Available online at www.ujpronline.com
Universal Journal of Pharmaceutical Research
An International Peer Reviewed Journal
ISSN: 2831-5235 (Print); 2456-8058 (Electronic)

RESEARCH ARTICLE

PREVALENCE AND RISK FACTORS OF LATENT TUBERCULOSIS AMONG HEALTHCARE WORKERS IN SANA'A CITY, YEMEN USING WHOLE BLOOD INTERFERON-Γ RELEASE ASSAY

Khaled Saad Abdulrahman Al-Khamesy[1], Mohammed Mohammed Al-Shehari[2], Khaled Abdul-Karim A Al-Moyed[3], Jalal Yahia Yahia Atf-allah[4], Hassan Abdulwahab Al-Shamahy[3,5], Ahmed Mohamed Al-Hadad[6]

[1]*Physiology Department, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen.*
[2]*General surgery Department, Faculty of Medicine and Health Sciences, Sana'a University, Republic of Yemen.*
[3]*Medical Microbiology and Clinical Immunology Department, Faculty of Medicine and Health Sciences, Sana'a University.*
[4]*Department of community and family medicine, Faculty of Medicine, Science and technology University, Sana'a city.*
[5]*Medical Microbiology department, Faculty of Medicine, Genius University for Sciences & Technology, Dhamar city.*
[6]*Department of Medical Microbiology, Faculty of Medicine and Health Sciences, Hadhramout University, Republic of Yemen.*

Article Info:

Article History:
Received: 2 August 2023
Reviewed: 11 September 2023
Accepted: 24 October 2023
Published: 15 November 2023

Cite this article:
Al-Khamesy KSA, Al-Shehari MM, Al-Moyed KAA, Atf-allah JYY, Al-Shamahy HA, Al-Hadad AM. Prevalence and risk factors of latent tuberculosis among healthcare workers in Sana'a city, Yemen using whole blood interferon-γ release assay. Universal Journal of Pharmaceutical Research 2022; 7(5):1-7.
https://doi.org/10.22270/ujpr.v7i5.833

***Address for Correspondence:**
Dr. Hassan A. Al-Shamahy, Faculty of Medicine and Heath Sciences, Sana'a University, Faculty of Medicine, Genius University for Sciences and Technology Dhamar/Sana'a, Yemen. Tel- +967-1-239551.
E-mail: *shmahe@yemen.net.ye*

Abstract

Background and aims: Tuberculosis (TB) is a critical problem of public health. Diagnosis and screening of latent *Mycobacterium tuberculosis* infections (LTBI) are essential to control their spread. The goal of the study was to clarify the prevalence and risk factors for LTBI using IGRA among healthcare works (HCWs) in Sana'a city, Yemen.

Methods: The cross-sectional study was performed in three chosen tertiary hospitals in Sana'a city. Healthcare workers who participated in this survey were asked to complete a questionnaire and donate 5 ml of blood to perform the IGRA. A total of 180 healthcare workers were involved in this study; aged 20-60 years, 45.6% males and 54.4% females. Blood samples were collected and then tested by Interferon-gamma (IFN-γ)release assays that measure the presence of specific *M. tuberculosis* reactive T-cells sensitized by a previous infection with *M. tuberculosis* using the Quanti FERON-TB Gold In Tube assay (QFT-GIT). The data were evaluated for the positive association of interferon-gamma.

Results: The overall positivity rate IFN-γ of our healthcare workers was 20%, and for females it was 28.6%, with an associated odds ratio equal to 3.7, *CI*=1.5-8.7, *p*=0.001, while for males it was only 9.7%. Positive rates IFN-γ increased with increasing age, as a high IFN-γ positive rate occurred in the 50-60-year age group was 50%, with *OR*=5.5, *CI*=2.2-13.6, *p*<0.001. There was a significant association between IFN-γ positive latent tuberculosis and unimmunized childhood BCG (*OR*=2.2, *CI*=1.03-4.7, *p*=0.03), diabetics (*OR*=4.2, *CI*=1.5-12, *p*=0.003), smoking (*OR*=2.7, *CI*=1.2-6.1, *p*=0.009) and contacting cases with active TB (*OR*=4.1, *CI*=1.4-12.2, *p*=0.007).

Conclusion: It was found that the rate of LTBI among HCWs is high in Sana'a, central Yemen. Factors at both the institutional and individual level can influence the prevalence of LTBI among HCWs. Since contact with active TB patients has been identified as a risk factor for LTBI, more effective TB infection control measures are necessary in health care facilities and congregate settings and to create awareness about TB risk factors in hospitals and as an occupational hazard.

Keywords: Health care workers (HCWs), Interferon (IFN)-γ release assays (IGRAs), Latent TB, Tuberculosis (TB), Sana'a, Yemen.

INTRODUCTION

Yemen is one of the developing countries where infectious microorganisms are the main causes of human suffering including tuberculosis, limited research has been conducted in investigating infectious diseases such as viral hepatitis[1-7], parasitic infections[8,9], leptospirosis[10], trachoma[11], tuberculosis[12], fungal infections[13]. Tuberculosis is one of the serious public health problems in Yemen[12], as tuberculosis is one of

the main causes of death, although it is a curable infectious disease, as well as a major cause of morbidity in developing countries such as Yemen[14]. Approximately 9 million new cases were expected worldwide in 2021, but only half were reported[15]. Detecting and monitoring latent TB infection is crucial to controlling its spread. TST and drug treatment to prevent LTBI from progressing to overt disease are vital strategies for the elimination of tuberculosis in low-incidence countries and especially among high-risk groups such as HCWs[16].

Improving diagnostic methods for LTBI is an important step towards the goal of tuberculosis eradication, as stipulated in the WHO Tuberculosis Control Strategy[16] and the Ministry of Health and Population Action Plan for Tuberculosis Control in Yemen. As part of reaching this goal, individuals with tuberculosis should be identified and prophylactic treatment offered to halt the progression to active tuberculosis and prevent further transmission of *Mycobacterium tuberculosis*. Thus, there is a need to develop more accurate methods for detecting LTBI, and to provide evidence-based guidance on the use of these methods before they can be adopted by national TB programmes. In Yemen, the determination of LTBI is based on the TST. This diagnostic test has been comprehensively evaluated for its potential and the limitations of its use in preventive strategies to eliminate tuberculosis. However, the TST does not distinguish between possible infection with tuberculosis and prior vaccination with Bacillus Calmette-Guerin (BCG), or possible infection with *Mycobacterium non-tuberculosis* (NTM) [17]. IFN-γ release assays (IGRAs) are *in vitro* immune tests that have been introduced in ten years ago as an alternative to the TST for the diagnosis of LTBI. IGRAs are established on the recognition of a T-cell immune response towards *M. tuberculosis* complex specific antigens (early secretary antigenic target (ESAT)-6, culture filtrate protein (CFP)-10 and/or TB7.7) [17]. The adoption and implementation of IGRAs in Yemen's national tuberculosis programs must be evidence-based. To date, many countries have adopted IGRAs for the diagnosis of LTBI within their tuberculosis screening programmes, and guiding documents are available on their use[17]. Clinical guidance for the diagnosis of LTBI is particularly vital for immune-compromised individual's care, eg patients experience and undertaking tumor necrosis factor (TNF) therapies, who have an increased risk of developing active tuberculosis. Numerous studies and subsequent systematic reviews and meta-analyses have been performed to assess the accuracy of IGRA in diagnosing LTBI[17]. The purpose of the study was to determine the prevalence and risk factors for LTBI using IGRA among HCWs in Sana'a city, Yemen. In addition, this study provides important information about the use of IGRAs to support the development of evidence-based guidelines for tuberculosis screening programmes.

MATERIALS AND METHODS

Study tools: A questionnaire

All HCWs who participated in this survey were asked to finish the questionnaire. The questionnaire consisted of things connected to age, sex, occupation, length of work, current place of work, history of BCG vaccination, history of active tuberculosis, and medical history, containing smoking, diabetes, autoimmune diseases, and malignancies. Additional information acquired included employment history in the tuberculosis department classified as the departments in which HCWs with a high potential for contact with respiratory tuberculosis patients work: including tuberculosis management in medical institutions; hospital ward or outpatient pulmonology unit; hospital ward or outpatient infectious disease unit; Bronchoscopy room, laboratory *M. tuberculosis*; pulmonary Function Test Room, Intensive Care Unit; Emergency department; Pulmonary clinic and chest x-ray room. Furthermore, the participating subjects given a history of their contact with active tuberculosis, both in and out of the hospital.

Sample size: The sample size was calculated using Epi info version 7 and based on the following assumption: The total number of HCWS in Sana'a city tertiary hospitals (Population size) is 6335. The percentage of LTBI among HCWs is about 14%[17], the accepted margin of error=5%, the design effect=1, and the confidence level=95%, the calculated sample size is 180.

Collection, transport, and testing of specimens: Blood specimens were obtained and directly stored in a cooler box. The samples were transported to the laboratory on the same day, and on arrival at the laboratory, the specimens centrifuged and the serum was divided into three aliquots and stored at −20°C. One aliquot was tested by IFN-γ release assays which determine the presence of specific *M. tuberculosis* reactive T-cells sensitized by previous infection with *M. tuberculosis* using the Quanti FERON-TB Gold In-Tube assay (QFT-GIT) (Cellestis Ltd., Australia).

DRG IFN-γ ELISA: The DRG IFN-γ ELISA is a solid phase enzyme amplified sensitivity immunoassay performed on micro-titer plate, the assay uses monoclonal antibodies (MAbs) directed against distinct epitopes of IFN-γ. Standards and samples react with the capture monoclonal antibody (MAb 1) coated on micro-titer well and with a monoclonal antibody (MAb 2) labelled with horseradish peroxides (HRP). After an incubation period allowing the formation of a sandwich-coated MAb1-human IFN-γ MAb2-HRP, the micro-titer plate is washed to remove unbound enzyme labeled antibody. Bound enzyme-labelled antibody is measured through a chromogenic reaction.

Chromogenic solution is added and incubated. The reaction is stopped with the addition of stop solution and the micro-titer plate is then read at the appropriate wavelength, the amount of substrate turnover is determined calorimetrically by measuring the absorbance, which is proportional to the IFN-γ concentration.

Statistical Analysis: To correlate possible risk factors for latent TB, the data were inspected in a case-control study arrangement. For HCWs with confirmation of latent TB were matched up with those who were latent TB negative. The chi-square was used to see the association *Odds ratios* (*OR*) and their 95% confidence intervals (*CI*). Values of *OR*, *CI*, and χ^2 were determined using 2x2 tables to identify possible *odds ratio* on the occurrence of latent TB and their significance. The result at *p* value of 0.05 was considered statistically significant.

Ethical approval: The ethical approval for this study was No. 782 dated March, 2022 and was taken from the Medical Ethics and Research Committee of Sana'a University, Faculty of Medicine and Health Sciences, and all procedures were in accordance with the ethical guidelines of the review committee. We approached all participants for their consent, and prior to enrollment information sheets in Arabic were provided. We required that all participants provide written informed consent before the information was collected.

RESULTS

The study included 180 HCWs, males were 82 (45.6%), and females were 98 (54.4%) (Table 1). The HCWs included in the latent tuberculosis study were broken down by occupation and were nurses (39%), physicians (34%), technicians (16.7%) and administrators (10%) (Figure 1).

Table 1: Gender and age distribution of health care workers included in studies of latent tuberculosis.

Age groups Years	Male No (Rate %)	Female No (Rate %)	Total No (Rate %)
20-29	24 (29.2)	28 (28.6)	52 (28.9)
30-39	22 (26.8)	34 (34.7)	56 (31.1)
40-49	22 (26.8)	26 (26.5)	48 (26.7)
50-60	14 (17.1)	10 (10.2)	24 (13.3)
Total	82 (45.6)	98 (54.4)	180 (100)

The total IFN-γ positive for our healthcare workers was 20%, and for females it was 28.6%, with an associated *odds ratio* equal to 3.7, *CI*=1.5-8.7, *p*=0.001, while for males it was only 9.7%. Positive IFN-γ rates increased with age, with a significant increase in IFN-γ positive rates occurring in the 50–60-year age group, where *OR*=5.5, *CI*=2.2–13.6, *p*<0.001(Table 2). There was no significant association between positive IFN-γ indicative of latent tuberculosis with any specific occupations of health workers in the current study (Table 3).

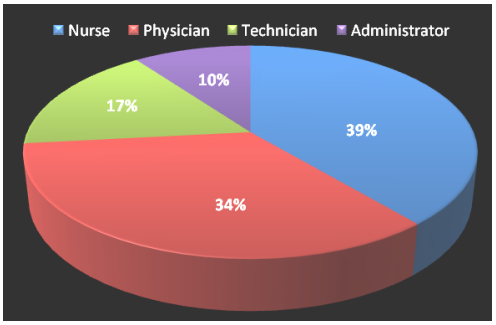

Figure 1: The distribution of health care workers included in study of latent tuberculosis according to specific occupations.

There was no significant association between positive IFN-γ indicative of latent tuberculosis with duration of works for the HCWs in the current study (Table 4). There was a significant association between IFN-γ positive latent tuberculosis and unimmunized childhood BCG (*OR*=2.2, *CI*=1.03-4.7, *p*=0.03), diabetics (*OR*=4.2, *CI*=1.5-12, *p*=0.003), smoking (*OR*=2.7, *CI*=1.2-6.1, *p*=0.009) and contacting cases with active TB (*OR*=4.1, *CI*=1.4-12.2, *p*=0.007) (Table 4).

DISCUSSION

This is one of the first studies to compare the performance of the QFT while examining Yemeni HCWs. TB is known to be a biological health hazard for HCWs, and continues a very significant occupational hazard for HCWs in middle-and low-income countries and workers in various institutions in high-income countries. Risks appear particularly high when there is increased exposure such as working in infectious disease hospitals, emergency rooms and laboratory settings, combined with inadequate infection control measures[16-18].

Table 2: Association of positive *interferon gamma* indicative of latent tuberculosis with age and sex of health workers.

Characters	Positive *gamma interferon*		*OR*	*CI*	X^2	*P*
	NO	Rate (%)				
Sex						
Male n=82	8	9.7	0.27	0.1-0.6	9.8	0.001
Female=98	28	28.6	3.7	1.5-8.7	9.8	0.001
Age group (Years)						
20-29 n=52	2	3.8	0.11	0.025-0.47	11.9	0.0005
30-39 n=56	10	17.8	0.8	0.36-1.8	0.2	0.62
40-49 n=48	12	25	1.5	0.68-3.3	1.02	0.31
50-60 n=24	12	50	5.5	2.2-13.6	15.6	<0.001
Total n=180	36	20				

OR= odds ratio, *CI*= confidence interval; X^2= Chi-square; *p*<0.05 (significant)

Table 3: Association of positive *interferon gamma* indicative of latent tuberculosis with specific occupations of health workers.

	Positive *gamma interferon*	*OR*	*CI*	X^2	*p*
	No (Rate %)				
Nurses, n =70	12 (17.1)	0.7	0.34-1.5	0.5	0.44
Physician, n=61	8 (12.9)	0.49	0.2-1.1	2.7	0.09
Technician, n= 30	10 (33.3)	2.4	1.0-5.6	4	0.04
Administrators, n=18	6 (33.3)	2.2	0.7-6.3	2.2	0.13
Total, n=180	36 (20)				

OR=odds ratio, *CI*= confidence interval; X^2=Chi-square; $p<0.05$ (significant)

De Vries *et al.*,[19] confirmed the importance of vigilance in TB control and emphasized that a high suspicion of TB by the clinician, sufficient infection control measures by hospital authorities and in the early time identification of latent TB infection by occupational and public-health specialists are necessary to prevent tuberculosis among HCWs. Efforts to combat tuberculosis in Yemen are huge but still ineffective. An important step in tuberculosis control is the identification of LTBI especially among HCWs. In this study, the prevalence of IFN-γ positive latent tuberculosis among HCWs was found to be 20% with a higher prevalence (50%, *OR*=5.5, $p<0.001$) among age groups 50-60 years. The results of the current study were comparable with those of Nienhaus *et al.*,[20] in Europe who found a positive 25% of IFN-γ suggestive of latent tuberculosis among HCWs and roughly similar to that done by Abbas *et al*.,[21] in Saudi Arabia; the positive rate of IFN-γ among HCWs was 18%. In addition, the positive rate of IFN-γ among HCWs in current study was lower than the rate reported by Chen *et al*., in southern China recently where the positive rate of IFN-γ among healthcare workers was 33.9%[22], while low rates were reported by Hung *et al.*, (14.5%)[23] and Shumba *et al.*,[24] (6.3%) among health care workers in central of China and Thailand respectively. There was also a strong association between older ages with positive outcomes, with the highest prevalence of positive IFN-γ (45%) among the age group of 60 years or older. On the other hand, lower rates of positive IFN-γ indicative of latent tuberculosis have been reported in other studies. For example, among HCWs in a pulmonary hospital in Germany, Schablon *et al.*,[25] found a prevalence of LTBI of 7.2%. Also in current study, the lowest IFN-γ positive prevalence among younger age group (20–29 years) was similar to that in HCWs <30 years of age in Germany where the positive prevalence of IFN-γ decreased to 3.5% in younger HCWS[25]. The positive IFN-γ index of latent tuberculosis among HCWs in current study (20%) is higher than that of the general population in Yemen by TST (2-4%)[26]. This higher rate in this study among HCWs compared to the general population can be explained by the fact that HCWs are usually more susceptible to tuberculosis infection [27].

In this study, female employees were associated with a higher prevalence of IFN-γ (28.6%) and an associated risk factor of 3.7 (*CI*=1-15, $p=0.02$), compared to a male prevalence of 9.7% (Table 2). This result is similar to that reported elsewhere where females showed a higher prevalence of latent TB than males[28]. This result can be explained by that female staffs are exposed to sources of infections more than male staff and sex susceptibility for which overall importance remains undefined[28]. There was a significant association between IFN-γ positive latent tuberculosis and contacting cases with active TB (*OR*=4.1, *CI*=1.4-12.2, $p=0.007$) (Table 4). These findings can be explained by those people with frequent, prolonged, or close connection with people with TB patients as HCWs are at predominantly high risk of developing infected, with an estimated 22% infection rate[29].

Table 4: Association of positive *interferon gamma* indicative of latent tuberculosis with BCG vaccination, work duration, diabetics, smoking, and TB contact for health workers.

	Gamma interferon Positive N=36	*OR*	*CI*	X^2	*p*
	No (Rate %)				
BCG vaccination					
Unvaccinated, N=50	15 (30)	2.2	1.03-4.7	4.3	0.03
Vaccinated, n =130	21 (16.2)	0.4	0.2-0.9	4.3	0.03
Duration of works					
≤1 year, n=15	1 (6.7)	0.26	0.03-2	1.8	0.17
>1 to ≤5 years, n=51	7 (13.7)	0.6	0.2-1.4	1.2	0.27
>5 to ≤10 years, n=69	16 (23.2)	1.3	0.6-2.8	0.7	0.33
>10 years, n=45	12 (26.7)	1.7	0.7-3.7	1.6	0.19
Diabetes mellitus (DM), n=17	8 (47.1)	4.2	1.5-12	8.5	0.003
Smoking, n=41	14 (34.1)	2.7	1.2-6.1	6.6	0.009
Qat chewing, n=65	11 (16.9)	0.7	0.3-1.6	0.6	0.43
Contact active tuberculosis patients, n=15	7 (46)	4.1	1.4-12.2	7.2	0.007
Work in risk area, n=70	18 (25.7)	1.7	0.8-3.6	2.3	0.1

OR=odds ratio, *CI*=confidence interval; X^2=Chi-square; $p<0.05$ (significant)

An individual with active but untreated TB may infect 10-15 (or more) other people per year[30]. Transmission should only occur from people with active TB; those with latent infection are not thought to be contagious. The possibility of transmission from one individual to another depends upon a number of factors, comprising the effectiveness of ventilation, the number of infectious droplets expelled by the carrier, the level of immunity in the uninfected person, the duration of exposure and others[31]. Additionally high rate of IFN-γ might be indicated by the high infectivity and the virulence of the *M. tuberculosis* strain[31]. Also this high proportion of positive IFN-γ among HCWs staff may suggest that the HCWs may be unknowingly exposed to the risk of TB infection during working. After patients with active pulmonary TB sneeze, cough, spit, speak, or sing, they expel infectious aerosol droplets 0.5 to 5.0 μm in diameter. A single sneeze can release up to 40,000 droplets[32]. Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very low (the inhalation of fewer than 10 bacteria may cause an infection). HCWs staff are most times in contact with these patients making them at high risk of contacting TB infection. Occupational transmission of tuberculosis through contact between HCWs has been confirmed in previous reports. Current study covered a wide range of hospital personnel, including physicians (doctors and consulates), nurses, technicians and administrators but there were no significant differences in latent tuberculosis with specific occupation in the current study and this differed from the results of previous studies where specific occupations showed higher rate of latent TB[14,27,31].

In the current study, there was a significant association between IFN-γ positive latent tuberculosis and diabetes mellitus (DM) (*OR*=4.7, *CI*=1.5-12, *p*=0.003) (Table 4). Patients with DM are more likely to pass from latent TB to active TB. A diagnosis of diabetes also increases the risk of progression from primary infection to active TB. Case-control studies have shown that the *OR* of developing tuberculosis is 2.44 to 8.33 times higher in patients with DM compared with those without[33]. Poor DM control can lead to numerous complications, comprising raised susceptibility to infection. DM intense susceptibility to tuberculosis by numerous mechanisms, including hyperglycemia and cellular insulinopenia, which have roundabout consequences on macrophages and lymphocytes functions. Nevertheless, tuberculosis can in the short term cause damaged glucose tolerance, a risk factor for developing diabetes. Transient hyperglycemia can be caused by the inflammation that occurs during tuberculosis. Therefore, to establish a new diagnosis of diabetes, glucose levels should be measured again 4 weeks after TB treatment, especially after the patient has developed a fever[33,34].

There was a significant association between IFN-γ positive latent TB and smoking (*OR*=2.7, *CI*=1.2- 6.1, *p*=0.009) (Table 4). It is estimated that 1.3 billion people globally consume tobacco and the majority of them live in developing countries, where TB rates are high. Therefore, the biggest influence of smoking in terms of issues of public health associated with infection is probably the increased risk of developing tuberculosis. A number of meta-analyses and systematic reviews studies have revealed an adverse connection between universal epidemics of TB and smoking. In addition, the exposure to tobacco smoke has been associated with TB infection, active TB, and TB-related mortality[33,35]. The responsibility that cigarette smoke performing on the pathogenesis of TB is connected to ciliary dysfunction, to a reduced immune response, and to defects in the immune response of macrophages, with or without a decrease in the CD4 count, increasing susceptibility to infection with *M. tuberculosis*. Alveolar macrophages bind to the bacillus through complement receptors 1, 3 and 4. Activated lymphocytes release cytokines during the recruitment of macrophages, fibroblasts, and other lymphocytes. The most important cytokine implicated in granuloma formation is TNF-α, which is produced and released by macrophages directly after introduction to *M. tuberculosis* antigens. TNF-α activates macrophages and dendritic cells. In smokers, nicotine, acting through the α7 nicotinic receptor, reduces the production of TNF-α by macrophages, thus preventing its protective effect and favoring the development of tuberculosis[33,35].

In the current study childhood BCG vaccine were protective with significant *OR*=0.4, *CI*=0.2-0.9, *p*=0.03 (Table 4). The most contentious feature of BCG is the changeable efficacy found in different clinical trials, which become visible to depending on geography. Trials performed in the UK have reliably revealed a protective development of 60 to 80%. Obtained results are also supported by a 1994 systematic review that found that the BCG vaccine reduces the risk of TB by about 50%[36]. Differences in efficacy depend on county, due to factors for instance genetic variations in the population, alters in the environment, susceptibility to other bacterial infections, and conditions in the laboratory where the vaccine is grown, including genetic distinctions between the strains being cultured and selection medium growth. Also, a meta-analysis and systematic review conducted in 2014 demonstrated that the BCG vaccine reduced infections by 19–27% and reduced progression to active TB by 71%[37].

Limitation of the study

The prevalence of latent tuberculosis among health workers in Yemen has not been studied sufficiently and encourages follow-up treatment of latent tuberculosis cases in this group. The sample size of health workers was limited in this study, and a future study should be conducted to include all HCWs in Sana'a hospitals.

CONCLUSIONS

Evidence from this study among public hospital employees in Sana'a City, Yemen indicates that latent tuberculosis (IFN-positive) - among HCWs in Sana'a city public hospitals is even relatively common. The positive rate of females latent TB was higher than that of males and there is a higher risk of TB in older employees, unvaccinated childhood BCG, HCWs with diabetes, smoker-HCWs, and HCWs who have been in

contact with active TB cases. Since contact with active TB patients has been identified as a risk factor for LTBI, more effective TB infection control measures are necessary in health care facilities and congregate settings and to create awareness about TB risk factors in hospitals and as an occupational hazard.

ACKNOWLEDGEMENTS

The authors extend their thanks and appreciation to the National Center for Public Health Laboratories in Sana'a, and the Ministry of Health and Population who provided us with the reagents and place for laboratory tests.

AUTHOR'S CONTRIBUTIONS

Al-Khamesy KSA: writing original draft, study conception and design. **Al-Shehari MM:** conceptualization, methodology. **Al-Moyed KAA:** formal analysis, research design. **Atf-allah JYY:** data analysis, interpretation of results. **Al-Shamahy HA:** research design, supervision. **Al-Hadad AM:** data collection, writing, review, and editing. All the authors reviewed the results and approved the final version of the manuscript.

DATA AVAILABILITY

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST

No conflict of interest associated with this work.

REFERENCES

1. Al-kadassy AM, Al-Ashiry AFS, and Al-Shamahy HA. Sero-epidemiological study of hepatitis B, C, HIV and treponema pallidum among blood donors in Hodeida city-Yemen. Universal J Pharm Res 2019; 4(2): 1-8. *https://doi.org/10.22270/ujpr.v4i2.256*
2. AL-Shamahy HA. Prevalence of Hepatitis B surface antigen and Risk factors of HBV infection in a sample of healthy mothers and their infants in Sana'a, Yemen. Ann Saudi Medicine 2000; 20: 464-467. *https://doi.org/10.5144/0256-4947.2000.464*
3. Al-Shamahy HA, Rabbad IA, Al-Hababy A. Hepatitis B virus serum markers among pregnant women in Sana'a, Yemen. Ann Saudi Med 2003; 23:87-89. *https://doi.org/10.5144/0256-4947.2003.87*
4. Al-Shamahy HA, Hanash SH, Rabbad IA, Al-Madhaji NM, Naser SM. Hepatitis B vaccine coverage and the immune response in children under ten years old in Sana'a, Yemen. Sultan Qaboos Univ Med J 2011; 11(1):77-82. Epub 2011.
5. Amran OAA, Al-Shamahy HA, Al Hadad AM, Jaadan BM. Explosion of hepatitis B and C viruses among hemodialysis patients as a result of hemodialysis crisis in Yemen. Universal J Pharm Res 2019; 4(5):1-8. *https://doi.org/10.22270/ujpr.v4i5.311*
6. Hanash SH, Al-Shamahy HA, Bamshmous MHS. Prevalence and genotyping of hepatitis C virus in hemodialysis patients and evaluation of HCV-core antigen test in screening patients for dialysis in Sana'a city, Yemen. Universal J Pharm Res 2019; 4(2): 14-18. *https://doi.org/10.22270/ujpr.v4i2.251*
7. Rabbad IA, Al-Somainy AAM, Al-Shamahy HA, Nasser SM. Prevalence of hepatitis G virus infection among chronic hepatitis B, chronic hepatitis C and HIV patients in Sana'a, Yemen. J Chin Clin Med 2014; 5 (11), 654-658.
8. Alqaisi NANS, AL-Mekhlafi AM, Al-Shamahy HA, *et al*. Toxoplasmosis in pregnant women in Yemen: The immune status and potential risk factors. Universal J Pharm Res 2021; 6(2):1-6. *https://doi.org/10.22270/ujpr.v6i2.570*
9. Abu-Hurub AS, Okbah AA, Al-Dweelah HMA, Al-Shamahy HA, *et al*. Prevalence of visceral leishmaniasis among adults in Sana'a city-Yemen. Universal J Pharm Res 2022; 7 (2):1-6. *https://doi.org/10.22270/ujpr.v7i2.745*
10. Alastot E, Al-Shamahy HA. Prevalence of leptospirosis amongst slaughterhouse workers and butchers in Sana'a city-Yemen. Universal J Pharm Res 2018; 3(2):17-20. *https://doi.org/10.22270/ujpr.v3i2.133*
11. Al-Eryani SA, Alshamahi EYA, Al-Shamahy HA, *et al*. Prevalence and risk factors for trachoma among primary school children in Sana'a city, Yemen. Universal J Pharm Res 2021; 6(4):1-6. *https://doi.org/10.22270/ujpr.v6i4.636*
12. Al-Hrazi RMA, Al-Shamahy HA, Jaadan BM. Determination of rifampicin mono-resistance *Mycobacterium tuberculosis* in the National tuberculosis control programme in Sana'a city-Yemen: A significant phenomenon in war region with high prevalence tubercloisis. Universal J Pharm Res 2019; 4(3):1-6. *https://doi.org/10.22270/ujpr.v4i3.266*
13. Alhasani AH, Al-Akwa AA, Al-Shamahy HA, Al-deen HMS, Al-labani MA. Biofilm formation and antifungal susceptibility of candida isolates from oral cavity after the introduction of fixed orthodontic appliances. Universal J Pharm Res 2020; 5(4):1-6. *https://doi.org/10.22270/ujpr.v5i4.435*
14. WHO. Global Tuberculosis Control 2021. World Health Organization. Retrieved 15 September 2022.
15. World Health Organization. Epidemiology. Global tuberculosis control: Epidemiology, strategy, financing. 2009; ISBN 978-92-4-156380-2.
16. El-Sokkary, RH, Abu-Taleb AM, El-Seifi OS, *et al*. Assessing the prevalence of latent tuberculosis among health care providers in Zagazig city, Egypt, Using Tuberculin Skin Test and Quanti-FERON-TB Gold In-Tube Test. Cent Eur J Public Health 2015; 23, 324–330. *https://doi.org/10.21101/cejph.a4101*
17. Yeon JH, Seong H, Hur H, *et al*. Prevalence and risk factors of latent tuberculosis among Korean healthcare workers using whole-blood interferon-γ release assay. Sci Rep 2018; 8:10113. *https://doi.org/10.1038/s41598-018-28430-w*
18. World Health Organization. The use of tuberculosis interferon-gamma release assays (IGRAs) in low- and middle-income countries. Policy Statement. Geneva, WHO, 2011
19. De Vries G, Sebek MM, Lambregts-van Weezenbeek CS. Healthcare workers with tuberculosis infected during work. Eur Respir J 2006; 28(6):1216-21.
20. 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(9):613-6.
21. Abbas M, AlHamdan N, Fiala FA, *et al*. 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(1):2-10
22. Chen B, Gu H, Wang X , *et al*. Prevalence and determinants of latent tuberculosis infection among frontline tuberculosis healthcare workers in southeastern China: A multilevel analysis by individuals and health facilities. Int J infect Dis 2019; 79:26-33. *https://doi.org/ 10.1016/j.ijid.2018.11.010*
23. Hung WT, Lee SS, Sy CL, *et al*. 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; 48(2):147-52. *https://doi.org/10.1016/j.jmii.2013.07.008*

24. Chumpa N, Kawkitinarong K, Wongpiyabovorn J, *et al*. Prevalence of latent tuberculosis infection among pre-clinical and clinical medical students using QuantiFERON-TB gold plus and tuberculin skin test at a teaching hospital in Thailand: A cross-sectional study. J Infect Public Health 2022; 15(4):400-405. *https://doi.org/10.1016/j.jiph.2022.02.010*
25. Ringshausen FC, Schlösser S, Nienhaus A, Schablon A, Schultze-Werninghaus G, Rohde G. In-hospital contact investigation among health care workers after exposure to smear-negative tuberculosis. J Occup Med Toxicol 2009; 4:11. *https://doi.org/10.1186/1745-6673-4-11*
26. MHP. News letter. Tuberculosis in Yemen 2021.
27. Kumar V, Abbas AK, Fausto N, Mitchell RN. Robbins Basic Pathology (8th ed.). Saunders Elsevier 2007; 516–522. ISBN 978-1-4160-2973-1.
28. Lawn SD, Zumla AI. Tuberculosis. Lancet 2011; 378 (9785): 57–72. *https://doi.org/10.1016/S0140-6736(10)62173-3*
29. *Ahmed N, Hasnain* S. Molecular epidemiology of tuberculosis in India: Moving forward with a systems biology approach. Tuberculosis 2011; 91 (5): 407–3. *https://doi.org/10.1016/j.tube.2011.03.006*
30. World Health Organization. Tuberculosis. Fact sheet N°104, March, 2010.
31. CDC. Core Curriculum on Tuberculosis: What the Clinician Should Know" (5th ed.). 2011. Centers for Disease Control and Prevention (CDC), Division of Tuberculosis Elimination. 2011:24.
32. Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: Emission of respirable pathogens. J Occup Environ Hyg 2005; 2 (3): 143–54.
33. Silva DR, Muñoz-Torrico M, Duarte R, *et al*. Risk factors for tuberculosis: diabetes, smoking, alcohol use, and the use of other drugs. J Bras Pneumol 2018; 44(2):145-152. *https://doi.org/10.1590/s1806-37562017000000443*
34. Workneh MH, Bjune GA, Yimer SA. Prevalence and associated factors of tuberculosis and diabetes mellitus comorbidity A systematic review. PLoS One 2017;12(4):e0175925. *https://doi.org/10.1371/journal.pone.0175925*
35. Bates MN, Khalakdina A, Pai M, Chang L, Lessa F, Smith KR. The risk of tuberculosis from exposure to tobacco smoke a systematic review and meta-analysis. Arch Intern Med 2007;167(4):335–342. *https://doi.org/10.1001/archinte.167.4.335*
36. Colditz GA, Brewer TF, Berkey CS, Wilson ME, Burdick E, Fineberg HV, Mosteller F. Efficacy of BCG vaccine in the prevention of tuberculosis. Meta-analysis of the published literature. JAMA 1994; 271 (9): 698–702. *https://doi.org/10.1001/jama.1994.03510330076038*
37. Roy A, Eisenhut M, Harris RJ, Rodrigues LC, Sridhar S, Habermann S, *et al*. Effect of BCG vaccination against *Mycobacterium tuberculosis* infection in children: Systematic review and meta-analysis. BMJ 2014; 349: g4643. *https://doi.org/10.1136/bmj.g4643*