



Risk Factors and Prevalence for Latent Tuberculosis Infection among Health Care Workers in Al-Quwayiyah General Hospital Riyadh, KSA

Enas Sh. Khater^{1,2*} and Khalid H. M. Abdo³

¹*Department of Microbiology and Immunology, Faculty of Medicine, Benha University, Egypt.*

²*Microbiology Laboratory, Al-quwayiyah General Hospital, Riyadh, KSA.*

³*Department of Chest, Al-quwayiyah General Hospital, Riyadh, KSA.*

Authors' contributions

This work was done in collaboration between both authors. Author ESK planned and designed the study, wrote the protocol, collected the samples, performed the practical laboratory activities, participated in the interpretation of the results and analysis, drafted and critically revised the manuscript. Author KHMA participated in planning and designing the study, sample collection, performing tuberculin test, evaluate cases clinically, participated in the interpretation of the results. Both authors reviewed and approved the final manuscript.

Article Information

DOI: 10.9734/MRJI/2019/v29i630183

Editor(s):

(1) DR. Rajarshi Kumar Gaur, Professor, Department of Biotechnology D.D.U. Gorakhpur University, Gorakhpur, Uttar Pradesh, India.

Reviewers:

(1) Binit Vaidya, National Centre for Rheumatic Diseases (NCRD), Nepal.

(2) Many Mashako Ruhanga, Kisangani University, Democratic Republic of Congo.

(3) Tsuyoshi Ogata, Japan Anti-tuberculosis Association, Japan.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/53796>

Original Research Article

Received 10 November 2019

Accepted 13 January 2020

Published 18 January 2020

ABSTRACT

Background: All health care facilities should intensify TB screening and encourage treatment of latent tuberculosis infection (LTBI) among Healthcare workers (HCWs) to prevent progression to tuberculosis (TB) disease.

Aim: This study was conducted to determine the prevalence and associated risk factors of LTBI among HCWs in Al Quwayiyah General hospital as well as to compare the performance of QuantiFERON-TB Gold Plus (QFT-Plus) to TST in identifying LTBI.

Methods: A cross sectional study and prospective cohort study was performed from January to July 2019 in Al Quwayiyah General hospital involving a total of 718 HCWs. questionnaire with socio-

*Corresponding author: E-mail: drenaskhater@yahoo.com;

demographic data and work history was filled, and both tests were done TST and QFT test for each Healthcare worker.

Results: The study showed that The prevalence of latent tuberculosis diagnosed was 9.05% and 9.19% using QFT-Plus and TST respectively. Only 26 (3.62%) subjects were positive for both tests whereas 131 (18.25%) were positive by either test. Comparing the results of the QFT-Plus with those of the TST, both tests had a significant total agreement of 88.8. Negative concordance comprised 85.37% of the results, and positive concordance comprised 3.62%. However, positive TST but negative QFT-Plus comprised 5.57% of the results, and negative TST but positive QFT-Plus comprised 5.43%. The association between risk factors and QFT-Plus test results in the studied groups showed that the smoking, health status, immunosuppression, housing, occupation, contact T.B. at work place, past history of TB and diabetes mellitus appear as significant risk factors. The association between the studied risk factors and TST in the studied groups showed significant difference noted for smoking, BCG vaccination, immunosuppression, housing, occupation, contact T.B. at work place, past history of TB and diabetes mellitus.

Conclusion: The prevalence of latent tuberculosis diagnosed was 9.05% and 9.19% using QFT-Plus and TST respectively. Testing of HCWs at hire and periodically can help in the detection of LTBI Large scale study is recommended to confirm such findings in Saudi Arabia, also the use of Quantiferon for detection of LTBI beside using TST is recommended as it reduce the false positive reports by TST and is not affected by prior BCG status.

Keywords: Latent tuberculosis; tuberculin skin; healthcare workers; QuantiFERON-TB gold plus.

1. INTRODUCTION

The World Health Organization (WHO) has declared tuberculosis as a global health emergency for more than two decades [1]. There are many risk factors that could lead to the reactivation of latent tuberculosis infection (LTBI), such as HIV co-infection, hemodialysis, immunosuppressive therapy, organ transplantation, malignancy, diabetes, alcoholism, cigarette smoking, underweight, and malnutrition [2,3]. Healthcare workers (HCWs) are at high risk rate of LTBI and (tuberculosis) TB disease, because of their prolonged occupational exposure to these infections [4].

Early detection and treatment of LTBI may reduce further spread of TB, which remains a challenge. For many years, LTBI diagnosis has been dependent on the tuberculin skin test (TST) but a rapid and reliable alternative is needed [5]. Placing and reading the TST requires experience and a second patient visit 48–72 h after doing the procedure to determine the reading. This has made the TST a difficult and challenging diagnostic tool to identify LTBI cases [6]. QuantiFERON-TB Gold Plus (QFT-Plus), on the other hand, was created using TB-specific antigens conducted on a single blood specimen [7,8].

QFT-Plus has novel CD8 specific antigens in the second antigen tube (QFT-Plus Tube 2, TB2) which lead to stimulate both CD8+ T-cells and

CD4+ T-cells. This complements the first antigen tube (QFT-Plus Tube 1, TB1), which has ESAT-6 and CFP-10 peptides which stimulate cell-mediated immune responses from CD4+ T-helper lymphocytes [9,10].

The WHO end TB policy took action to decrease the incidence of TB by 90% and TB death by 95% until 2035. To achieve this ambitious goal in the TB control program, it is necessary to decrease LTBI reservoirs by administering anti-TB preventive therapy [11].

As there is an elevated incidence rate of TB in Saudi Arabia without regular LTBI screening for HCWs, the risk of TB transmission and reactivation is a potential threat. Therefore, this study was conducted to determine the prevalence and associated risk factors of LTBI among HCWs in Al Quwayiyah General hospital as well as to compare the performance of QFT-Plus to TST in identifying LTBI.

2. MATERIALS AND METHODS

2.1 Study Design

A cross sectional study and prospective cohort study was performed from 1st January to 30 July 2019 in Al Quwayiyah General hospital involving a total of 718 HCWs, including doctors, pharmacists, nurses, other clinical staff (dentists, medical assistants, physiotherapist, technicians), non clinical staff (administrative staff and cleaners) .

Inclusion criteria: all HCW in Al Quwayiyah General hospital were included and each agreed to be enrolled in the study with provision of written informed consent. Exclusion criteria were history of active TB and type I hypersensitivity reaction to the purified protein derivative used in the TST. A convenience sampling method was used. HCWs completed a questionnaire with demographic information, medical history and employment history.

2.2 Collection of Specimens

Blood samples were collected from each health care workers in Al Quwayiyah General hospital laboratory as follows:

1. Label tubes appropriately. Each tube (Nil, TB1, TB2 and Mitogen) was identifiable by its label or other means once the cap was removed. Blood collection tubes were at room temperature 17–25°C (62.6–77°F) at the time of blood collection.
2. For each HCW, 1 ml of blood was collected by venipuncture directly into each of the QFT-Plus Blood Collection Tubes. This procedure was performed by a trained phlebotomist. As 1 ml tubes were drawn blood relatively slowly, the tube was kept on the needle for 2–3 seconds once the tube appeared to have completed filling. This ensured that the correct volume was drawn.
3. Immediately after filling the tubes, the tubes were shaken ten (10) times just firmly enough to make sure the entire inner surface of the tube was coated with blood. This dissolved antigens on the tube walls. later the tubes were transferred to a 37°C incubator as soon as possible, and within 16 hours of collection. Prior to incubation, maintain tubes at room temperature (22°C) If QFT-Plus Blood Collection Tubes were not incubated at 37°C directly after blood collection and shaking, the tubes were inverted to mix 10 times prior to incubation at 37°C.
4. The QFT-Plus blood collection tubes were incubated upright at 37°C for 16 to 24 hours.

2.3 QuantiFERON-TB Gold in Tube

1. Within one hour of blood collection, tubes were incubated at 37±0.5°C for 23 to 24

hours and then centrifuged at 3,000 g for 10 minutes.

2. IFN- γ concentrations in plasmas in Nil tubes (Nil), TB antigen tubes (TB), and Mitogen tubes (Mitogen) were determined by ELISAs performed on the day after blood collection using reagents included in QFT-Plus kits. ELISAs were performed with the aid of an automated ELISA workstation (EVOLIS machine, Biorad, France) according to manufacture recommendations.
3. Test results were interpreted as indicated in the CDC guidelines and Cellestis package insert [12,13]. The interpretation was “positive” if the Nil was ≤ 8.0 IU/mL and the TB Response was ≥ 0.35 IU/mL and $\geq 25\%$ of the Nil. The interpretation was “negative” if the Nil was ≤ 8.0 IU/mL, the Mitogen Response was ≥ 0.5 IU/mL, and the TB Response was < 0.35 IU/mL or $< 25\%$ of the Nil. The interpretation was “indeterminate” if (1) the Nil was > 8.0 IU/mL or (2) the Nil was ≤ 8.0 IU/mL, the Mitogen Response was < 0.5 IU/mL, and the TB Response was < 0.35 IU/mL or $< 25\%$ of the Nil.

2.4 Tuberculin Skin Test

Tuberculin skin test was administered by injecting 0.1 mL of the standard test dose (5 tuberculin unit, TU) of PPD (BiocineTest-PPD®; Chiron S.r.l., Sovicille, Siena, Italy) according to the Mantoux method. Skin induration was evaluated after 72 hours and considered positive if ≥ 10 mm.

2.5 Radiological Examination

Any HCWs with positive QuantiFERON-TB Gold Plus or positive TST underwent a chest X-ray (CXR) to exclude active TB. HCWs were divided according to the following areas for acquiring TB infection [14,15].

1. Low risk areas: administration units and surgery unit.
2. Moderate risk areas: pharmacy units and radiography units.
3. High risk areas: TB healthcare facilities, medical wards, laboratory units, and emergency units.

2.6 Statistical Analysis

Data were entered into SPSS software version 22 (Chicago, IL, USA). Categorical variables

were presented as frequencies and percentages. Chi square (X²) test and fisher exact test were used to find the association between the categorical variables. A *P*-value of less than 0.05 was considered significant.

3. RESULTS

Table 1 shows that of the 718 HCWs studied 437 (60.7%) were female and 281(39.1%) were male with a mean age of 30.25 ± 7.95. Also 391(54.5%) were Saudi and 327(45.5%) were non Saudi. 72(10.2%) were smokers while 646 (90%) were non smokers. Most of the HCWs 518 (72.1%) received the BCG vaccination. 220 (30.6%) had poor health status while 498(69.4%) had good health status. 107(14.9%) of HCWs had immunosuppression conditions (like cancer, chronic renal failure or undergoing immunosuppressive treatment). The HCWs examined were physicians 105 (14.6%), nurses 220 (30.6%), other clinical staff including pharmacists, technicians and physiotherapists were 183 (25.5%) and non-clinical staff including administration staff and cleaners were 210 (29.3%). 151(21.0%) had contacts with TB cases in work place. 15(2.1%) of HCWs studied had past history of T.B. 127(17.7%) were diabetics.

Table 2 shows that LTBI was positive by QFT-Plus in 65 (9.05%) subjects and by TST in 66 (9.19%) subjects. Only 26 (3.62%) subjects were positive for both tests whereas 131 (18.3%) were positive by either test. Comparing the results of the QFT-Plus with those of the TST, both tests had a significant total agreement of 88.8%; $\kappa = 0.332$; 95% confidence interval = 0.23–0.43; $P < 0.001$). The LTBI prevalence index was 0.83 and prevalence-adjusted kappa was 0.79 ($P < 0.001$). Negative concordance comprised 85.4% of the results, and positive concordance comprised 3.62%. However, positive TST but negative QFT-Plus comprised 5.57% of the results, and negative TST but positive QFT-Plus comprised 5.43%.

Table 3 shows the association between risk factors and QFT-Plus test results in the studied groups, where the Smoking, Health status, Immunosuppression, Occupation, Contact T.B. at work place, Past history of TB and diabetes mellitus appear as significant risk factors [16].

Table 4 shows the association between the studied risk factors and Tuberculin skin test results in the studied groups, with significant difference noted for Smoking, BCG vaccination, Immunosuppression, Occupation, Contact T.B. at

work place, Past history of TB and diabetes mellitus.

Tables 3,4 shows also that the LTBI prevalence among females using QFT-Plus was 44 (67.7%) which was higher than males 21(32.3%) but with no significant difference. By using TST LTBI prevalence among females was 40 (60.1%) which was higher also than males 26(39.9%) but also with no significant difference. Healthcare workers aged ≤30 years had the higher prevalence of LTBI 40(61.53%) using QFT-Plus and 39(59.09%) using TST than aged >30 years which was 25 (38.47%) using QFT-Plus and 27(40.91%) using TST. No significant difference detected using the two methods. The prevalence among Saudi was 53(53.0%) using both QFT-Plus and TST and non Saudi 31(46.92%) both QFT-Plus and TST with no significant difference regarding nationality. Non-smokers HCWs had a higher LTBI prevalence 42(64.6%) using QFT-Plus and 52(78.8%) using TST than smokers 23(35.4%) using QFT-Plus and 14(21.2%) using TST. There was significant difference using the two methods. The LTBI prevalence was higher in HCWs with previous BCG vaccination 58(87.9%) using TST while using QFT-Plus it was higher among non vaccinated 20 (30.8%). Poor health status HCWs had a higher LTBI prevalence 55(84.6%) than good health status HCWs 10(15.4%) with significant difference. Immunocompromised HCWs had a higher LTBI prevalence 52(80.0%) than non Immunocompromised HCWs 13(20.0%) with significant difference. Physicians in the medical domain had the highest prevalence of LTBI 12(18.6%) and 10 (15.2%) compared with the surgical domain 4(6.15%) and 1 (9.09%) using QFT-Plus and TST respectively. Nurses working in chest department had higher prevalence 11(16.9%) followed by nurses in female medical ward 10 (15.4%) using both methods of detection. The LTBI prevalence among HCWs who work and contact TB at work place was 58(89.2%). HCWs who had past history of TB had higher LTBI prevalence 60(92.3%). Diabetics also had a higher LTBI prevalence 55(84.6%) and 21(31.8%) than non diabetics using QFT-Plus and TST respectively.

All HCWs with positive LTBI underwent CXR examination, and the results were normal CXR. Those HCWs with positive LTBI, who had sputum, underwent AFB smear microscopy and, subsequently, their results were negative. In conclusion, there were no active TB cases among HCWs with LTBI.

4. DISCUSSION

Examination of the health care workers for latent tuberculosis infection is an important step in the identification of cases which have a high risk of tuberculosis disease [17].

Seven hundred and eighteen health care workers were enrolled in our study, The prevalence of latent tuberculosis diagnosed was 9.19% and 9.05% using TST and QFT-Plus methods respectively which is similar to results obtained in KSA by Abbas et al., 2010 who reported 11%

Table 1. Healthcare workers demographic data

Characteristics	HCW tested	
	NO	%
Sex		
Male	281	39.1%
Female	437	60.9%
Age (SD) years	30.25 ± 7.95	
Age		
≤30	345	33.4%
>30	373	38.0%
Nationality		
Saudi	391	54.5%
Non saudi	327	45.5%
Smoking		
Yes	646	90.0%
No	72	10.0%
BCG vaccination		
YES	200	27.7%
NO	518	72.1%
Health status		
Poor	220	30.6%
Good	498	69.4%
Immunosuppression		
Yes	107	14.9%
No	611	85.1%
Occupation		
Doctors		
Medical	54	7.52%
Surgical	51	7.10%
Total	105	14.6%
Nurses		
Chest department	14	1.90%
Female medical	16	2.23%
Male medical	16	2.23%
Nephrology	19	2.65%
others	155	21.6%
Total	220	30.6%
Other clinical staff	183	25.5%
Non clinical staff	210	29.3%
Contact T.B. at work place		
Yes	151	21.0%
No	567	79.0%
Past history of TB		
Yes	15	2.1%
No	703	97.9%
diabetes		
Yes	127	17.7%
No	591	82.3%

Table 2. Comparison between TST and QFT-Plus results

TST			
QFT-Plus	Negative <10 mm	Positive ≥10 mm	Total
Negative	613	40	653
Positive	39	26	65
Total	652	66	718

Table 3. Association between risk factors and QFT-Plus

Risk factors	QFT-Plus				X²	P
	Positive =65		Negative =653			
	No.	%	No.	%		
Male	21	32.30%	260	39.82%	1.40	0.237
Female	44	67.70 %	393	60.18%		
Age						
≤30	40	61.53%	305	46.70%	5.21	0.022
>30	25	38.47%	348	53.30%		
Nationality						
Saudi	34	53.04	356	54.60%	0.056	0.807
Non saudi	31	46.96	296	45.40%		
Smoking						
Yes	23	35.38%	49	7.50%	50.9	<0.001*
No	42	64.62%	604	92.50%		
BCG vaccination						
YES	20	30.76%	490	75.04%	0.030	0.781
NO	45	67.16%	163	24.96%		
Health status						
Poor	55	84.62%	165	25.27%	98.0	<0.001*
Good	10	15.38%	488	74.73%		
Immunosuppression						
Yes	52	80%	55	8.42%	99.8	<0.001*
No	13	20%	598	91.58%		
Occupation						
Doctors						
Medical	12	18.46%	42	6.74%	4.20	0.040*
Surgical	4	6.15%	47	7.19%		
Nurses						
Chest	11	16.92%	3	0.46%	111.0	<0.001*
Female medical	10	15.38%	6	0.92%		
Male medical	8	12.31%	8	1.23%		
Nephrology	9	13.85%	10	1.53		
Others	1	1.52%	154	23.58%		
Other clinical staff	9	13.85%	174	26.64%	7.78	0.005*
Non clinical staff	1	1.52%	209	32.01%		
Contact T.B. at work place						
Yes	58	89.23%	93	14.24%	200.2	<0.001*
No	7	10.77%	560	85.76%		
Past history of TB						
Yes	5	7.69%	10	1.53%	11.0	<0.001*
No	60	92.31%	643	98.47%		
Diabetes						
Yes	55	84.62%	72	11.03%	220.0	<0.001*
No	10	15.38%	581	88.97%		

prevalence of latent tuberculosis in HCWs in four major tertiary care hospitals in Riyadh, Saudi Arabia[18] and also our results agreed with that reported by Nienhaus et al. which was 10.5% in

HCW working in in geriatric care units[19]. Our data were lower compared to other studies in low and middle income countries with a prevalence 33% [20]. Because these studies were almost based on the use of the TST, while, several reports of LTBI in HCWs using TST and the interferon gamma release assay (IGRA) have shown a high proportion of TST-positive/IGRA-negative results, which was most likely explained by BCG vaccination [21], [22].

In our study LTBI test was positive by TST in 66 (9.19%) subjects and by QFT-Plus in 65 (9.05%) subjects. Only 26 (3.62%) subjects were positive for both tests whereas 131 (18.3%) were positive by either test. On comparison of the results of the QFT-Plus with those of the TST, both tests had a significant overall agreement of 88.8%. The agreement of the results by adjusted kappa testing of QFT-Plus and TST test was 0.332, which is considered fair agreement.

Table 4. Association between risk factors and TST

Risk factors	TST				X ²	P
	Positive =66		Negative =652			
	No.	%	No.	%		
Male	26	39.93%	255	39.11%	0.002	0.964
Female	40	60.07%	397	60.89%		
Age					3.54	0.0595
≤30	39	59.09%	306	46.93%		
>30	27	40.91%	346	53.07%		
Nationality					0.06	0.807
Saudi	35	53.04	356	54.60%		
Non saudi	31	46.96	296	45.40%		
Smoking					10.1	<0.001*
Yes	14	21.21%	58	8.90%		
No	52	78.79%	594	91.10%		
BCG vaccination					95.1	<0.001*
YES	58	87.88%	142	21.78%		
NO	8	12.12	510	78.22%		
Health status					2.14	0.143
Poor	15	22.73	205	31.44%		
Good	51	77.27%	447	68.56%		
Immunosuppression					139.3	<0.001*
Yes	42	63.63%	65	9.97%		
No	24	36.37%	588	90.03%		
Occupation					2.81	0.003*
Doctors						
Medical	10	15.15%	44	6.75%		
Surgical	1	9.09%	50	6.90%		
Nurses					111.4	<0.001*
Chest	11	16.92%	3	0.46%		
Female medical	10	15.15%	6	0.92%		
Male medical	9	13.63%	7	1.07%		
Nephrology	9	13.63%	10	1.53%		
others	1	1.52%	154	23.62%		
Other clinical staff	11	(36.07%)	172	26.38%	10.12	<0.001*
Non clinical staff	1	(36.07%)	209	32.06%		
Contact T.B. at work place					103.7	<0.001*
Yes	46	69.70%	105	16.10%		
No	20	30.30%	547	83.90%		
Past history of TB					47.4	<0.001*
Yes	9	2.09%	6	0.92%		
No	57	97.91%	646	99.08%		
Diabetes					9.97	<0.001*
Yes	21	31.82%	106	16.26%		
No	45	68.18%	546	83.74%		

Many studies showed a fair to good agreement from 65.4% to 92.5% among HCWs, [23,24,25] while other reports showed a much lower agreement rate among HCWs [26,27]. Other studies showed total agreement of 82% among army personnel [28]. In Saudi Arabia a recent study among HCWs showed 73.7% overall agreement between the two tests ($\kappa = 0.33$, $P < 0.01$) with 60.1% negative concordance and 13.5% positive concordance [29]. Another recent study reported overall agreement of TST and QFT-Plus of 90.9% ($\kappa = 0.46$) among HCWs [30]. However, the sample size of these studies was small, and the results may not be representative of a larger population.

In our study as the overall agreement was 88.8% for both positive and negative concordance, it is noticed that both tests being positive were in only 3.62% whereas positive TST but negative QFT-Plus comprised 5.57% of the results, and negative TST but positive QFT-Plus comprised 5.43%. The era that either test conducted alone for screening LTBI among HCWs will miss 5.57%, and 5.43% for QFT-Plus and TST, respectively, is of concern while screening both tests simultaneously. In fact, guidelines from other countries such as the UK, Spain, Italy, and Canada have provided special scenarios in which a two-step testing is applied [31].

Among risk factors associated with latent tuberculosis infection, it was found that LTBI prevalence among females using both QFT-Plus and TST methods was higher than males with no significant difference and these results also reported by Belo and Naidoo, 2017 who showed that was very similar results of LTBI prevalence between males and females (34.8% vs 34.3% respectively) [32]. In this study positive results of our two tests were higher in age groups (> 30 years old) than (< 30 years old) with no significant value which agreed with other similar study that declared that age was an independent risk factor for tuberculosis and the prevalence of latent tuberculosis infection in health care workers increased by 1.04 times for each year of age [18].

Non-smokers HCWs had a higher LTBI prevalence 42 (64.62%) using QFT-Plus and 52(78.8%) using TST than smokers 23(35.4%) using QFT-Plus and 14(21.2%) using TST. There was significant difference using the two methods. Although, it was observed that the positive results of QFT-GIT test were significantly higher among smokers as reported in a study

conducted in the United States [33]. These findings may be explained with high proportion of non smokers among studied population.

The LTBI prevalence was higher in HCWs with previous BCG vaccination 58(87.9%) using TST while using QFT-Plus it was higher among non vaccinated 20 (30.8%).The results of Tuberculin skin test in BCG vaccinated individuals were significantly affected by their BCG vaccination status. Higher proportions of vaccinated individuals were positive when tested by Tuberculin skin test, while the results of individuals tested by QFT-Plus were not affected by vaccination status. This could be due to the fact that QFT-Plus depended on specific *M. tuberculosis* antigens not affected by vaccination status. Therefore, it reduced the risk of latent tuberculosis infection overestimation via cross-reactions with BCG vaccination or environmental mycobacteria. These findings made examination by QFT-Plus in people who were repeatedly exposed to tuberculosis (e.g. health care providers) more feasible. QFT-Plus is therefore a useful tool in detecting latent tuberculosis infection cases in a country where BCG vaccination is a national policy [34].

In our study poor health status HCWs had a higher LTBI prevalence 55(84.6%) than good health status HCWs 10(15.4%) with significant difference. Immunocompromised HCWs had a higher LTBI prevalence 52(80.0%) than non Immunocompromised HCWs 13(20.0%) with significant difference. Immunosuppression is a very important individual risk factor with a high LTBI prevalence however Van Rie et al. found immunosuppression associated with a high prevalence of LTBI and an increased probability of progression to TB disease [35].

In our study regarding profession as a risk factor, Physicians in the medical domain had the highest prevalence of LTBI 12(18.6%) and 10 (15.2%) compared with the surgical domain 4(6.15%) and 1 (9.09%) using QFT-Plus and TST respectively which was similarly to what Tan et al. found [36] that healthcare workers working in the medical domain reported a higher prevalence of LTBI compared to the surgical domain. Also latent tuberculosis infection among Nurses working in chest department had higher prevalence 11(16.9%) followed by nurses in female medical ward 10 (15.4%) using both methods of detection. These results were in agreement with previous studies which reported

that the prevalence of latent tuberculosis infection in nurses was higher than that in other health care workers [37]. Results revealed that a higher percentage of infection was present among chest nurses. This was because they provided care for tuberculosis patients and were continuously directly exposed.

In our study the LTBI prevalence among HCWs who works in Contact T.B. at work place was 58(89.2%). also CDC agreed that the work hours, working conditions, and the condition of patient who work closely with them are important risk factors for LTBI prevalence among HCWs. CDC also reported that if an individual has been around someone with TB disease, he or she can get TB infection. However, not everyone infected with TB germs becomes sick. A person with latent TB infection cannot spread germs to other people, but can develop TB disease in the future [34,35].

In this study past history of tuberculosis represents a higher risk of developing latent tuberculosis infection by the two tests which is similar to the results of another study done in the United States [38].

In current study diabetics also had a higher LTBI prevalence 55(84.6%) and 21(31.8%) than non diabetics using QFT-Plus and TST respectively. This was similar to results obtained by Jeon and Murray,2008 who revealed that People with diabetes had a 2–3 times higher risk of tuberculosis compared to people without diabetes [39] These findings coincide with the concept of increased susceptibility to tuberculosis by decreased immunity (diabetes).

5. CONCLUSION

The prevalence of latent tuberculosis diagnosed was 9.05% and 9.19% using QFT-Plus and TST respectively and the overall agreement of TST and QFT-Plus for the detection of LTBI among the studied population was 88.8%. Testing of HCWs at hire and periodically can help in the detection of LTBI and using prophylaxis treatment for positive TST cases can reduce the number of HCWs who may develop TB later on. Large scale study is recommended to confirm such findings in Saudi Arabia health care settings, also the use of Quantiferon for detection of LTBI beside using TST is recommended as it reduces the false positive reports by TST and is not affected by prior BCG status.

CONSENT

All HCW in Al Quwayiyah General hospital were included and each agreed to be enrolled in the study with provision of written informed consent.

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. World Health Organization. What Is DOTS?: A guide to understanding the WHO-recommended TB control strategy known as DOTS; World Health Organization: Geneva, Switzerland, 1999.
2. Kiazky S, Ball T. Tuberculosis (TB): Latent tuberculosis infection: An overview. *Can. Commun. Dis. Rep.* 2017;43- 62.
3. Sidhu A, Verma G, Humar A, Kumar D. Outcome of latent tuberculosis infection in solid organ transplant recipients over a 10-year period. *Transplantation.* 2014;98:671–675.
4. Corbett EL, Muzangwa J, Chaka K, Dauya E, Cheung YB, Munyati SS, Reid A, Hakim J, Chandiwana S, Mason PR. Nursing and community rates of Mycobacterium tuberculosis infection among students in Harare, Zimbabwe. *Clin. Infect. Dis.* 2007; 44:317–323.
5. Abdalhamid B, Hinrichs S, Garrett J, O'Neill J, Hansen-Cain J, Armbrust A,2 and Iwen1P: Utilization of the QuantiFERON-TB gold test in a two-step process with the tuberculin skin test to evaluate health care workers for latent tuberculosis. *Journal Of Clinical Microbiology.* 2010;2955–2956.
6. Taggart EW, Hill HR, Ruegner RG, Martins TB, Litwin CM. Evaluation of an *in vitro* assay for gamma interferon production in response to Mycobacterium tuberculosis infections. *Clin Diagn Lab Immunol.* 2004; 11:1089–93.
7. Andersen P, Munk ME, Pollock JM, Doherty TM. Specific immune-based diagnosis of tuberculosis. *Lancet.* 2000; 356:1099–104.

8. Pai M, Riley LW, Colford JM, Jr Interferon-gamma assays in the immunodiagnosis of tuberculosis: A systematic review. *Lancet Infect Dis.* 2004;4:761–76.
9. Petruccioli E, Chiacchio T, Pepponi I, et al. First characterization of the CD4 and CD8 T-cell responses to QuantiFERON-TB Plus. *J Infect.* 2016;73:588–597.
10. Qiagen. QuantiFERON®-TB gold plus (QFT®-Plus) ELISA Package Insert. Available: <http://www.quantiferon.com/irm/content/PI/QFT/PLUS/2PK-Elisa/UK.pdf>
11. Uplekar M, Weil D, Lonroth K, Jaramillo E, Lienhardt C, Dias HM, Falzon D, Floyd K, Gargioni G, Getahun H. WHO's new end TB strategy. *Lancet.* 2015;385:1799–1801.
12. Andersen P, et al. Specific immune-based diagnosis of tuberculosis. *Lancet.* 2000; 356:1099.
13. Turner J, et al. Stimulation of human peripheral blood mononuclear cells with live *Mycobacterium bovis* BCG activates cytolytic CD8+ T cells in vitro. *Immunology.* 1996;87:339.
14. 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;3: 494-499.
15. Bennett DE, Courval JM, Onorato I, Agerton T, Gibson JD, Lambert L, et al. Prevalence of tuberculosis infection in the United States population: The national health and nutrition examination survey, 1999-2000. *Am J Respir Crit Care Med.* 2008;177(3):348-55.
16. Jeon CY, Murray MB. Diabetes mellitus increases the risk of active tuberculosis: A systematic review of 13 observational studies. *PLoS Med.* 2008;5(7):e152.
17. Costa JT, Silva R, Sá R, Cardoso MJ, Ferreira J, Ribeiro C, et al. Tuberculosis – risk of continued transmission in health-care workers. *Rev Port Pneumol.* 2010; 16(1):5-21.
18. Abbas MA, AlHamdan NA, Fiala LA, AlEnezy AK, AlQahtani MS. Prevalence of latent TB among health care workers in four major tertiary care hospitals in Riyadh, Saudi Arabia. *J Egypt Public Health Assoc* 2010;85:61-71.
19. Nienhaus A, Schablon A, Loddenkemper R, Hauer B, Wolf N, Diel R. Prevalence of latent tuberculosis infection in healthcare workers in geriatric care. *Pneumologie* 2007;61:613-616.
20. 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;3: 494.
21. 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
22. Vinton P, Mhrshahi S, Johnson P, Jenkin GA, Jolley D, et al. Comparison of QFT-Plus test and tuberculin skin test for identification of latent mycobacterium tuberculosis Infection in healthcare staff and association between positive test results and known risk factors for infection. *Infect Control Hosp Epidemiol.* 2009;30: 215–221.
23. Caglayan V, Ak O, Dabak G, Damadoglu E, Ketenci B, Ozdemir M, et al. Comparison of tuberculin skin testing and QuantiFERON-TB gold-in tube test in health care workers. *Tuberk Toraks.* 2011; 59:43–7.
24. Pai M, Gokhale K, Joshi R, Dogra S, Kalantri S, Mendiratta DK, et al. *Mycobacterium tuberculosis* infection in health care workers in rural India: Comparison of a whole-blood interferon gamma assay with tuberculin skin testing. *JAMA.* 2005;293:2746–55.
25. Khoury NZ, Binnicker MJ, Wengenack NL, Aksamit TR, Buchta WG, Molella RG. Preemployment screening for tuberculosis in a large health care setting: Comparison of the tuberculin skin test and a whole-blood interferon-gamma release assay. *J Occup Environ Med.* 2011;53:290–3.
26. Zhao X, Mazlagic D, Flynn EA, Hernandez H, Abbott CL. Is the QuantiFERON-TB blood assay a good replacement for the tuberculin skin test in tuberculosis screening. A pilot study at Berkshire Medical Center? *Am J Clin Pathol.* 2009; 132:678–86.
27. Jong Lee K, Ae Kang Y, Mi Kim Y, Cho SN, Wook Moon J, Suk Park M, et al. Screening for latent tuberculosis infection in South Korean healthcare workers using a tuberculin skin test and whole blood interferon-gamma assay. *Scand J Infect Dis.* 2010;42:672–8.
28. Talebi-Taher M, Javad-Moosavi SA, Entezari AH, Shekarabi M, Parhizkar B. Comparing the performance of

- QuantiFERON-TB gold and mantoux test in detecting latent tuberculosis infection among Iranian health care workers. *Int J Occup Med Environ Health*. 2011;24:359–66.
29. Franken WP, Timmermans JF, Prins C, Slootman EJ, Dreverman J, Bruins H, et al. Comparison of Mantoux and QuantiFERON TB Gold tests for diagnosis of latent tuberculosis infection in Army personnel. *Clin Vaccine Immunol*. 2007; 14:477–80.
30. El-Helaly M, Khan W, El-Saed A, Balkhy HH. Pre-employment screening of latent tuberculosis infection among healthcare workers using tuberculin skin test and QuantiFERON-TB Gold test at a tertiary care hospital in Saudi Arabia. *J Infect Public Health*. 2014;7:481–8.
31. Hassan H, Shorman M, Housawi A, Elsammak M. Detecting latent tuberculosis infection prior to kidney transplantation in a tertiary hospital in Saudi Arabia: Comparison of the T-SPOT. TB test and tuberculin test. *Br Microbiol Res J*. 2013; 3:116–27.
32. Belo C, S. Prevalence and risk factors for latent tuberculosis infection among healthcare workers in Nampula Central Hospital, Mozambique *BMC Infect Dis*. 2017;17: 408.
33. Tan LH, Kamarulzaman A, Liam CK, Lee TC. Tuberculin skin testing among healthcare workers in the University of Malaya Medical Centre, Kuala Lumpur. *Malaysia Infect Control Hosp Epidemiol*. 2002;23(10):584–590.
34. CDC. Protect Your Family and Friends from TB: The TB Contact Investigation. Available:http://www.CDC.gov/tb/publications/pamphlets/TB_contact_investigation.pdf
35. TB Control Programs. Available:<http://www.CDC.gov/tb/links/tboffices.htm>
36. Dodig S, Zrinski Topić R, Živčić J. Latent tuberculosis infection in a subject with diabetes mellitus – a case report. *Biochem Med (Zagreb)*. 2008;18(3):368-73.
37. Haley CA, Cain KP, Yu C, Garman KF, Wells CD, Laserson KF. Risk-based screening for latent tuberculosis infection. *South Med J*. 2008;101(2):142-9.
38. 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;7(1):36-45.
39. Dheda K, Chang JS, Kim LU, Huggett JF, Johnson MA, Zumla A, et al. Interferon gamma assays for tuberculosis. *Lancet Infect Dis*. 2005;5(6):324-5.

© 2019 Khater and Abdo; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/53796>