International Journal of Infectious Diseases 79 (2019) 26–33

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Prevalence and determinants of latent tuberculosis infection among frontline tuberculosis healthcare workers in southeastern China: A multilevel analysis by individuals and health facilities

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ARTICLE INFO

Article history:
Received 27 September 2018
Received in revised form 7 November 2018
Accepted 14 November 2018
Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Keywords:
Tuberculosis
Latent tuberculosis infection
Healthcare workers

ABSTRACT

Objectives: Healthcare workers (HCWs) are at high risk of latent tuberculosis infection (LTBI), and the baseline prevalence of LTBI among frontline TB HCWs in southeastern China remains unknown. The aim of this study was to assess the prevalence of LTBI among TB HCWs and to analyze factors associated with LTBI at both the individual and institutional level.

Methods: Based on a cross-sectional study design, 31 out of 89 TB-designated hospitals in Zhejiang Province of China were selected. Information on TB infection control measures was collected through field visits to each of the selected hospitals. All TB HCWs from the selected hospitals were recruited to answer a questionnaire and to undergo LTBI testing by TB interferon gamma release assay. Univariate analyses and a generalized linear mixed model were applied to analyze factors associated with LTBI at both the individual and hospital level.

Results: A total of 487 TB HCWs were recruited at the 31 TB-designated hospitals; 33.9% of them tested positive for LTBI. At the institutional level, a low TB epidemic level, regular infection control training for HCWs, and regular maintenance of ultraviolet disinfection equipment were found to be significantly associated with a lower LTBI rate among HCWs. At the individual level, alcohol use, a greater number of years working on TB, and a longer weekly duration of contact with TB patients were identified as associated factors for LTBI among HCWs.

Conclusions: The LTBI rate among frontline TB HCWs was found to be high in southeastern China. Factors at the institutional and individual level could both affect the prevalence of LTBI among HCWs.

Introduction

China is one of the high-burden countries for tuberculosis (TB), HIV/TB co-infection, and multidrug-resistant TB (MDR-TB) (World Health Organization, 2017). In recent years, significant progress has been made in China, with a 3.1% annual decline in the reported TB incidence from 2010 to 2015 (Chen et al., 2016b). Zhejiang Province, a coastal and developed province located in the southeast of China, is also experiencing a dramatic decline in the TB epidemic, with a reported incidence rate of 50.8/100 000, which was lower than the national level in 2015 (Chen et al., 2016b). However, with a population of 55 million, the TB burden remains high in this province. In 2015, local TB hospitals diagnosed and reported a total of 30 476 cases of TB (Zhejiang Provincial Center for Disease Control and Prevention, 2016). Moreover, the province was estimated to have 2000 new MDR-TB cases (CZTV.com, 2013).

TB healthcare workers (HCWs) are at high risk of TB infection, as they work at the frontline of TB treatment and prevention (Joshi et al., 2006; World Health Organization, 2015; Zwerling et al., 2012b). A systematic review reported a prevalence of latent tuberculosis infection (LTBI) of 54% (33–79%) in low and middle-income countries (Joshi et al., 2006). In China, previous studies have revealed high LTBI rates among HCWs ranging from 34% to

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https://doi.org/10.1016/j.ijid.2018.11.010

77% in the northern provinces, including Inner Mongolia, Heilongjiang, Henan, and Beijing (He et al., 2010, 2012; Wang et al., 2007; Wei et al., 2013b; Zhang et al., 2013). Although China has greatly improved its ability to find and treat cases of TB, TB infection control measures have been ignored in many TB-designated hospitals (Chen et al., 2016a; He et al., 2010). The LTBI status of TB HCWs has not been tested systematically as conditionally recommended in the World Health Organization guidelines (World Health Organization, 2015).

The QuantiFERON-TB Gold In-Tube test (QFT-GIT; Cellestis Ltd, Carnegie, Victoria, Australia) and T-SPOT.TB test (Oxford Immunotec, Oxford, UK) are two commonly used interferon-gamma release assays (IGRAs) used to test for LTBI (King et al., 2015; Mazurek et al., 2010; World Health Organization, 2015; Zhang et al., 2013; Zwerling et al., 2012b). Despite disagreements regarding the stability of serial tests, the easily operated IGRAs have been recommended and are used widely to detect LTBI among different populations (He et al., 2010; Joshi et al., 2012; Zhang et al., 2013; Zwerling et al., 2012a,b). In China, TB-IGRA (Beijing Wantai Biopharm Co., Ltd, China) is a domestic TB IGRA licensed by the China Food and Drug Administration (Liu et al., 2015). This assay has been evaluated in previous research and has shown equal sensitivity and specificity to QFT-GIT and T-SPOT.TB for the detection of TB infection among patients, non patients, and healthy individuals (Liu et al., 2015; Qian et al., 2013; Qiu et al., 2015). It has been used clinically for the differential diagnosis of TB infection in hospitals in China.

In China, as of 2003, TB diagnostic and treatment services were supplied primarily by local Centers for Disease Control and Prevention (CDCs). In the past decade, these services have been assigned to local general hospitals designated as TB hospitals in most areas (Chen et al., 2016a; Wei et al., 2013a). Patient out-of-pocket costs and delays were shown to be dramatically reduced under the designated hospitals compared with the previous CDC treatment models (Sun et al., 2013; Wei et al., 2014). Under the TB-designated hospitals system, TB clinical services are often provided in a separate TB clinic where sputum testing and inpatient wards are located. However, other departments, such as the in-hospital pharmacy, radiology department and cashier counter, and registration areas are usually shared with other patients. Zhejiang Province is one of the pioneering provinces that have integrated TB clinical services into general hospitals. There is a concern regarding nosocomial TB infection in these hospitals (Chen et al., 2016a; He et al., 2010; Zhong et al., 2013). By 2014, a total of 89 TB-designated hospitals (13 prefectural and 76 county level) had been established in the province, in which around 900 registered TB HCWs served in 2015 (Zhejiang Online News, 2016). Prefectural-level TB-designated hospitals mainly provide medical services to patients with MDR-TB, patients with intractable TB, or critical TB patients. County-level TB-designated hospitals mainly provide care to local patients with normal TB.

The prevalence of LTBI among frontline TB HCWs in these TB-designated hospitals remains unknown in a provincial region of southeastern China. It appears that most previous studies have evaluated the risk factors of TB infection solely from the individual or facility perspective, but little research has been done at both levels (He et al., 2015; Jelip et al., 2004; Joshi et al., 2006). We conducted a provincial cross-sectional survey to investigate the LTBI status of TB HCWs. The risk factors for LTBI among TB HCWs were analyzed systematically at both the individual and the institutional level and it was aimed to provide evidence-based suggestions for TB infection control practices in China.

Methods

Study design and participants

A multistage stratified cluster sampling method was applied for the inclusion of sample hospitals and HCWs. Zhejiang Province has 11 prefectures and 90 counties. Each prefecture governs four to 13 counties. Each prefecture has at least one prefectural-level TB-designated hospital. Most counties have established a county-level TB-designated hospital in their administrative area, but some urban counties have not set their county-level TB-designated hospitals, and TB patients in those counties are treated at the upper-level (prefectural) TB-designated hospitals. First, one prefectural TB-designated hospital was selected from each prefecture as study objects. Second, two county-level TB-designated hospitals from each prefecture were randomly selected. An institutional survey was conducted to investigate all of the selected hospitals. Third, all eligible HCWs who served in the selected hospitals were invited to participate in the survey. The inclusion criteria were as follows: HCWs who worked in the independent TB departments or shared sections that had direct contact with TB patients (e.g., X-ray rooms, pharmacies, and fee-charging rooms); HCWs who did not have active TB disease; and HCWs who had worked with TB patients for more than 6 months.

The survey was conducted from January to June 2015. The sample size was calculated based on an expected LTBI rate of 54% (results from a systematic review on LTBI in HCWs) (Joshi et al., 2006) and a 5% two-sided level of significance. A sample size of 340 was calculated. Taking into account the possibility that 10% of the HCWs might decline to participate in the survey, it was determined that about 374 HCWs should be invited to participate in the survey.

Data collection and testing method

A trained survey team from the provincial CDC, including epidemiological investigators, laboratory technicians, and infection control practitioners, conducted the survey at the selected hospitals. An institutional questionnaire survey by direct observation and staff interviews was first conducted. Next, the eligible HCWs at the hospitals were invited to complete a self-administered questionnaire. The two questionnaires were designed based on the recommendations of the national TB infection control manual and were developed in Chinese (Wang et al., 2010). The questionnaires were pre-tested and adjusted at a prefectural-level TB-designated hospital. The institutional survey included questions that allowed basic hospital information and data on administrative, environmental, and personal protective infection control measures to be obtained. The questions in the individual questionnaire were used to obtain demographic information (e.g., sex, age, educational attainment, marital status, and so on); individual characteristics, such as weight, height, bacille Calmette–Guérin (BCG) vaccination status, and health-related behaviors; job characteristics and work experience; and knowledge, attitudes, and previous practice on TB infection control.

After completing the questionnaire, the laboratory technician collected 4–5 ml of venous whole blood from the respondents. The whole blood was stored in tubes containing heparin. The TB-IGRA (Beijing Wantai Biopharm Co., Ltd., China) was used to test for LTBI among the respondents. The laboratory technician added 1 ml of the heparinized venous whole blood sample to each of the three Eppendorf centrifuge tubes, which contained nil for negative control (N), mitogen for positive control (P), or TB antigen, and a recombinant fusion protein of CFP-10 (10-kDa culture filtrate protein) and ESAT-6 (T) (6-kDa early secreted antigen target).

The three tubes containing the blood sample were incubated at 37 °C and an enzyme-linked immunosorbent assay (ELISA) was used to measure the concentration of interferon-gamma (IFN-γ). The IFN-γ value (pg/ml) was corrected for the TB antigen and mitogen for background by subtracting the value of N, i.e., T − N and P − N. According to the manufacturer's recommendations, a test result of N ≤400 pg/ml, P − N = any value, T − N ≥14 pg/ml and ≥25% of N was recognized as positive. A test result of N ≤400 pg/ml, P − N ≥20 pg/ml, T − N <14 pg/ml or T − N ≥14 pg/ml but <25% of N were judged as negative. Other results were deemed to be intermediate.

Statistical analysis

The data from the valid questionnaires were double-entered and checked with EpiData software (EpiData 3.01 for Windows; The EpiData Association, Odense, Denmark). The data from the corresponding hospitals and the individuals were incorporated into one database. IBM SPSS Statistics version 20 (IBM Corp., Armonk, NY, USA) and SAS 9.4 (SAS Institute Inc., Cary, NC, USA) were used to perform the statistical analysis. Univariate analysis was applied to analyze the association between individual characteristics and LTBI results.

A generalized linear mixed model (GLIMMIX) was used to perform a multilevel risk factor analysis. Participant factors, such as demographic characteristics, job features, and personal infection control knowledge, attitudes, and previous practices, were considered as level 1 factors. Institutional factors, such as hospital basic information and infection control measures, were considered as level 2 factors. Factors that were identified as significant in the univariate analysis and variables that were important in the GLIMMIX model were included. The estimation method selected in the procedure was the maximum likelihood estimation. Backward selection helped in the selection of the best model. A logistic multivariate model was generated to determine which covariates would help predict the odds of LTBI, and hierarchical regression was applied to adjust the multilevel effect. A *p*-value of <0.05 was considered to be statistically significant.

Ethics statement

The survey was approved by the Ethics Review Board of Zhejiang Provincial CDC. Signed informed consent forms were obtained from the respondents and personal information was kept confidential. All respondents were informed of the results of their LTBI tests and a consultation was provided for those who needed further checks and prophylactic treatment.

Results

Basic information and infection control measures at the surveyed hospitals

Thirty-one TB-designated hospitals including nine prefectural-level hospitals (two hospitals refused to take part in the survey) and 22 county-level hospitals participated in the institutional survey. Table 1 lists the basic information of the hospitals and their implementation of TB infection control measures.

Table 1
Basic information for the investigated hospitals and TB infection control measures at the hospitals.

Hospital information and IC measures	Number or median	% or IQR
Hospital level		
Prefectural	9	29.0
County	22	71.0
Local TB epidemic (provincial notification rate level = 50.8/100 000)		
Lower than provincial average level	18	58.1
Higher than provincial average level	13	41.9
Annual number of outpatients in the TB section of each hospital	5000	2425–9167
Annual number of diagnosed TB patients in each hospital	371	208–505
Establishment of TB IC committee at the hospital		
Yes	17	54.8
No	14	45.2
Setting TB IC regulations in the hospital		
Yes	24	77.4
No	7	22.6
Setting rapid referral rules for patients with suspected TB (reducing waiting time)		
Yes	13	41.9
No	18	58.1
Separate entrance for HCWs in TB department		
Yes	7	22.6
No	24	77.4
Regular monitoring of ventilation (at least quarterly)		
Yes	17	54.8
No	14	45.2
Regular monitoring of ultraviolet facilities		
Yes	26	83.9
No	5	16.1
Regular provision of N95 respirators for HCWs		
Yes	29	93.5
No	2	6.5
Regular fitting test for usage of N95 respirators		
Yes	11	35.5
No	20	64.5
Regular TB IC training for HCWs (at least annually)		
Yes	28	90.3
No	3	9.7

TB, tuberculosis; IC, infection control; IQR, interquartile range; HCWs, healthcare workers.

Basic information for the HCWs and their LTBI rate

A total of 499 registered HCWs were eligible for enrollment at the 31 hospitals; seven HCWs from five hospitals declined to be surveyed. Two HCWs with active TB were excluded from the study. Finally, the remaining 490 HCWs agreed to be tested for LTBI and responded to the questionnaire. Excluding the three respondents who had intermediate test results, the test and questionnaire data of 487 HCWs were finally included. Among the HCWs, 359 were female (73.7%), and their mean age was 35.5 ± 9.6 years. The majority of the respondents (306/478) had graduated from university, and 364 (76.2%) were married. Table 2 lists more detailed information about the demographic characteristics of the respondents.

A total of 165 of the 487 TB HCWs tested positive for LTBI by TB-IGRA, giving an LTBI rate of 33.9%.

LTBI rate among different groups of TB HCWs

Compared with respondents younger than 30 years of age (LTBI rate = 22.7%), those in the age-groups of 30–39 years, 40–49 years, and ≥50 years had higher positive rates at 33.9%, 44.2%, and 46.3%, respectively. The unadjusted odds ratios (ORs) (95% confidence intervals (CI)) were 1.75 (1.07–2.85), 2.71 (1.59–4.61), and 2.95 (1.43–6.07), respectively. The LTBI rate among married HCWs was 36.5%, which was higher than the rate among single HCWs (OR 1.71, 95% CI 1.07–2.74). Smoking and drinking were significantly associated with higher LTBI rates (56.2% vs. 32.3% and 50.9% vs. 31.7%, respectively) with ORs of 2.69 (95% CI 1.30–5.67) and 2.23 (95% CI 1.27–3.93), respectively. There was no difference in the positive rate according to sex, education, annual family income, body mass index, BCG vaccination, or TB history (Table 2).

Prevalence of LTBI in groups of TB HCWs with different job features

In contrast to HCWs who had worked on TB for less than 2 years (25.3%), the positive rates among those who had worked for 6–10 years, 11–20 years, and >20 years were significantly higher at 37.1%, 46.7%, and 63.0%, respectively. Among the different professional groups, the physicians had the highest LTBI rate at 46.7%. The LTBI rates among nursing staff, laboratory technicians, and chest radiologists were significantly lower at 28.6%, 30.3%, and 26.8%, respectively. Compared with HCWs with a junior title (25.3%), HCWs with intermediate, associate-senior, and senior titles had significantly higher LTBI rates at 42.5%, 45.0%, and 56.2%, respectively (Table 3).

Association between knowledge, attitudes, and previous practice of infection control and LTBI in TB HCWs

No significant differences in LTBI rate were found among the groups with different knowledge, attitudes, and previous practice on TB infection control, except for the groups that held different attitudes about the protective effect of gauze masks. HCWs who believed gauze masks could prevent TB transmission had a higher LTBI rate than those who did not believe this (OR 1.86, 95% CI 1.14–3.04).

Results of multilevel risk factor analysis

The −2 log likelihood, Akaike's Information Criterion (AIC), and Bayesian Information Criterion (BIC) of the GLIMMIX model were 550.36, 592.36, and 622.48, respectively. The area under the receiver operating characteristic (ROC) curve of the model was 0.73, which showed a good fitness of the model.

At the individual level, the variables of education, drinking, annual family income, number of years working on TB, professional title, and weekly estimated contact hours with TB patients were

Table 2
Association between individual characteristics and positive TB-IGRA results among TB HCWs in Zhejiang Province, China.

Individual characteristic	Subgroups	Number	TB-IGRA positive, *n* (%)	Unadjusted OR (95% CI)
Sex	Male	128	51 (39.8)	(Reference)
	Female	359	114 (31.8)	0.70 (0.46–1.07)
Age (years)	<30	150	31 (22.7)	(Reference)
	30–39	183	62 (33.9)	1.75 (1.07–2.85)[a]
	40–49	113	50 (44.2)	2.71 (1.59–4.61)[a]
	≥50	41	19 (46.3)	2.95 (1.43–6.07)[a]
Education	High middle school or below	54	13 (24.1)	(Reference)
	Junior college	127	38 (29.9)	1.35 (0.65–2.80)
	University	306	114 (37.3)	1.87 (0.96–3.64)
Marital status	Single	115	29 (25.2)	(Reference)
	Married	364	133 (36.5)	1.71 (1.07–2.74)[a]
	Divorced/widowed	8	3 (37.5)	1.78 (0.40–7.91)
Annual family income (USD)	<15 000	53	21 (39.6)	(Reference)
	15 000–30 000	305	100 (32.8)	0.75 (0.41–1.36)
	≥30 000	129	44 (34.1)	0.79 (0.41–1.52)
BMI (kg/m^2)	<18.5	63	20 (31.7)	(Reference)
	18.5–23.9	328	112 (34.1)	1.12 (0.63–1.99)
	≥24	96	33 (34.4)	1.13 (0.57–2.22)
Smoking	No	455	147 (32.3)	(Reference)
	Yes	32	18 (56.2)	2.69 (1.30–5.67)[a]
Drinking	No	432	137 (31.7)	(Reference)
	Yes	55	28 (50.9)	2.23 (1.27–3.93)[a]
BCG vaccination	Yes	340	117 (34.4)	(Reference)
	No	147	48 (32.7)	0.92 (0.61–1.39)
History of TB, but now cured	No	470	158 (33.6)	(Reference)
	Yes	17	7 (41.2)	0.72 (0.27–1.94)
Total		487	165 (33.9)	

TB, tuberculosis; IGRA, interferon gamma release assay; HCWs, healthcare workers; OR, odds ratio; CI, confidence interval; BMI, body mass index; BCG, bacille Calmette–Guérin.

[a] Significant, $p < 0.05$.

Table 3
Association between job features and positive TB-IGRA results among TB HCWs in Zhejiang Province, China.

Job feature	Subgroups	Number	TB-IGRA positive, *n* (%)	Unadjusted OR (95% CI)
Years working in healthcare	≤2	60	15 (25.0)	(Reference)
	3–5	74	17 (23.0)	0.78 (0.40–1.98)
	6–10	110	36 (32.7)	1.46 (0.72–2.96)
	11–20	133	46 (34.6)	1.59 (0.72–2.96)
	>20	110	51 (46.4)	2.59 (1.30–5.19)[a]
Years working on TB	≤2	162	41 (25.3)	(Reference)
	3–5	107	29 (27.1)	1.10 (0.63–1.91)
	6–10	116	43 (37.1)	1.74 (1.04–2.92)[a]
	11–20	75	35 (46.7)	2.58 (1.45–4.59)[a]
	>20	27	17 (63.0)	5.02 (2.14–11.83)[a]
Work department	TB outpatient clinic	77	30 (39.0)	(Reference)
	TB ward	258	91 (35.3)	0.85 (0.51–1.44)
	TB microbiology laboratories	76	23 (30.3)	0.68 (0.35–1.33)
	Radiology unit	41	11 (26.8)	0.57 (0.25–1.32)
	Pharmacies, fee charging rooms, and other administrative sections	35	10 (28.6)	0.63 (0.26–1.45)
Professional group	Physician	136	63 (46.7)	(Reference)
	Nursing staff	189	54 (28.6)	0.46 (0.29–0.74)[a]
	Laboratory technician	76	23 (30.3)	0.50 (0.28–0.91)[a]
	Chest radiologist	41	11 (26.8)	0.43 (0.20–0.92)[a]
	Administrative and other support staff	45	14 (31.1)	0.52 (0.26–1.07)
Professional title	Junior	251	61 (24.3)	(Reference)
	Intermediate	160	68 (42.5)	2.30 (1.50–3.53)[a]
	Associate-senior	60	27 (45.0)	2.55 (1.42–4.57)[a]
	Senior	16	9 (56.2)	4.00 (1.43–11.21)[a]
Weekly estimated contact hours with TB patients	≤10	63	16 (25.4)	(Reference)
	10–40	258	86 (33.3)	1.47 (0.78–2.74)
	≥40	166	63 (38.0)	1.80 (0.94–3.44)
Total		487	165 (33.9)	

TB, tuberculosis; IGRA, interferon gamma release assay; HCWs, healthcare workers; OR, odds ratio; CI, confidence interval.
[a] Significant, $p < 0.05$.

included in the final model. HCWs who had the habit of drinking alcohol showed a higher odds of TB infection, with an OR of 2.63 (95% CI 1.38–5.00). HCWs who had worked for more than 20 years had an OR of 3.41 (95% CI 1.29–9.02) compared with HCWs who had worked for less than 2 years. The estimated weekly contact hours with TB patients showed a similar pattern: HCWs who reported 10–40 hours and more than 40 h of contact had an OR of 2.15 (95% CI 1.06–4.37) and 2.88 (95% CI 1.36–6.09), respectively, compared with those who reported less than 10 h of contact (Table 4).

At the institutional level, the local level of the TB epidemic, annual outpatient turnover, and infection control measures, including establishing a separate entrance for HCWs in the TB department, regular monitoring of ultraviolet (UV) facilities, regular fitting tests for the usage of N95 respirators, and regular TB infection control training for HCWs, were included in the final model. Among these, the hospitals located in a higher level TB epidemic area had an OR of 1.91 (95% CI 1.23–2.96). Regular monitoring of UV facilities by the hospital was identified as a protective factor (OR 0.34). However, hospitals that reported failing to organize infection control training on a regular basis had higher odds of LTBI (OR 3.63) (Table 4).

Discussion

This study investigated LTBI among TB HCWs at 31 frontline TB-designated hospitals and obtained a province-wide baseline LTBI rate of 33.9% in southeastern China. This rate is lower than those in other high-burden countries and those reported in the northern provinces of China (Dorman et al., 2014; Evans and Bekker, 2016; He et al., 2012; Joshi et al., 2006; Wang et al., 2007; Wei et al., 2013b; Zhou et al., 2014; Zwerling et al., 2012b). However, it is higher than that of a large-scale study among the rural community population (13–20%), indicating higher odds of TB infection among HCWs in China (Gao et al., 2015).

The GLIMMIX offered an opportunity to systematically analyze factors associated with LTBI at both the individual and institutional level in the same context. Previous research has indicated that the TB contact frequency is an important risk factor for LTBI in HCWs (He et al., 2012; Joshi et al., 2006; Whitaker et al., 2013). In the present research, the local TB epidemic level was identified as a factor associated with LTBI at the facility level. A higher epidemic level led to more TB patient visits and a higher volume of contact with TB, which increased the chance of coming into contact with TB during daily work (Joshi et al., 2006; Sherman et al., 2011; Tudor et al., 2016). At the individual level, it was found that a greater intensity of contact with TB during routine HCW working practices increased the risk of TB infection. Other factors, such as older age and longer working time, have been recognized as additional risk factors for LTBI among HCWs (He et al., 2012; Joshi et al., 2006; Zhou et al., 2014). The present study indicated that longer working years on TB might be the major factor affecting LTBI rates among HCWs when adjusted for age-group in the multilevel model.

The implementation of multiple infection control measures, including administrative, personal, and engineering controls in TB facilities, has proven to be effective for the reduction of TB infection (Joshi et al., 2006; Roth et al., 2005; Yanai et al., 2003). In the present study, it was found that regular monitoring of UV equipment was a protective factor for LTBI, which suggests the importance of ensuring that facilities are maintained and disinfected properly. Regular infection control training for HCWs was associated with a lower LTBI rate and the study also found that regular TB infection control training was a protective factor for a lower LTBI rate at the institutional level. Regular training could

Table 4
Multilevel analysis for risk factors for positive TB-IGRA results among TB HCWs in Zhejiang Province, China.

Variables		Indicators				
		Estimate	SE	*t*	*p*-Value	OR (95% CI)
Intercept		−3.27	0.94	−3.48	0.001	–
Institutional level:						
Local TB epidemic level	Lower than the provincial average level	(Reference)				
	Higher than the provincial average level	0.64	0.23	2.85	0.005	1.90 (1.22–2.97)[a]
Separate entrance for HCWs in TB department	No	(Reference)				
	Yes	−0.28	0.28	−0.99	0.322	0.75 (0.43–1.32)
Regular monitoring of UV facilities	Yes	(Reference)				
	No	1.07	0.38	2.84	0.005	2.92 (1.39–6.14)[a]
Regular fitting test for usage of N95 respirators	No	(Reference)				
	Yes	−0.25	0.24	−1.08	0.281	0.78 (0.49–1.23)
Regular TB IC training for HCWs (at least annually)	Yes	(Reference)				
	No	1.29	0.48	2.7	0.007	3.63 (1.42–9.28)[a]
Individual level:						
Education level	High middle school or below	(Reference)				
	Junior college	0.45	0.41	1.09	0.275	1.57 (0.70–3.51)
	University	0.62	0.39	1.57	0.117	1.85 (0.86–4.01)
Drinking	No	(Reference)				
	Yes	0.96	0.33	2.95	0.003	2.62 (1.38–4.98)[a]
Annual family income (USD)	≥30 000	(Reference)				
	15 000–30 000	0.12	0.26	0.46	0.646	1.13 (0.67–1.89)
	<15 000	0.69	0.41	1.68	0.094	1.99 (0.89–4.45)
Years working on TB	≤2	(Reference)				
	3–5	−0.05	0.31	−0.17	0.861	0.95 (0.52–1.73)
	6–10	0.31	0.31	1.01	0.312	1.36 (0.75–2.48)
	11–20	0.57	0.35	1.63	0.105	1.77 (0.89–3.52)
	>20	1.25	0.49	2.53	0.012	3.49 (1.32–9.22)[a]
Weekly estimated contact hours with TB patients	≤10	(Reference)				
	10–40	0.81	0.36	2.22	0.027	2.25 (1.10–4.59)[a]
	≥40	1.11	0.39	2.88	0.004	3.04 (1.42–6.50)[a]
Professional title	Senior	(Reference)				
	Associate-senior	−0.49	0.62	−0.79	0.429	0.61 (0.18–2.07)
	Intermediate	−0.33	0.59	−0.56	0.577	0.72 (0.22–2.30)
	Junior	−1.07	0.61	−1.74	0.082	0.34 (0.10–1.15)

TB, tuberculosis; IGRA, interferon gamma release assay; HCWs, healthcare workers; SE, standard error; OR, odds ratio; CI, confidence interval; HCWs, healthcare workers; IC, infection control.
[a] Significant, $p < 0.05$.

make HCWs more knowledgeable of TB and infection control measures, which may help HCWs practice TB infection control measures well and protect them from infection in their routine work (Mirtskhulava et al., 2015).

At the individual level, smoking and alcohol drinking were determined to be risk factors for LTBI among the normal population in a large-scale survey (Gao et al., 2015). In the present study, both drinking and smoking were recognized as factors associated with LTBI among HCWs in the univariate analysis and drinking was recognized as a risk factor in the final multilevel model. Simet and Sisson considered that the lung is affected adversely by alcohol, and individuals with an alcohol use disorder are more likely to develop pneumonia and TB (Simet and Sisson, 2015).

Occupational factors are important factors associated with LTBI among HCWs (Sherman et al., 2011; Tudor et al., 2016; Yanai et al., 2003; Zhou et al., 2014). In the present study, physicians tended to have higher odds of LTBI in the univariate analysis (47.7%), whereas other occupational groups showed a lower infection rate. Previous studies have proven that clinical staff members who have direct contact with TB patients are in a risk group for LTBI (He et al., 2010; Tudor et al., 2016; World Health Organization, 2015). Sherman et al. found that housekeeping HCWs had the highest risk of TB infection at a tertiary university medical center (Sherman et al., 2011). Zhang et al. found that the laboratory staff had a higher T-SPOT.TB positive rate at the Beijing Chest Hospital, China (Zhang et al., 2013). The risk groups might be different because of differences in the study settings. In the present study, physicians in the clinic room or inpatient ward took on higher patient turnover, which could be the cause of the higher risk in the lower level TB hospitals. In addition, it was found that the incorrect belief of the protective value of gauze masks was associated with a higher LTBI rate in the univariate analysis. In China, there is a long history of gauze mask usage due to the lack of N95 respirators. This result indicates that TB infection control training is needed to correct the wrong belief of the protective value of gauze masks, particularly in the groups of young and senior HCWs.

This study had several limitations. First, the retrospective questionnaire survey may have resulted in information loss. The study was explained to the respondents and they were informed of the information loss in order to mitigate this as much as possible. Second, the study could not provide the incidence of LTBI and the causal relationship of some factors was not clear. The social association between alcohol drinking and smoking may affect the factor analysis of LTBI among HCWs, and this deserves further study in the future. Due to the cross-sectional design, serial IGRA testing was not conducted and it was not possible to obtain the conversion rate among the TB HCWs. We are planning to conduct another round of testing with a cohort design in a future study. Finally, the sample size was sufficient to determine the overall LTBI level among the TB HCWs in southeastern China, but these HCWs might not be representative of the whole country.

In conclusion, this study revealed a high risk of LTBI among frontline TB HCWs in southeastern China. Senior TB HCWs who have worked with the TB population for a longer time and who have worked more extensively on TB should be prioritized for periodic testing for LTBI and active TB. Comprehensive TB infection control measures such as regular maintenance of UV facilities and regular TB infection control training should be well implemented at the TB facilities, particularly in high-epidemic areas. Health interventions to reduce alcohol drinking could be provided to TB HCWs to reduce nosocomial TB infection.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (71640019), Zhejiang Major Science and Technology Projects2014C03034), Zhejiang Social Science Project (19NDJC243YB), and Zhejiang Provincial Medical Research Project (2016RCA007 and 2015KYA052). We would like to thank the staff from the local centers for diseases control and prevention (CDCs) and local TB-designated hospitals for their help in the field survey.

Author contributions

J.J. and X.L.W. conceived the idea and designed the study. B.C. and H.G. wrote the article. X.M.W., F.W., and Y.P collected the data. E.G. and R.D. analyzed the data. R.U. provided suggestions and revised the article.

Conflict of interest

The authors declare no conflict of interest.

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