19	Muzzi et al. [6]	2014	Italy	Cross-sectional study	388	TST	TST at T1 was positive: 11 (4.3%). ARTI was 1.6 (95% CI: 0.9–2.9) per 100 person-years. TST at T2 was positive: 9 (3.7%). HWs PEARTI was 26 (95% CI 13.6–50) per 100 person-years
20	Wei et al. [18]	2013	China	Observational study	210	IGRA, TST	QFT-GIT positive: 161 (76.7%). QFT-GIT negative: 10 (19.01%). Indeterminate results: 9 (4.3%) (κ = 0.456, p < 0.001)
21	Gran et al. [8]	2013	Norway	Cross-sectional study	387	QFT, TST	QFT-GIT positive: 3.4%. TST (≥ 6 mm): 214 (55.3%). TST (≥ 15 mm): 53 (13.7%). QFT, TST positive: 10 (4.7%)
22	Whitaker et al. [9]	2013	Georgia	Prospective longitudinal study	319	TST, QFT-GIT	HWs from TB unit had higher prevalence of positive QFT-GIT and TST than those from non-TB unit: 107/194 (55%) vs. 30/125 (31%) QFT-GIT positive (p < 0.0001) and 128/189 (69%) vs. 64/119 (54%) TST positive (p = 0.01)
23	Kiertiburanakul et al. [15]	2012	Thailand	Prospective study	1,438	TST	TST positive: 66.3%. TST conversion: 4.8 per 100 HCP-year. 9 (0.6%) HCP were diagnosed with active TB
24	Larcher et al. [53]	2012	Italy	Cross-sectional study	621	TST, QFT	TST positive: 29.1%. QFT positive: 18.5%
25	Zwerling et al. [29]	2012	Canada	Prospective longitudinal study	388	TST, QFT	TST positive: 5.7% (22/388, 95% CI: 3.6%–8.5%). QFT positive: 6.2% (24/388, 95% CI: 4%–9.1%)
26	Borroto et al. [30]	2011	Cuba	Cross-sectional study	350	TST	LTBI prevalence: 15.4%: it was highest in professionals (20.6%); 60.3% were non-reactors, and at the second test a year later 1.4% were converters
27	Moon et al. [21]	2011	Korea	Cross-sectional study	173	TST, QFT	QFT-GIT positive: 21.4%. TST positive: 33.3%. κ = 0.234
28	Sherman et al. [10]	2011	Germany	Retrospective cohort study	450	TST	TST conversion: 93
29	Kehinde et al. [54]	2011	Nigeria	Descriptive study	271	Pre-tested questionnaire	AFB stain positive: 9 (3.3%). Culture positive: 6 (2.2%). The culture contamination: 1.8 per cent
30	Costa et al. [12]	2011	Portugal	Cross-sectional study	376	QFT, TST	TST positive: 61
31	Rafiza et al. [23]	2011	Malaysia	Cross-sectional study	954	QFT, TST	The overall prevalence of latent tuberculosis infection among Health workers was 10.6% (CI: 8.6%–12.6%)
32	Park et al.[55]	2010	Korea	Prospective study	322	QFT, TST	Both positive: 25 subjects (8%). Follow-up after 1 year. QFT-GIT positive: between 3.3% and 5.7%
33	Cadmus et al. [56]	2010	Nigeria	Retrospective study	101	AFB	AFB positive: 10 (13%)
34	Escombe et al. [26]	2010	Peru	Cross-sectional study	845	QFT	QFT-GIT positive: 39 (56%)
35	Lambert et al. [28]	2012	USA	Cross-sectional study	200,744	TST	TST positive: 6,049 (3%)
36	Schablon et al. [11]	2010	Germany	Cross-sectional study	2,028	IGRA	QFT-GIT positive: 198 (9.9%). TST positive: 480 (24.0%)
37	Jo et al. [20]	2013	Korea	Cross-sectional study	493	TST, QFT	Doctors (n = 99): TST positive: 63 (41.4%)/QFT-GIT positive: 36 (23.7%). Nurse (n = 168): TST positive: 119 (34.9%)/QFT-positive: 49 (14.4%)

TB: tuberculosis; HW: health worker; IGRA: interferon-gamma releasing assay; QFT-GIT: QuantiFERON-TB Gold-In-Tube; CXR: chest X-ray; LTBI: latent TB infection; CI: confidence interval; TST: tuberculin skin test; QFT: QuantiFERON-TB; AFB: acid fast bacilli; BCG: Bacillus Calmette-Guerin; QFT-G: QuantiFERON-TB Gold; PEARTI: post-exposure rate of tuberculosis infection.

(Portugal, 2011) [12]. Asia, like Europe, had an average of about 30% positive cases. However, Taiwan and Thailand had particularly higher rates, as follows: 24.4% (Taiwan, 2015, AFB staining) [13]; 88.8% (Taiwan, 2015, TST) [14]; 66.3% (Thailand, 2012, AFB staining) [15]. In China, the rates decreased slightly in 2015 (11.4%) [16] but again increased to 33.9% in 2019 [17], similar to the trend seen in 2013 (33.6%) [18]. In Korea, the infection rate showed a decreasing trend: 26.9% (2017) [19]; 41.4% (2013) [20]; and 33.3% (2011) [21]. Nepal and Malaysia had lower prevalence rates of 10.4% (2017) [22] and 10.6% (2011), respectively [23], while India's rate in 2017 was 36.8% [24]. In the American continent, the reported prevalence was 39.4% (Brazil, 2017) [25]; 56% (Peru, 2010) [26]; 4.2% (USA, 2014) [27]; 3% (USA, 2012) [28]; 5.7% (Canada, 2012) [29]; and 15.4% (Cuba, 2011) [30].

There were 4 articles reported the prevalence of LTBI from thirty-eight articles about TB infection status. The status of LTBI was different by countries, in Korea 5.8% [19]; in Malaysia 10.6% [23]; in Cuba 15.4% [30]; in Brazil 27.0% [25].

Higher TB infection rates were identified in women (women, 58.0% and men, 42.0%) [31]. The positive rates with the QFT-GIT test (5.8%, 52/902) were lower than those with the TST (26.9%, 243/902) for LTBI [32]. Several other studies showed a similar trend as follows: TST: 38% and QFT: 13%–22% [33]; TST: 88.8% and QFT: 14.5% [14]; TST: 6.9% and QFT: 3.0% [34]; and TST: 55.3% and QFT: 3.4% [8].

The risk factors of TB among HWs

Table 2 showed TB infection related risk factors status among HWs. Risk factors such as old age, long work-duration, lack of Bacillus Calmette-Guerin (BCG) vaccination, nursing professionals, TB contacts, and lower body mass index (BMI) were identified. Patients older than 51 years showed a higher TB infection rate (OR: 6.17, 95% confidence interval [CI]: 1.35–28.28) [35]. Age > 30 years was associated with a positive TST (p = 0.02 [19]; age ≥ 30 years, OR: 18.88, 95% CI: 1.52–234.36 [36]; being older, OR: 1.10, 95% CI: 1.06–1.13, p < 0.001 [37]).

Table 2. Summary of published studies meeting inclusion criteria for risk factors of TB among HWs

Number	Author	Year	Country	Study design	Participants	Tuberculosis assessment	Estimate of risk
1	Wang et al. [35]	2018	China	Cross-sectional study	212	Positive sputum acid-fast stains	TB: 760/100,000, RF: 51 years and above (aOR: 6.17, 95% CI: 1.35–28.28), being a nurse (aOR: 3.09, 95% CI: 1.15–8.32)
2	Kim et al. [19]	2017	Korea	Prospective cohort study	872	TST, CXR	Age over 30 years: (p = 0.02), LTBI point prevalence: 6.6%, LTBI incidence: 2.4 per 100 HWs
3	Davidson et al. [57]	2017	UK	Retrospective cohort study	2,320	TB surveillance, genotyping data	HWs: 23.4 (95% CI: 22.5–24.4), non-HWs: 16.2 (95% CI: 16.0–16.3)
4	Belo et al. [38]	2017	Mozambique	Cross-sectional study	316	Symptom screening questionnaire	LTBI: 34.4%, working > 8 years: 39.3%, no BCG vaccine: 39.6%, immunocompromised: 78.1%
5	Du et al. [48]	2017	China	Cross-sectional study	186	Questionnaires	Medical professionals (PR = 2.40), laboratory technicians (PR = 2.17), other hospital staff (PR = 1.04)
6	Bonini et al. [39]	2017	Italy	Cross-sectional study	580	Questionnaires, TST	Previous BCG vaccination: OR: 344, CI: 43.72–2,718.41, p < 0.001, origin in high-risk countries: OR: 401.68, CI: 50.60–3,188.69, p < 0.001
7	Weng et al. [58]	2016	Swaziland	Cross-sectional study	186	Questionnaires	Nurses (OR: 39.87, 95% CI: 2.721–584.3), other HWs (OR: 99.34, 95% CI: 7.469–1,321)
8	Nonghanphithak et al. [36]	2016	Thailand	Cross-sectional study	112	QFT, questionnaires	Age ≥ 30 years (OR: 18.88, 95% CI: 1.52–234.36), nurse (OR: 2.78, 95% CI: 1.19–6.49), job for ≥ 10 years (OR: 8.78, 95% CI: 1.26–61.29)
9	Tudor et al. [43]	2016	South Africa	Case-control study	307	Questionnaires	HWs living with HIV (OR: 6.35, 95% CI: 3.54–11.37) spent time working in areas with patients (OR: 2.24; 95% CI: 1.40–3.59)

Table 2. (Continued) Summary of published studies meeting inclusion criteria for risk factors of TB among HWs

Number	Author	Year	Country	Study design	Participants	Tuberculosis assessment	Estimate of risk
10	Ito et al. [41]	2016	Japan	Retrospective study	875	IGRA, CXR	Multivariate analysis (OR: 8.2, 95% CI: 1.3–78.3, p = 0.03), longer duration of contact (> 7 days, 12/12 [100%], vs. ≤ 7 days, 18/43 [41.9%]; p = 0.0002), fewer symptoms (> 7 days, 5/12 [41.7%] vs. ≤ 7 days, 35/43 [81.4%]; p = 0.01).
11	Tsang et al. [59]	2015	Hong Kong	Prospective cohort study	279	IGRA, QFT	QFT-GIT positive: (exposed: 19.5%, non-exposed: 20.8%, RR = 0.96, 95% CI: 0.74–1.25, p > 0.05)
12	Agaya et al. [60]	2015	Kenya	Cross-sectional survey	1,416	Standardized questionnaire	LTBI prevalence: (p = 0.72), work year: p < 0.01
13	McCarthy et al. [61]	2015	South Africa	Cross-sectional study	199	IGRA, TST	Incident LTBI (IGRA): 25/97 (26%; incident rate 29 cases/100 person-years, 95% CI: 20–44), TST: 25/93 (27%; incident rate 29 cases/100 person-years, 95% CI: 19–42)
14	Rutanga et al. [62]	2015	Rwanda	Cross-sectional study	1,131	TST	LTBI prevalence: (62.1%), TST positive odds TST: 2.71 times greater (95% CI: 2.01–3.67), work year odds: increasing 4% (aOR: 1.04, 95% CI: 1.02%–1.05%) per year
15	Chu et al. [63]	2014	Taiwan	Population-based cohort study	11,811	Chart review	TB incidence: HWs vs matched subjects (61.08 vs. 37.81 per 100,000 person-years) Risk of TB: HWs (aHR: 1.62, 95% CI: 1.08–2.43)
16	Tudor et al. [43]	2014	South Africa	Retrospective cohort study	1,313	Chart review	HWs living with HIV had a greater incidence of TB (IRR: 3.2, 95% CI: 1.54–6.66) than HIV-negative HWs
17	Zhou et al. [64]	2014	China	Cross-sectional study	712	TST	TB hospital: 58.0% (n = 127), non-TB hospital: 33.9% (n = 105) (OR: 2.40, 95% CI:1.59–3.62), (6–10 years vs. ≤ 5 years [OR: 1.89, 95% CI: 1.10–3.25] and > 10 vs. ≤ 5 [OR:1.80; 95% CI: 1.20–2.68])
18	Claassens et al. [65]	2013	South Africa	Cross-sectional study	133	Sputum smear	The infection control audit score: OR: 1.04, 95% CI: 1.01–1.08, p = 0.02, the number of staff: OR: 3.78, 95% CI: 1.77–8.08, the number of staff remained: OR: 3.33, 95% CI: 1.37–8.08
19	Durando et al. [66]	2013	Italy	Cross-sectional study	881	TST	Born in high TB incidence areas (≥ 20 cases per 100,000 population)
20	Kim et al. [37]	2013	Korea	Cross-sectional study	2,132	TST	TST positive: 778 (36.5%), being older (OR: 1.10, 95% CI: 1.06–1.13, p < 0.001), male (OR: 1.78, 95% CI: 1.21–2.62, p = 0.003), re-joining the hospital workforce (OR: 1.58, 95% CI: 1.04–2.40, p = 0.032)
21	Casas et al. [67]	2013	Spain	Cohort analysis	614	TST	High risk worker hazard ratio: 1.55 (95% CI: 1.05–2.27) gender, age and professional status
22	Mathew et al. [42]	2013	South India	Case-control study	101	TST	BMI < 19 kg/m^2 (OR: 2.96, 95% CI: 1.49–5.87), contact with patients (OR: 2.83, 95% CI: 1.47–5.45), being employed in medical wards (OR: 12.37, 95% CI: 1.38–110.17), microbiology laboratories (OR: 5.65, 95% CI: 1.74–18.36)
23	He et al. [68]	2012	China	Cross-sectional study	999	TST, QFT-GIT	QFT-GIT-positive: 683 (68%) associated with greater age, longer HW career, TB disease in a co-worker and greater daily patient exposure using multivariable analysis

TB: tuberculosis; HW: health worker; RF: risk factor; aOR: adjusted odds ratio; CI: confidence interval; TST: tuberculin skin test; CXR: chest X-ray; LTBI: latent tuberculosis infection; BCG: Bacillus Calmette-Guerin; PR: prevalence ratio; OR: odds ratio; QFT: QuantiFERON-TB; HIV: human immunodeficiency virus; IGRA: interferon-gamma releasing assay; QFT-GIT: QuantiFERON-TB Gold-In-Tube; RR: risk ratio; BMI: body mass index.

The longer the number of work years of the HWs was, the higher the TB infection rate was. For instance, 39.3% HWs with work years > 8 years were TB positive [38], work years ≥ 10 years were also associated with a higher risk [36]. TB infection rates were also higher in the HWs (39.6%) [38] who did not receive the BCG vaccination with a study reporting an OR of 344 (CI: 43.72–2,718.41, p < 0.00001) [39].

Nurses had a higher OR than the other HWs (being a nurse, OR: 3.09, 95% CI: 1.15–8.32 [35]; nurses OR: 39.87, 95% CI: 2.721–584.3 and other HWs, OR: 99.34, 95% CI: 7.469–1,321 [40]; and nurses, OR: 2.78, 95% CI: 1.19–6.49 [36]).

There was an increased risk for TB with longer working durations (> 7 days, 12/12 [100%] vs. ≤ 7 days, 18/43 [41.9%]; $p = 0.0002$) [41] and direct contact with patients (OR: 2.83, 95% CI: 1.47–5.45) [42]. The infection was also observed more frequently in underweight HWs (BMI < 18.5, OR: 2.96, 95% CI: 1.49–5.87) [42], or in HWs with human immunodeficiency virus (OR: 6.35, 95% CI: 3.54–11.37) [43].

Discussion

Our results showed that the risk for TB among HWs was higher than that of the general population worldwide. Furthermore, differences were found in this association according to the geographical location. Risk factors for LTBI included old age, long work-duration, nursing professionals, lack of BCG vaccination, and lower BMI.

Overall, 29.94% of the HWs were found to be TB test positive. The rates were lower in Italy (4%–6%) and higher in Thailand and Taiwan. However, there was no significant difference between the TB infection rate of HWs in Taiwan and that of the general population. This suggests that HWs in countries with intermediate TB burden, face a similar risk of exposure to TB as the community, and that appropriate personal protection equipment and good infection control practices within a hospital effectively mitigates the transmission of TB in healthcare settings. Further, HWs who did not report an exposure to TB may have been unknowingly exposed to it either within the hospital or in the community [14]. However, these results must be interpreted with caution because TB infection status could be different by TB diagnosis tools.

Studies from different geographical locations were examined. As TB prevalence is still high in Asia and continental Europe, the research in these regions appeared to be more active than in the Americas. In France, the incidence of TB among the nurses and paramedics was not higher than the general public. This probably reflects the effectiveness of the measures implemented over the last decade to prevent the transmission of TB in the health care industry, as well as an overall decline of TB in the general population.

In our review, the prevalence of TB positive in doctors and nurses were high, which was similar to the existing literature. In terms of the occupation, TB prevalence was highest in the nurses, followed by doctors. This was probably due to their close proximity with the patients, particularly those with severe infections requiring high-risk investigations, such as bronchoscopy [35].

For the diagnosis, most of the studies used IGRA and TST together, while some others used either IGRA or TST, individually. Others employed questionnaires alone or along with the test. Additionally, AFB stains, CXR, and genotyping data were also used. TST and IGRA are currently used as the basis for LTBI screening and have different guidelines in different countries. Two or more screening methods are recommended for TB screening in adult and immunocompromised populations. Sometimes one test can provide an advantage over the other. For example, the IGRA is preferred over TST in groups where BCG is administered after infancy or at multiple times. However, none of the present LTBI tests fulfil the requirement of early diagnosis of TB. In a study comparing the results of IGRA and TST conducted in Saudi Arabia for medical workers, the following results were found. The disagreements between the two tests were relatively high (kappa co-efficient = 0.312 ± 0.026, $p < 0.00001$) as TST positive/QFT negative discordance was 54.8% while TST negative/QFT positive discordance was 15.7% [44]. Therefore, supplementary testing methods such as CXR, AFB stains and questionnaires should be used.

Various risk factors were identified. Aging, diabetes mellitus and low BMI, are known factors of immunological imbalance associated with TB development in the general population [45]. The reason for higher TB infection in older HWs and longer work years was due to an increased contact with TB patients in addition to the aging and decline in the immunity [35]. Although a low BMI is associated with active TB, it can be interpreted as a consequence of TB rather than as a risk factor [42,46].

According to the World Health Organization (WHO) guidelines, strict clinical observation and close monitoring for the development of active TB for at least two years is preferred over the provision of preventive treatment for contacts of multidrug-resistant-TB cases. In cases where preventive therapy is considered for such individuals, the program should ensure that the necessary resources are available to provide quality-assured drug susceptibility testing and the necessary medications, and to closely monitor for any harm, breakthrough disease, and acquired resistance [47].

In many of the countries, despite the increasing risk of TB infection in HWs, the quality of occupational health and safety, and infection prevention and control have not improved significantly. Evidence-based investment of effort is required for the effective risk reduction for HWs [48,49].

The Republic of Korea has a moderate TB prevalence (85–110/100,000 population per year) and BCG vaccination is recommended at birth [37]. Until 1997, the BCG vaccine was given at birth and repeated at the age of 12 or 13 years if the child proved to be a TST non-responder. However, revaccination was stopped in 1997 according to the WHO recommendation in 1995 due to the lack of evidence [50].

Further research is needed to assess the change in regional surveillance systems in different countries, depending on the development of respective national health conditions. We also need a country- and age-wise evaluation of the effectiveness of the BCG vaccination.

In conclusion, this study showed that HWs were at higher risk for developing TB. It further emphasized on the need for sound TB infection control measures, including early diagnosis and prompt treatment, for its effective prevention in HWs and the general public.

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