

# Predictors of low prevalence of latent tuberculosis infection among Egyptian health care workers at intensive care and bronchoscopy units

## Geringe Prävalenz von Prädiktoren für eine latente Tuberkulose bei ägyptischem medizinischem Personal auf Intensivtherapie- und Bronchoskopieeinheiten

### Abstract

**Aim:** Latent tuberculosis infections (LTBI) contain a significant reservoir for future epidemics. Screening of health care workers (HCWs) in a high-risk tuberculosis (TB) environment is an important strategy in TB control. The study aimed to assess the prevalence of LTBI among high risk Egyptian HCWs and to assess infection associated risk factors.

**Methods:** Fifty-two HCWs who work at intensive care unit (ICU), bronchoscopy unit, and chest diseases department were tested for LTBI using both tuberculin skin test (TST) and QuantiFERON TB Gold in-tube test (QFT). Risk factors for infection, knowledge of HCWs towards different aspects of TB infection and agreement between TST and QFT were also evaluated.

**Results:** Prevalence of LTBI in this study was 13.5% by QFT and TST. It was 13.6% by TST alone and 10.3% by QFT alone. There was good concordance between both tests ( $\text{Kappa}=0.713$ ). There was a statistically significant association between prevalence of LTBI and age of staff  $\geq 30$  yr ( $p=0.002$ ), period of working experience ( $p=0.006$ ) and working at the Bronchoscopy Unit ( $p=0.001$ ). The total knowledge of HCWs towards different aspects of TB infection was generally good.

**Conclusion:** Although the participants in the current study were among high risk HCWs, the prevalence of LTBI was low. Bacille Calmette-Guerin (BCG) vaccination, young age, short employment duration, good knowledge and a good infection control were the predictors of low risk of contracting TB at our hospitals. The risk of TB infection in resource-limited countries can be reduced with simple continuous educational and administrative infection control programmes.

**Keywords:** health care workers, infection control, latent tuberculosis, QuantiFERON-TB Gold test, tuberculin skin test

### Zusammenfassung

**Zielsetzung:** Eine latente Tuberkuloseinfektion (LTBI) ist ein Reservoir für Epidemien. Daher ist das Screening von medizinischem Personal (HCWs) in einem Hochrisikobereich eine wichtige Strategie zur Kontrolle der Tuberkulose (TB). In der Untersuchung sollten die Prävalenz von LTBI bei ägyptischem medizinischem Personal und mit der Infektion assoziierte Risikofaktoren bestimmt werden.

**Methode:** 52 HCWs, die auf einer Intensivtherapieeinheit (ITS), einer Bronchoskopieeinheit und einer Abteilung für Thoraxerkrankungen tätig waren, wurden auf das Vorkommen einer LTBI mittels Tuberkulin-Hauttest (THT) und QuantiFERON-TB Gold (QFT) untersucht. Ferner wurden Risikofaktoren für eine Infektion, Kenntnisse der HCWs zu verschiedenen Aspekten der TB-Infektion und die Übereinstimmung zwischen THT und QFT evaluiert.

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**Ergebnisse:** Die Prävalenz von LTBI betrug 13,5% mittels QFT und TST (13,6% mittels TST allein und 10,3% mittels QFT allein). Damit war eine gute Konkordanz zwischen beiden Tests gegeben ( $Kappa=0.713$ ). Es war eine statistisch signifikante Assoziation zwischen der Prävalenz von LTBI und Alter der HCWs  $\geq 30$  Jahre ( $p=0.002$ ), Zeitdauer der Tätigkeit ( $p=0.006$ ) und Tätigkeit in der Bronchoskopieeinheit ( $p=0.001$ ) nachweisbar. Die Kenntnisse der HCWs zu verschiedenen Aspekten der TB-Infektion waren im Allgemeinen gut.

**Schlussfolgerung:** Obwohl die Teilnehmer der Studie in Hochrisikobereichen tätig waren, war die Prävalenz der LTBI niedrig. Bacillus Calmette-Guérin (BCG)-Impfung, junges Alter, kurze Zeitdauer der Berufstätigkeit, gute Kenntnisse und eine gute Infektionskontrolle erwiesen sich als Prädiktoren für ein geringes Risiko zum Erwerb einer LTBI. Das Risiko einer TB-Infektion kann in Ländern mit begrenzten Ressourcen durch einfache kontinuierliche Erziehung und Infektionskontrollprogramme reduziert werden.

**Schlüsselwörter:** medizinisches Personal, Infektionskontrolle, latente Tuberkulose, QuantiFERON-TB Gold Test, Tuberkulin-Hauttest

## Introduction

Tuberculosis (TB) is one of the common and, in many cases, lethal infectious disease in the world. In several studies, health care workers (HCWs) appear as a subpopulation with a higher risk of a TB infection than the remaining population without occupational exposure [1]. Nosocomial transmission of *Mycobacterium tuberculosis* (*M. tuberculosis*) from patients to HCWs has been identified for many years; the risk of transmission is the greatest in facilities with a high burden of infectious TB cases [2].

Currently, two methods are available for the evaluation of latent tuberculosis infection (LTBI): a tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) [1]. TST depends on delayed hypersensitivity reaction to purified protein derivative (PPD) of *Mycobacterium bovis*. TST sensitivity ranges from 75%–90% with limited specificity, especially when exposure to *M. tuberculosis* is common, due to cross-reactivity of PPD with the Bacille Calmette-Guérin (BCG) vaccine and non-tuberculous mycobacteria (NTM). The inter-observer variability, boosting phenomenon and the need for a reading visit besides false-negative results in older persons, young persons and immune-compromised patients are other limitations of the TST use [3].

A hallmark of the immune reaction to *M. tuberculosis* infection is the interferon (IFN)- $\gamma$  release by CD4 cells. Measurement of this response in blood samples to culture filtrate protein 10 (CFP10) and early-secreted antigen 6 (ESAT6), highly specific MTB antigens, is the basis of IGRAs test. These antigens are not present in BCG or NTM, thus IGRAs are more specific than TST. Other important advantages of the IGRAs include objective output and a single patient visit [4].

Latent TB infections contain a significant reservoir for future epidemics. Screening of HCWs working in a high-risk TB environment by chest X-rays and TST, LTBI targeted treatment and chemoprophylaxis administration

in high-risk groups are important strategies in TB control [5]. TB transmission in health-care facilities can be prohibited with implementation of effective infection control measures [6]. Control measures of TB infection have been highly spotted recently by data of the development and spread of extensively drug resistant (XDR)-TB which is linked with mortality and morbidity [7].

Incidence of TB in Egypt was last measured as 15 (per 100,000 people) in 2014, according to the World Health Organization (WHO) [8] but little is known about the prevalence of LTBI among Egyptian HCWs. The current study aimed to assess the prevalence of LTBI among HCWs at Fayoum University Hospital (FUH) who are at high risk using both TST and Quantiferon TB Gold in-tube test (QFT) which is an IGRA test. Assessment of risk factors for infection and agreement between TST and QFT were also evaluated.

## Methods

### Study participants

This cross-sectional study was conducted from August 2015 to January 2016 at FUH. The centre is a 500-bed referral hospital that serves Fayoum Governorate which is a rural governorate with about three millions population. Annual prevalence of active TB has been reported as 200 cases per year. About 300 brochosopes are performed yearly at FUH. The study aimed to assess the prevalence of LTBI among HCWs who are at high risk, based on exposure to patients with active tuberculosis. They were from Intensive Care Unit (ICU), Bronchoscopy Unit, and Chest Diseases Department. All participants gave their written informed consent before their inclusion in the study. The study protocol was approved by the Research Ethical Committee at Faculty of Medicine, Fayoum University.

## Data collection

Each participant included into the study has completed a self-administered questionnaire containing information about: possible risk factors (sociodemographic, occupation history, smoking, BCG vaccination, co-morbid diseases, history of previous TB, and history of contact or living with TB patient) and knowledge about LTBI among physicians, nurses and housekeepers at FUH. This second part contained questions with 28 items covering knowledge about TB transmission, LTBI, TB vaccination and treatment, TST and prevention of TB transmission (personal protective equipment and hand washing). This questionnaire was modified from that developed by Montagna et al. [9]. Degree of knowledge was ascertained by means of “yes”, “no” or “don't know” questions on each item being evaluated.

The questionnaire was translated into Arabic to be easily understood and answered. It took approximately 15 minutes to complete it. Before administration of the questionnaire, the purpose of the study was explained to each respondent and confidentiality of the information was assured. Each statement of knowledge was measured on three points; a right answer was scored two points, an “I do not know” answer was scored one point, and a wrong answer was scored zero points with a maximum total score of 56. In this study, a diagnosis of LTBI was made if the respondent was tested positive by TST and/or QFT.

## Quantiferon TB Gold in-tube test

Quantiferon TB Gold in-tube test (QFT) (Cellestis/Qiagen) was performed according to the manufacturer's instructions. Briefly, one ml of whole blood was sampled in each of the three QFT tubes containing TB specific antigen (CFP-10, ESAT-6 and TB7.7), mitogen antigen (positive control) and no antigen (negative control). Tubes were incubated for 16 to 24 hr at 37 °C then plasma was harvested from each tube. An enzyme-linked immunosorbent assay (ELISA) reader was used to measure the IFN- $\gamma$  concentrations (IU/ml) in plasma and this value was calculated by the 'QFT-TB-analysis software'. A value  $\geq 0.35$  IU/ml (TB antigens minus negative control) was considered as a positive test.

## Tuberculin skin test

TST was done after blood for QFT has been withdrawn to avoid the possibility of reaction boosting. The test was administered using the Mantoux method i.e. intradermal injection of 0.1 ml of PPD containing 5TU (Tuber test, vacsera, Egypt) and read after 48–72 h. Induration of  $\geq 10$  mm was considered a positive result for HCWs.

The study participants with a positive QFT or TST were followed according to clinical practice with clinical and radiological examination to rule out active TB.

## Data analysis

All HCWs who agreed to participate were included for the analysis. The collected data was organized, tabulated and statistically analyzed using SPSS software statistical computer package version 18 (SPSS Inc, USA). For quantitative data, the mean and standard deviation (SD) were calculated. Independent t-test or one way ANOVA were used, when appropriate, to test the differences between several study variables as regards mean values of knowledge score. For qualitative data the number and percentage were calculated. Chi squared test ( $\chi^2$ ) was used as a test of significance. Agreement between the two tests, TST and QFT, and Kappa values were calculated. The general significance was adopted at  $P \leq 0.05$ .

## Results

### Socio-demographic characteristics of study population

This was a cross-sectional study included 52 HCWs who are at high risk for exposure to TB patients and therefore infection. The age of participating HCWs ranged between 19 and 50 years old with the mean age was  $28.8 \pm 7.5$ , 24 (46.2%) of participants were males and 28 (53.8%) were females. Their job distribution was as follows; 31 (59.6%) were nurses, 13 (25.0%) were housekeepers and 8 (15.4%) were physicians. Experience of HCWs in working at health care facility ranged from 0.5 year to 20 years with mean  $\pm$  SD of  $4.9 \pm 4.7$ . All respondents were BCG vaccinated as assessed by history and/or vaccination scar. Seventeen HCWs (32.7%) reported a suspected exposure to TB case or infected specimen and one participant (1.9%) to a diseased relative. Socio-demographic and occupational data of participants is shown in Table 1.

### Knowledge of studied participants as regards latent TB

Table 2 demonstrates the responses and scores of knowledge of HCWs towards different aspects of TB infection. The total knowledge of the study group regarding TB was generally good with a total score of  $44.2 \pm 5.2$  out of 52. Regarding LTBI, the majority of participants have mentioned the correct answers with a percentage over 50 for all items except for two questions; TB is mostly asymptomatic and there are many methods for diagnosing LTBI where less than half of HCWs mentioned the correct answer.

For questions about treatment and specific protection against TB, participants mentioned the correct answers with a percentage over 50 for three questions; treatment of TB need long duration, treatment of TB is complicated and there is a vaccine for TB. On the other hand, less than half of HCWs gave correct answers for the other questions (Table 2). According to TST, the majority of

**Table 1: Socio-demographic characteristics of the study participants**

Variable	N	%
<b>Age</b>		
<25	18	34.6
25–30	19	36.5
≥30	15	28.8
<b>Sex</b>		
Male	24	46.2
Female	28	53.8
<b>Marital status</b>		
Single	25	48.1
Married	27	51.9
<b>Smoking</b>		
Non smoker	48	92.3
Smoker	4	7.7
<b>Working experience</b>		
Physician	8	15.4
Nurse	31	59.6
Housekeeper	13	25.0
<b>Place of work</b>		
ICU	31	59.6
Chest Diseases Department	14	26.9
Bronchoscopy Unit	7	13.5
<b>Suspected exposure</b>		
Exposure to case or specimen	17	32.7
Diseased relative	1	1.9

participants could not mention the correct answers for all items except one question; negative TST results mean no infection where more than half of HCWs identified the correct answer. Knowledge of the HCWs as regards measures of prevention was high. The majority of participants could mention the correct answers with a percentage over 80 for almost all items (Table 2).

Table 3 specifies that there was a statistically significant difference between total knowledge score among different age groups, working experience and working activities,  $P=0.004$ ,  $0.024$  and  $<0.0001$ , respectively. Poor knowledge score was found among older age ( $\geq 30$  years old), working experience  $\geq 10$  years and housekeepers.

## Prevalence and risk factors of LTBI among study participants

Overall prevalence rate of LTBI among the studied HCWs, detected by TST and/or QFT, was 13.5% (7/52). By TST alone, prevalence was 13.6% (6/44), while by QFT alone it was found to be 10.3% (4/39), as shown in Table 4. Thirty one of participants agreed to be tested by both tests with 26 (83.9%) were negative by both tests, three (9.7%) were positive in both tests, one was positive by TST alone and one was positive by QFT alone. There was good concordance between both tests (Kappa=0.713). Out of the study participants, 39 agreed to be tested for LTBI with QFT. Of the respondents, four participants gave

positive results but only three of them were positive when tested with TST. Of the participants with negative results by QFT (=35), 27 were screened for LTBI by TST and one participant only gave positive results.

Table 5 reveals a statistically significant association between prevalence of LTBI and age of staff  $\geq 30$  yr ( $p=0.002$ ). There was a statistically significant association between prevalence of LTBI and period of working experience ( $p=0.006$ ) and working at the Bronchoscopy Unit ( $p=0.001$ ). Although, LTBI was more common in housekeepers (30.8 %) than nurses (9.7%) no statistically significant association was found ( $p>0.05$ ). Other socio-demographic parameters were not significantly associated with prevalence of LTBI ( $p>0.05$ ). Table 5 demonstrates prevalence of LTBI among different socio-demographic and occupational groups of participants.

Table 6 specifies that there was no statistically significant difference between mean total knowledge score of the infected and the not infected groups. As regards, subtotal knowledge scores, there was a statistically significant difference between the infected and the not infected groups in knowledge about LTBI, (mean  $\pm$  SD was  $6.7 \pm 1.8$  for who has vs.  $8.6 \pm 2.0$  for who doesn't have LTBI,  $p=0.025$ ).

**Table 2: Knowledge of study participants**

Question	True		False		I do not know	
	N	%	N	%	N	%
<b>Transmission of TB</b>						
Causative agent	34	65.4	8	15.4	10	19.2
Modes of transmission	43	82.7	2	3.8	7	13.5
Subtotal score* (4)	3.3 ± 1.0					
<b>Latent TB infection</b>						
TB is mostly asymptomatic	24	46.2	15	28.8	13	25.0
Body does not destroy TB bacteria	26	50.0	12	23.1	14	26.9
TSH can detect latent TB infection	35	67.3	5	9.6	12	23.1
Latent TB needs treatment	40	76.9	2	3.8	10	19.2
There are many methods for diagnosing latent TB infection	25	48.1	10	19.2	17	32.7
TB affects lung only	27	51.9	12	23.1	13	25.0
Subtotal score* (12)	8.3 ± 2.1					
<b>Treatment and specific protection</b>						
Treatment of TB is complicated	38	73.1	5	9.6	9	17.3
Treatment of TB needs long duration	41	78.8	2	3.8	9	17.3
Fatality rate of active TB cases without treatment is more than 50%	23	44.2	5	9.6	24	46.2
There is a vaccine for TB	36	69.2	2	3.8	14	29.6
The vaccine of TB is called BCG	20	38.5	7	13.5	25	48.1
The vaccine is not highly protective	19	36.5	10	19.2	23	44.2
Subtotal score* (12)	8.8 ± 2.0					
<b>TST</b>						
TST recognizes infection	33	32.7	2	3.8	17	32.7
Negative TST results mean no infection	27	51.9	7	13.5	18	34.6
TST is a treatment	23	44.2	11	21.2	18	34.6
TST is a seroprophylaxis	22	42.3	7	13.5	23	44.2
TST is a diagnostic test	23	44.2	6	11.5	23	44.2
Subtotal score* (10)	6.8 ± 1.9					
<b>Prevention</b>						
Wearing mask is necessary	49	94.2	1	1.9	2	3.8
Wearing PPE is necessary	48	92.3	1	1.9	3	5.8
Hand washing removes bacteria	45	86.5	3	5.8	4	7.7
HW is necessary before and after wearing gloves	47	90.4	2	3.8	3	5.8
HW with aseptic soap is necessary	49	94.2	1	1.9	2	3.8
Wearing gloves replaces HW	33	63.5	2	3.8	17	32.7
HW is the effective measure	43	82.7	7	13.5	2	3.8
Covering mouth during coughing decreases transmission of infection	50	96.2	0	0.0	2	3.8
Main control measures include identification, isolation & treatment of case	44	84.6	1	1.9	7	13.5
Subtotal score* (18)	16.9 ± 1.5					
Total knowledge score* (56)	44.2 ± 5.2					

Table 3: Differences between characteristics of participants as regards knowledge score

Variable	Knowledge score Mean $\pm$ SD	P-value
<b>Age</b>		
<25	46.7 $\pm$ 3.1	<b>0.004*</b>
25–30	44.4 $\pm$ 4.9	
$\geq$ 30	40.9 $\pm$ 5.9	
<b>Sex</b>		
Male	45.2 $\pm$ 4.3	0.176
Female	43.3 $\pm$ 5.7	
<b>Working experience</b>		
<5 years	45.6 $\pm$ 4.6	<b>0.024*</b>
5–10 years	42.9 $\pm$ 5.4	
$\geq$ 10 years	40.0 $\pm$ 5.1	
<b>Working activity</b>		
Physician	48.6 $\pm$ 3.4	<b>&lt;0.0001**</b>
Nurse	45.8 $\pm$ 3.3	
Housekeeper	37.4 $\pm$ 2.9	
<b>Place of work</b>		
ICU	44.0 $\pm$ 5.2	0.911
Chest Diseases Department	44.6 $\pm$ 4.4	
Bronchoscopy Unit	43.7 $\pm$ 7.6	

\* significant \*\* highly significant

Table 4: Prevalence of latent TB infection

Variable	N	%
<b>TST (44)</b>		
Positive	6	13.6
Negative	38	86.4
<b>QFT (39)</b>		
Positive	4	10.3
Negative	35	89.7
<b>TST and/or QFT (52)</b>		
Positive	7	13.5
Negative	45	86.5

Table 5: Relation between latent TB and socio-demographic factors

Variable	Latent TB				P-value
	Positive		Negative		
	N	%	N	%	
<b>Age</b>					
<25	1	5.6	17	94.4	<b>0.002*</b>
25–30	0	0.0	19	100.0	
$\geq$ 30	6	40.0	9	60.0	
<b>Sex</b>					
Male	4	16.7	20	83.3	0.690
Female	3	10.7	25	89.3	
<b>Marital status</b>					
Single	2	8.0	23	92.0	0.422
Married	5	18.5	22	81.5	
<b>Smoking</b>					
Non smoker	7	14.6	41	85.4	0.412
Smoker	0	0.0	4	100.0	
<b>Working experience</b>					
<5 years	1	3.2	30	96.8	<b>0.006*</b>
5–10 years	3	20.0	12	80.0	
$\geq$ 10 years	3	50.0	3	50.0	
<b>Working activity</b>					
Physician	0	0.0	8	100.0	0.083
Nurse	3	9.7	28	90.3	
Housekeeper	4	30.8	9	69.2	
<b>Place of work</b>					
ICU	2	6.5	29	93.5	<b>0.001*</b>
Chest Diseases Department	1	7.1	13	92.9	
Bronchoscopy Unit	4	57.1	3	42.9	

\* Significant



Table 6: Relation of latent TB to knowledge of participants

Knowledge items	Latent TB		P-value
	Positive	Negative	
	Mean $\pm$ SD		
Transmission	3.1 $\pm$ 0.9	3.3 $\pm$ 1.0	0.688
Latent TB	6.7 $\pm$ 1.8	8.6 $\pm$ 2.00	<b>0.025*</b>
Treatment and specific protection	8.7 $\pm$ 2.4	8.8 $\pm$ 1.9	0.896
TST	6.4 $\pm$ 1.9	6.9 $\pm$ 1.9	0.564
Prevention	17.3 $\pm$ 0.9	16.8 $\pm$ 1.5	0.462
Total knowledge	42.3 $\pm$ 6.6	44.4 $\pm$ 4.9	0.309

\* Significant

## Discussion

In low and middle income countries with high and intermediate TB burden, TB is a prominent occupational hazard among HCWs. In this cross-sectional study we aimed to assess the prevalence of LTBI among BCG vaccinated Egyptian HCWs from ICU, Bronchoscopy unit, and Chest Diseases Department. Those locations were identified as high-risk locations for LTBI within facilities [10], [11]. Prevalence of LTBI in this study was 13.5% by QFT and TST. It was 13.6% by TST alone and 10.3% by QFT alone. However, it is difficult to decide if the prevalence of LTBI among HCWs is significantly higher or lower than the community as data on concurrent LTBI prevalence in the community is not available to the authors.

This low prevalence in Egypt, an intermediate TB burden country, was in concordance with prevalence of LTBI among HCWs in Malaysia, also an intermediate TB burden country, where overall prevalence was 10.6% [12]. The prevalence in Germany and Japan was 9.9% [13], [14]. Even though the prevalence is close to our findings, it should be prominent that Germany and Japan are, according to TB-burden, low-burden countries. Definitely, our findings are higher than those obtained from studies from countries with low TB burden like Denmark and Norway with prevalence of 1% and 3.4% respectively [15], [16]. The prevalence of LTBI in this study was relatively low in comparison with other low or middle income African countries where researchers found rates of LTBI among HCWs of 33% in South Africa, 57% in Uganda up to 79% in Côte d'Ivoire [17], [18], [19] with estimated pooled prevalence of 54% (95% CI 53–55) [2]. These higher values could be attributed to high prevalence of HIV infection in these countries or use of TST only for diagnosing LTBI which accounts for this higher prevalence with false positive reactions that could be attributed to NTM infections or BCG vaccination [20].

Although the participants in the current study were among high risk HCWs, the prevalence of LTBI was low. Concurrent data was obtained from Malaysia and Taiwan where no increased risk of LTBI among HCWs in direct contact with TB patients was reported [12], [21]. Also, the inclusion of young aged HCWs with short duration of occupation could be another explanation.

In this, BCG-vaccinated, studied population only 31 respondents accepted to be investigated by both TST and QFT with 93.5% agreement between both tests, Kappa=0.713. All TST positive respondents had readings  $\geq 15$  mm, this can explain the agreement between both tests. These findings parallel those obtained by Rafiza et al., where concordance between TST and QFT at cut-off values of 15 mm was 82.1% [12]. In agreement with our results, an earlier study in India reported high concordance between the two tests although majority of the respondents were BCG vaccinated [22]. A study in Germany, where BCG vaccination is not mandatory, Nienhaus et al., found good concordance among those who did not receive BCG vaccination and poor agreement among those who received vaccination [23]. This poor agreement between both tests has been attributed to BCG vaccination, NTM exposure and the cumulative occupational plus non-occupational exposure to *M. tuberculosis* [21]. Increasing age, more exposure to TB patients and duration of employment in the health care setting (denoting longer accumulative exposure), were risk factors for acquiring infection, which supports nosocomial transmission. Researchers reported about one time increase in the prevalence of LTBI in HCWs with each additional year of age [19], [10], and 1.5–2.4 times increase with employment duration of more than one year [24], [10] and 3-fold higher risk with more than 10 years of employment [22]. By univariate analysis, findings of this study support this data as there was a significant association between LTBI and age  $\geq 30$  years ( $p=0.002$ ) and period of working experience  $\geq 10$  years ( $p=0.006$ ). Similar results were reported in earlier studies [12], [19], [21], [25]. Another study from Rwanda found that within health care facilities, risk of infection did not differ significantly between occupations and work locations and reported that increased infection with TB within health care settings is affected by duration of employment in health facilities, regardless of department type or occupation [26]. In contrast, Gran et al. did not find any relation between age and the QFT results [27]. Also, Franchi et al. found that TST conversion was not associated with duration of time in contact with the infectious TB patient, but related to unprotected brief exposure to a highly infectious person in a closed and poorly ventilated confined spaces [28].

As both women and men in our study shared the same workplace medium, this may have reduced the significant association between sex and LTBI. In contrast, being male was significantly associated with LTBI in a study by Rafiza et al. [12]. Although LTBI was more common in housekeepers (30.8 %) followed by nurses (9.7%) but there was no statistically significant association was found ( $p > 0.05$ ). Sherman et al., also reported higher prevalence of LTBI among housekeepers [11]. A previous study, reported a lower prevalence in nurses, compared to other HCWs [29]. In contrast, it was reported in several studies that the prevalence of LTBI in nurses was higher than that in other HCWs [10], [12], [30].

The total knowledge of study group regarding TB was generally good which can explain the generally low prevalence of LTBI among the studied group. But there was a statistical significant difference between the infected and the not infected groups in knowledge about LTBI, (mean  $\pm$  SD was  $6.7 \pm 1.8$  for who have vs.  $8.6 \pm 2.0$  for who do not have LTBI,  $p = 0.025$ ). In a case-control study by Jelip et al., HCWs with TB infection were about six times (95% CI 0.76–46.4) more likely to have poor knowledge about transmission of TB, and about four times (95% CI 0.95 to 19.8) less aware about the need for respiratory protection [31]. A 2.6-fold (95% CI 1.06 to 6.64) increase in risk of TB disease was associated with failure of personal protection among HCWs [32]. In the current work, poor knowledge score was found among older age ( $\geq 30$  years old), working experience  $\geq 10$  years and housekeepers ( $P = 0.004$ ,  $0.024$  and  $< 0.0001$ , respectively), which are the same risk factors associated with prevalence of LTBI. This indirectly reflects the positive correlation between poor knowledge and prevalence of LTBI.

## Conclusion

Based on our results we can conclude that young age, short employment duration, good knowledge and good infection control are the predictors of low risk of contracting TB at our hospital. Taken together, the risk of TB infection in resource-limited countries can be reduced with simple continuous educational and administrative controls, development of suitable infection control, surveillance programs and BCG vaccination. But larger studies are needed to evaluate this neglected chronic problem of health care associated TB in low income countries especially with the extensive drug resistant tuberculosis recent emergence.

## Notes

## Competing interests

The authors declare that they have no competing interests for this work.

## Funding

No funds were received for this work.

## References

1. Targowski T, Chelstowska S, Plusa T. Tuberculin skin test and interferon-gamma release assay in the detection of latent tuberculosis infection among Polish health care workers. *Pol Arch Med Wewn.* 2014;124(1-2):36-42.
2. Joshi R, Reingold AL, Menzies D, Pai M. Tuberculosis among health-care workers in low- and middle-income countries: a systematic review. *PLoS Med.* 2006 Dec;3(12):e494. DOI: 10.1371/journal.pmed.0030494
3. Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep.* 2000 Jun 9;49(RR-6):1-51.
4. Herrera V, Perry S, Parsonnet J, Banaei N. Clinical application and limitations of interferon-gamma release assays for the diagnosis of latent tuberculosis infection. *Clin Infect Dis.* 2011 Apr;52(8):1031-7. DOI: 10.1093/cid/cir068
5. Rubbo PA, Nagot N, Le Moing V, Brabet M, Bourdin A, Nogué E, Bolloré K, Vendrell JP, Van De Perre P, Tuailon E. Multicytokine detection improves latent tuberculosis diagnosis in health care workers. *J Clin Microbiol.* 2012 May;50(5):1711-7. DOI: 10.1128/JCM.00117-12
6. Mazurek GH, Jereb J, Lobue P, Iademarco MF, Metchock B, Vernon A; Division of Tuberculosis Elimination, National Center for HIV, STD, and TB Prevention, Centers for Disease Control and Prevention (CDC). Guidelines for using the QuantiFERON-TB Gold test for detecting *Mycobacterium tuberculosis* infection, United States. *MMWR Recomm Rep.* 2005 Dec;54(RR-15):49-55.
7. Gandhi NR, Shah NS, Andrews JR, Vella V, Moll AP, Scott M, Weissman D, Marra C, Laloo UG, Friedland GH; Tugela Ferry Care and Research (TF CARES) Collaboration. HIV coinfection in multidrug- and extensively drug-resistant tuberculosis results in high early mortality. *Am J Respir Crit Care Med.* 2010 Jan;181(1):80-6. DOI: 10.1164/rccm.200907-0989OC
8. WHO. Global tuberculosis report. 20th ed. Geneva: WHO; 2015 [cited 2016 Mar 19]. Available from: [http://www.who.int/entity/tb/publications/global\\_report/en/index.html](http://www.who.int/entity/tb/publications/global_report/en/index.html)
9. Montagna MT, Napoli C, Tafuri S, Agodi A, Auxilia F, Casini B, Coscia MF, D'Errico MM, Ferrante M, Fortunato A, Germinario C, Martinelli D, Masanotti GM, Massenti MF, Messina G, Montuori P, Mura I, Orsi GB, Quaranta A, Sotgiu G, Stefanati A, Tardivo S, Torregrossa MV, Tortorano AM, Veronesi L, Zarrilli R, Pasquarella C. Knowledge about tuberculosis among undergraduate health care students in 15 Italian universities: a cross-sectional study. *BMC Public Health.* 2014;14:970. DOI: 10.1186/1471-2458-14-970
10. García-García ML, Jiménez-Corona A, Jiménez-Corona ME, Ferreyra-Reyes L, Martínez K, Rivera-Chavira B, Martínez-Tapia ME, Valenzuela-Miramontes E, Palacios-Martínez M, Juárez-Sandino L, Valdespino-Gómez JL. Factors associated with tuberculin reactivity in two general hospitals in Mexico. *Infect Control Hosp Epidemiol.* 2001 Feb;22(2):88-93. DOI: 10.1086/501869
11. Sherman HA, Karakis I, Heimer D, Arzt M, Goldstein W, Bouhnik L, Maimon MN. Housekeeping health care workers have the highest risk for tuberculin skin test conversion. *Int J Tuberc Lung Dis.* 2011 Aug;15(8):1050-5. DOI: 10.5588/ijtld.10.0344
12. Rafiza S, Rampal KG, Tahir A. Prevalence and risk factors of latent tuberculosis infection among health care workers in Malaysia. *BMC Infect Dis.* 2011;11:19. DOI: 10.1186/1471-2334-11-19



13. Harada N, Nakajima Y, Higuchi K, Sekiya Y, Rothel J, Mori T. Screening for tuberculosis infection using whole-blood interferon-gamma and Mantoux testing among Japanese healthcare workers. *Infect Control Hosp Epidemiol*. 2006 May;27(5):442-8. DOI: 10.1086/504358
14. Schablon A, Harling M, Diel R, Nienhaus A. Risk of latent TB infection in individuals employed in the healthcare sector in Germany: a multicentre prevalence study. *BMC Infect Dis*. 2010;10:107. DOI: 10.1186/1471-2334-10-107
15. Soborg B, Andersen AB, Larsen HK, Weldingh K, Andersen P, Kofoed K, Ravn P. Detecting a low prevalence of latent tuberculosis among health care workers in Denmark detected by M. tuberculosis specific IFN-gamma whole-blood test. *Scand J Infect Dis*. 2007;39(6-7):554-9. DOI: 10.1080/00365540601148483
16. Drobniowski F, Balabanova Y, Zakamova E, Nikolayevskyy V, Fedorin I. Rates of latent tuberculosis in health care staff in Russia. *PLoS Med*. 2007 Feb;4(2):e55. DOI: 10.1371/journal.pmed.0040055
17. Naidoo S, Jinabhai CC. TB in health care workers in KwaZulu-Natal, South Africa. *Int J Tuberc Lung Dis*. 2006 Jun;10(6):676-82.
18. Kassim S, Zuber P, Wiktor SZ, Diomande FV, Coulibaly IM, Coulibaly D, Kadio A, Yapi A, Touré KC, Blekou PB, Irié B, Greenberg AE, Binkin NJ. Tuberculin skin testing to assess the occupational risk of Mycobacterium tuberculosis infection among health care workers in Abidjan, Côte d'Ivoire. *Int J Tuberc Lung Dis*. 2000 Apr;4(4):321-6.
19. Kayanja HK, Debanne S, King C, Whalen CC. Tuberculosis infection among health care workers in Kampala, Uganda. *Int J Tuberc Lung Dis*. 2005 Jun;9(6):686-8.
20. Andersen P, Munk ME, Pollock JM, Doherty TM. Specific immune-based diagnosis of tuberculosis. *Lancet*. 2000 Sep 23;356(9235):1099-104. DOI: 10.1016/S0140-6736(00)02742-2
21. Hung WT, Lee SS, Sy CL, Wu KS, Chen JK, Tsai HC, Chen YS. Prevalence of latent tuberculosis infection in BCG-vaccinated healthcare workers by using an interferon-gamma release assay and the tuberculin skin test in an intermediate tuberculosis burden country. *J Microbiol Immunol Infect*. 2015 Apr;48(2):147-52. DOI: 10.1016/j.jmii.2013.07.008
22. Pai M, Gokhale K, Joshi R, Dogra S, Kalantri S, Mendiratta DK, Narang P, Daley CL, Granich RM, Mazurek GH, Reingold AL, Riley LW, Colford JM Jr. Mycobacterium tuberculosis infection in health care workers in rural India: comparison of a whole-blood interferon gamma assay with tuberculin skin testing. *JAMA*. 2005 Jun;293(22):2746-55. DOI: 10.1001/jama.293.22.2746
23. Nienhaus A, Schablon A, Diel R. Interferon-gamma release assay for the diagnosis of latent TB infection – analysis of discordant results, when compared to the tuberculin skin test. *PLoS ONE*. 2008;3(7):e2665. DOI: 10.1371/journal.pone.0002665
24. Alonso-Echanove J, Granich RM, Laszlo A, Chu G, Borja N, Blas R, Olortegui A, Binkin NJ, Jarvis WR. Occupational transmission of Mycobacterium tuberculosis to health care workers in a university hospital in Lima, Peru. *Clin Infect Dis*. 2001 Sep;33(5):589-96. DOI: 10.1086/321892
25. He GX, van den Hof S, van der Werf MJ, Wang GJ, Ma SW, Zhao DY, Hu YL, Yu SC, Borgdorff MW. Infection control and the burden of tuberculosis infection and disease in health care workers in china: a cross-sectional study. *BMC Infect Dis*. 2010;10:313. DOI: 10.1186/1471-2334-10-313
26. Rutanga C, Lowrance DW, Oeltmann JE, Mutembayire G, Willis M, Uwizeye CB, Hinda R, Bassirou C, Gutreuter S, Gasana M. Latent Tuberculosis Infection and Associated Factors among Health Care Workers in Kigali, Rwanda. *PLoS ONE*. 2015;10(4):e0124485. DOI: 10.1371/journal.pone.0124485
27. Gran G, Aßmus J, Dyrhol-Riise AM. Screening for latent tuberculosis in Norwegian health care workers: high frequency of discordant tuberculin skin test positive and interferon-gamma release assay negative results. *BMC Public Health*. 2013;13:353. DOI: 10.1186/1471-2458-13-353
28. Franchi A, Richeldi L, Parrinello G, Franco G. Room size is the major determinant for tuberculin conversion in health care workers exposed to a multidrug-resistant tuberculosis patient. *Int Arch Occup Environ Health*. 2007 May;80(6):533-8. DOI: 10.1007/s00420-006-0160-1
29. Orrett FA. Prevalence of tuberculin skin test reactivity among health care workers at a teaching hospital in Trinidad. *Clin Microbiol Infect*. 2000 Jan;6(1):45-8. DOI: 10.1046/j.1469-0691.2000.00015-2.x
30. Yanai H, Limpakarnjanarat K, Uthavivoravit W, Mastro TD, Mori T, Tappero JW. Risk of Mycobacterium tuberculosis infection and disease among health care workers, Chiang Rai, Thailand. *Int J Tuberc Lung Dis*. 2003 Jan;7(1):36-45.
31. Jelip J, Mathew GG, Yusin T, Dony JF, Singh N, Ashaari M, Lajanin N, Shanmuga Ratnam C, Yusof Ibrahim M, Gopinath D. Risk factors of tuberculosis among health care workers in Sabah, Malaysia. *Tuberculosis (Edinb)*. 2004;84(1-2):19-23. DOI: 10.1016/j.tube.2003.08.015
32. Harries AD, Nyirenda TE, Banerjee A, Boeree MJ, Salaniponi FM. Tuberculosis in health care workers in Malawi. *Trans R Soc Trop Med Hyg*. 1999 Jan-Feb;93(1):32-5. DOI: 10.1016/S0035-9203(99)90170-0

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#### Please cite as

Hefzy EM, Wegdan AA, Elhefny RA, Nasser SH. Predictors of low prevalence of latent tuberculosis infection among Egyptian health care workers at intensive care and bronchoscopy units. *GMS Hyg Infect Control*. 2016;11:Doc22.  
DOI: 10.3205/dgkh000282, URN: urn:nbn:de:0183-dgkh000282

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Published: 2016-10-12

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