Int.J.Curr.Microbiol.App.Sci (2017) *6*(6): 2360-2368

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 6 Number 6 (2017) pp. 2360-2368**
Journal homepage: http://www.ijcmas.com

Original Research Article https://doi.org/10.20546/ijcmas.2017.606.280

Interferon Gamma Release Assay and Tuberculin Skin Test in the Diagnosis of Latent Tuberculosis among Health Care Workers – A Comparative Study

Reshmi Gopalakrishnan[1*] and G.S. Vijay Kumar[2]

[1]Department of Microbiology, Malabar Medical College Hospital and Research Centre, Calicut, Kerala, India
[2]Kodagu Institute of Medical Science, Madikeri, Karnataka, India
**Corresponding author*

Keywords

Latent tuberculosis infection, Healthcare workers, Interferon gamma release assay.

Article Info

Accepted:
26 May 2017
Available Online:
10 June 2017

A B S T R A C T

Health Care Workers (HCWs) are vulnerable to tuberculosis exposure. Non availability of a reliable test has resulted in underestimation of latent tuberculosis infection (LTBI) among HCWs. The aim is to detect the rate of LTBI among nursing and medical students, Compare Interferon Gamma Release Assay (IGRA) and Tuberculin Skin Test (TST), Detect conversions and reversions. Total of 100 (83 nursing and 17 medical) students were included in the study. QuantiFERON®-TB Gold In-Tube test (QFT) and TST were carried out for the participants and results at various thresholds were noted. The prevalence of LTBI was found to be 16 - 26% among the students using TST and 7 – 8% using QFT. TST The conversion was 2.5% for TST and 2.5 % for QFT when thresholds were kept low. The conversion was 7.5% for TST and 2.5 % for QFT, with stringent threshold. With low thresholds, 25% students had reversions and with stringent threshold values 20% had reversion. No single test is reliable for detecting LTBI. Routine TST and IGRA of HCWs with patient contact should be part of the screening program with a major effort to institute treatment for LTBI.

Introduction

Tuberculosis (TB) infects an estimated of one-third of the world's population, and about 9 million cases occur every year. 90% of the infected people develop LTBI. Though the individuals are not infectious, they risk progression to active TB at a later stage (Mack *et al*., 2009). About 3 to 5% of Latent tuberculosis (LTB) develops into active TB in first year and about 5 to 15% later.

People with LTBI can serve as potential reservoirs for future acute infections if the host immune system is compromised. A person with LTBI progressing to active TB can be reduced by 90% with proper treatment. Screening of HCWs for TB is an important component of infection control program. The risk of transmission of *M. tuberculosis* from patients to HCWs is a neglected problem in many low and middle-income countries (Joshi *et al*., 2006). LTBI is difficult to diagnose because MTB is difficult to detect by smear study and needs alternative methods like TST and the latest method of Interferon Gamma Release Assays (IGRAs).

Materials and Methods

A descriptive study was conducted in a tertiary care hospital. A total of 100 health care students participated in the study. A written consent was taken from all the participants. The participants included 83 first year nursing students and 17 second year medical students. Average age of the subjects ranged from 17 to 19 years. Students with past history of active tuberculosis, those receiving anti tuberculosis medications were excluded from the study. Clinical history, physical examination findings, BCG scar appearance were recorded for each participant. Data such as exposure with an index case was also recorded.

Blood required for the QFT assay were drawn in the QFT tubes. TST was performed by using the Mantoux technique, by injecting 0.1ml of 5TU of PPD on the volar aspect of forearm. TST results were read after 48 hours. The transverse diameter of the in duration was recorded in millimetres after 48 hours. A cut-off of $\geq$ 15mm in duration was considered strongly positive, in duration of 10 to 14mm was considered weakly positive and in duration <10mm was considered negative for the study.

IGRA test was carried out using commercially available kit (QuantiFERON®-TB Gold In-Tube test (Cellestis, Australia)) and manufacturer's instructions were followed. QuantiFERON®-TB Gold IT Analysis Software was used to analyse raw data and calculate results. As recommended by the manufacturer, a positive QFT was defined as IFN – γ greater than or equal to 0.35 IU/ml.

All students underwent AFB smear study, culture analysis for sputum samples and chest radiograph to rule out active tuberculosis.

TST and IGRA tests were repeated after 18 months to look for conversions and reversions.

Statistical analyses

Sensitivity, specificity, confidence interval were calculated for both TST and IGRA tests using SPSS Version 16 software. MediCalc software was used for diagnostic test evaluation. Association between TST and QFT changes were also evaluated at various thresholds, with TST and QFT treated as continuous measures.

Results and Discussion

Base line testing

100 students participated for baseline testing. Among the 100 participants, 83 (83%) were nursing students and 17 (17%) were medical students. There were 84 (84%) female and 16 (16%) male participants. Baseline testing was done for all the 100 participants by TST and QFT. 27 (27%) students were positive by either TST or QFT; when TST cut-off was ≥ 10mm and IGRA cut-off was ≥ 0.35 IU/ml. 26 (26%) of the total 100 students had a TST of ≥ 10mm and 16 (16%) had a TST of ≥ 15mm. 8 (8%) had IGRA ≥ 0.35 IU/ml and 7 (7%) had IGRA ≥ 0.70 IU/ml.

At baseline, when less stringent thresholds were used i.e., TST ≥ 10mm and IGRA ≥ 0.35 IU/ml, 7 (7%) students were concordant positive by both TST and IGRA. 73 (73%) students were concordant negative by both the tests. 20 (20%) out of 100 participants were discordant; 19 were TST positive and IGRA negative and 1 student was TST negative and IGRA positive (Table 1).

When the TST and IGRA thresholds were increased to ≥ 15mm and ≥ 0.70 IU/ml respectively, 5 (5%) students were concordant

positive and 83 (83%) students were concordant negative by both TST and IGRA. 12 (12%) students were discordant; 10 were TST positive and IGRA negative and 2 students were TST negative and IGRA positive (Table 2).

Results were also evaluated for threshold of TST ≥ 15mm and IGRA ≥ 0.35 IU/ml. It was found that 6 students (6%) were concordant positive and 83 (83%) were concordant negative. 11 (11%) had discordant results of which 2 (2%) were TST negative and IGRA positive and 9 (9%) were TST positive and IGRA negative (Table 3).

The concordance between TST and IGRA was high (k = 0.585) at low threshold when compared to concordance at high threshold (k = 0.052). It was observed that when less stringent thresholds were used for both the tests, there was greater discordance between TST and IGRA.

During baseline testing, when less stringent thresholds were used for both TST and QFT, the sensitivity was 87.50% (95% CI = 47.38 – 97.93%) and specificity was 79.35% (95% CI = 69.64 – 87.08%). When stringent thresholds were used for both TST and QFT, the sensitivity was 71.43% (95% CI = 29.27 - 95.48%) and specificity was 88.17% (95% CI = 79.82 – 93.94%). It was also found that with TST ≥ 15mm and IGRA ≥ 0.35 IU/ml, the sensitivity was 37% (95% CI = 15.29 – 64.23%) and specificity was 97% (95% CI = 91.64 – 99.64%) (Table 4).

Serial testing

Serial testing was carried out in 40 nursing students after 18 months by both TST and IGRA to look for conversions and reversions. Out of the 40 students, 37 (92.5%) were female students and 3 (7.5%) were male students.

TST conversion was defined as baseline TST < 10mm and follow-up TST ≥ 10mm. QFT conversion was defined as baseline IGRA ≤ 0.35 IU/ml and follow-up IGRA ≥ 0.35 IU/ml. TST reversion was defined as baseline TST ≥ 10mm and follow-up TST < 10mm. QFT reversion was defined as baseline IGRA of ≥ 0.35 IU/ml and follow-up IGRA of ≤ 0.35 IU/ml.

Conversion and reversion were also analyzed by increasing the TST and IGRA threshold. TST conversion was defined as baseline TST < 15mm and follow-up TST ≥ 15mm; and baseline IGRA ≤ 0.70 IU/ml and follow-up IGRA ≥ 0.70 IU/ml. TST reversion was defined as baseline TST ≥ 15mm and follow-up TST < 15mm. QFT reversion was defined as baseline IGRA of ≥ 0.70 IU/ml and follow-up IGRA of ≤ 0.70 IU/ml.

Out of the 40 nursing students who participated for serial testing, 9 (22.5%) had a TST of ≥ 10mm and 7 (17.5%) had a TST of ≥ 15mm. 4 (20%) had IGRA ≥ 0.35 IU/ml and 3 (7.5%) had IGRA ≥ 0.70 IU/ml.

At serial testing, when less stringent thresholds were used i.e., TST ≥ 10mm and IGRA ≥ 0.35 IU/ml, 4 (10%) students were concordant positive by both TST and IGRA. 31 (77.5%) students were concordant negative by both the tests. 5 (12.5%) out of 40 participants were discordant; 5 were TST positive and IGRA negative (Table 5).

When the TST and IGRA thresholds were increased to ≥ 15mm and ≥ 0.70 IU/ml respectively, 3 (7.5%) students were concordant positive and 33 (82.5%) students were concordant negative by both TST and IGRA. 4 (10%) students were discordant; 4 were TST positive and IGRA negative (Table 6). With stringent thresholds it was observed that there was reduced discordance (10%) between TST and IGRA when compared to

discordance with lesser stringent thresholds (12.5%).

With less stringent thresholds, 2 (5%) students were noticed to have conversions. 1 (2.5%) had TST conversion and 1 (2.5%) had QFT conversion. 10 (25%) students had reversions. 8 (20%) students had TST reversion and 2 (5%) had QFT reversion.

When the thresholds for TST and IGRA were raised, 4 (10%) students had conversions. 3 (7.5%) students had TST conversions and 1 (2.5%) had QFT conversion. 8 (20%) had reversions. 6 (15%) students had TST reversion and 2 (5%) had QFT reversion.

During serial testing in 40 participants, when less stringent thresholds were used for both TST and QFT, the sensitivity was 100 % (95% CI = 40.23 – 100%) and specificity was 86.11% (95% CI = 70.49 – 95.28%). When stringent thresholds were used for both TST and QFT, the sensitivity was 100% (95% CI = 30.24 – 100%) and specificity was 89.19% (95% CI = 74.56 – 96.91%). With TST ≥ 15mm and IGRA ≥ 0.35 IU/ml, the sensitivity was 100% (95% CI = 40.23 – 100%) and specificity was 91.67% (95% CI = 77.51 – 98.15%) (Table 7).

During baseline testing, sensitivity was higher (87.5%) when less stringent thresholds were used for both TST and IGRA (i.e., TST ≥ 10mm and IGRA ≥ 0.35 IU/ml); and specificity was higher (97 %) with TST cut-off ≥ 15mm and IGRA cut-off ≥ 0.35 IU/ml. With TST threshold ≥ 15mm and IGRA threshold ≥ 0.70 IU/ml sensitivity was 71.43 % and specificity was 88.17 %; and agreement was higher with higher thresholds.

The use of less stringent thresholds for TST or QFT could potentially result in misclassification of nonspecific variations as new infections. Therefore, a TST value of ≥ 15mm and IGRA value of ≥ 0.70 IU/ml might be more specific for detecting new infections.

During serial testing, sensitivity was 100 % with both less stringent and stringent thresholds; specificity was higher (91.67 %) with TST cut-off ≥ 15mm and IGRA cut-off ≥ 0.35 IU/ml. So, TST threshold of ≥ 15mm and IGRA threshold ≥ 0.35 IU/ml might be more specific for detecting conversions and reversions.

Over all, the results showed that conversions, reversions and nonspecific variations occur with serial IGRA testing, as they do with TST. TST and QFT results are threshold dependent.

An estimated 40% of the Indian population is infected and the annual risk of infection is 1.5% (Devasahayam *et al*., 2010; Chadha, 2003). The risk of transmission of MTB between patients and HCWs is well recognized. HCWs in India are constantly exposed to infectious TB patients (Devasahayam *et al*., 2010).

With the emergence of MDR-TB and XDR-TB there has been a renewed interest in TB infection control, especially in resource limited settings with high TB and HIV prevalence (Basu *et al*., 2007; 2009). Nosocomial transmission appears to play an important role in amplifying XDR – TB transmission (Veriko *et al*., 2008).

Several studies have shown a positive association between TST response and subsequent risk of active TB, and randomizes trials have shown that treatment of LTBI, diagnosed using TST, reduces the risk of active TB by 60 % to 90 % (American Thoracic Society, 2000). The TST has limitations with respect to accuracy and reliability (Huebner *et al*., 1993). Advances in genomics and immunology have led to a

promising alternative, the in vitro IFN-γ assay (Pai *et al*., 2004; Andersen *et al*., 2000; Lalvani, 2003), based on the concept that T-cells of infected individuals release IFN-γ.

Recent data from India suggests that nearly 40% of HCWs may have LTBI, as measured by positivity in either TST or IGRA, and increasing age and years in the health profession were significant risk factors for positivity. The ARTI among medical and nursing trainees has been estimated to be approximately 5% (Pai *et al*., 2006), which is substantially higher than the ARTI in the general population which is estimated at 1.5% (Chadha *et al*., 2005).

In this study, during baseline testing, 27% were positive either by TST or IGRA. When the TST and IGRA thresholds were kept low, 26% were TST positive and 8% were QFT positive; 7% were concordant positive and 73% were concordant negative. 20% were discordant i.e., 19 were TST positive and IGRA negative and 1 student was TST negative and IGRA positive. When thresholds were stringent, 16% were TST positive and 7% were QFT positive.

The prevalence of LTBI was found to range from 16 -26% among the nursing and medical students using TST; and 7 – 8% using QFT. The prevalence of approximately 26% may an underestimate because of the small sample size.

With stringent thresholds, 5 (5%) students were concordant positive and 83% students were concordant negative. 12% were discordant i.e., 10 were TST positive and IGRA negative and 2 students were TST negative and IGRA positive. The concordance between TST and IGRA was high (k = 0.585) at low threshold when compared to concordance at high threshold (k = 0.052). Although TST and IGRA use different antigen combination, it was noticed that these tests had high level of agreement at low threshold values. This was comparable to the study conducted by Pai *et al*., (2006) in HCWs in rural India.

During baseline testing, when less stringent thresholds were used for both TST and QFT, the sensitivity was 87.50% (95% CI = 47.38 – 97.93%) and specificity was 79.35% (95% CI = 69.64 – 87.08%). When stringent thresholds were used for both tests, the sensitivity was 71.43% (95% CI = 29.27 - 95.48%) and specificity was 88.17% (95% CI = 79.82 – 93.94%). It was also found that with TST $\geq$ 15mm and IGRA $\geq$ 0.35 IU/ml, the sensitivity was 37% (95% CI = 15.29 – 64.23%) and specificity was 97% (95% CI = 91.64 – 99.64%). This showed that during baseline testing stringent thresholds should be used for detection of LTBI because the use of less stringent thresholds could potentially result in false-positives.

Serial testing was done 18 months after the base-line testing to look for conversions and reversions. 40 nursing students, who had initially undergone baseline testing, participated for the serial testing. With less stringent thresholds, 2 (5%) students were noticed to have conversions. 1 (2.5%) had TST conversion and 1 (2.5%) had QFT conversion. 10 (25%) students had reversions. 8 (20%) students had TST reversion and 2 (5%) had QFT reversion. When the thresholds for TST and IGRA were raised, 4 (10%) students had conversions. 3 (7.5%) students had TST conversions and 1 (2.5%) had QFT conversion. 8 (20%) students had reversions. 6 (15%) students had TST reversion and 2 (5%) had QFT reversion.

It was noticed that some students who were positive by either TST/IGRA during the baseline testing reverted to negative during serial testing without any treatment, suggesting transient, non-progressive LTBI.

Table.1 Results obtained at low threshold value during baseline testing

TST and IGRA Threshold Values	Nursing Students (N = 83)	Medical Students (N = 17)	Total (N =100)
TST ≥ 10mm and IGRA ≥ 0.35 IU/ml	05	02	07 (7%)
TST < 10mm and IGRA ≥ 0.35 IU/ml	01	0	01 (1%)
TST ≥ 10mm and IGRA < 0.35 IU/ml	16	03	19 (19%)
TST < 10mm and IGRA < 0.35 IU/ml	61	12	73 (73%)

Table.2 Results obtained at stringent threshold values during baseline testing

TST and IGRA Threshold Values	Nursing Students (N = 83)	Medical Students (N = 17)	Total (N = 100)
TST ≥ 15mm and IGRA ≥ 0.70 IU/ml	04	01	05 (5%)
TST < 15mm and IGRA ≥ 0.70 IU/ml	01	01	02 (2%)
TST ≥ 15mm and IGRA < 0.70 IU/ml	10	0	10 (10%)
TST < 15mm and IGRA < 0.70 IU/ml	68	15	83 (83%)

Table.3 Results obtained at threshold of 15mm for TST and 0.35 IU/Ml for IGRA

TST and IGRA Threshold Values	Nursing Students (N = 83)	Medical Students (N = 17)	Total (N = 100)
TST ≥ 15mm and IGRA ≥ 0.35 IU/ml	05	01	06 (6%)
TST < 15mm and IGRA ≥ 0.35 IU/ml	01	01	02 (6%)
TST ≥ 15mm and IGRA < 0.35 IU/ml	09	0	09 (9%)
TST < 15mm and IGRA < 0.35 IU/ml	68	15	83 (83%)

Table.4 Sensitivity, specificity and 95% CI for various threshold value during baseline testing

Threshold Value	Sensitivity and Specificity	95% CI
TST ≥ 10mm and IGRA ≥ 0.35 IU/ml	Sensitivity = 87.5% Specificity = 79.35%	47.38 – 97.93% 47.38 – 97.93%
TST ≥ 15mm and IGRA ≥ 0.35 IU/ml	Sensitivity = 37 % Specificity = 97 %	15.29 – 64.23% 91.64 – 99.64%
TST ≥ 15mm and IGRA ≥ 0.70 IU/ml	Sensitivity = 71.43 % Specificity = 88.17%	29.27 - 95.48% 79.82 – 93.94%

Table.5 Results obtained at low threshold values during serial testing

TST and IGRA Threshold Values	Nursing Students (N = 40)
TST ≥ 10mm and IGRA ≥ 0.35 IU/ml	04 (10%)
TST < 10mm and IGRA ≥ 0.35 IU/ml	0 (0%)
TST ≥ 10mm and IGRA < 0.35 IU/ml	05 (12.5%)
TST < 10mm and IGRA < 0.35 IU/ml	31 (77.5%)

Table.6 Results obtained at stringent threshold values during serial testing

TST and IGRA Threshold Values	Nursing Students (N = 40)
TST ≥ 15mm and IGRA ≥ 0.70 IU/ml	03 (7.5%)
TST < 15mm and IGRA ≥ 0.70 IU/ml	0 (0%)
TST ≥ 15mm and IGRA < 0.70 IU/ml	04 (10%)
TST < 15mm and IGRA < 0.70 IU/ml	33 (82.5%)

Table.7 Sensitivity, specificity and 95% CI for various threshold value during serial testing

Threshold Value	Sensitivity and Specificity	95% CI
TST ≥ 10mm and IGRA ≥ 0.35 IU/ml	Sensitivity = 100% Specificity = 86.11%	40.23 – 100% 70.49 – 95.28%
TST ≥ 15mm and IGRA ≥ 0.35 IU/ml	Sensitivity = 100 % Specificity = 91.67 %	40.23 – 100% 77.51 – 98.15%
TST ≥ 15mm and IGRA ≥ 0.70 IU/ml	Sensitivity = 100 % Specificity = 89.19%	30.24 – 100% 74.56 – 96.91%

With low threshold values, 25% students had reversions. 20% had TST reversion and 5% had QFT reversion. With stringent threshold values, 20% had reversion. 15% students had TST reversion and 5% had QFT reversion. Pai *et al*., (2006) reported QFT reversion of 55% with low threshold value and 50% with high threshold value.

During serial testing, when less stringent thresholds were used for both TST and QFT, the sensitivity was 100 % (95% CI = 40.23 – 100%) and specificity was 86.11%. With stringent thresholds, the sensitivity was 100% and specificity was 89.19%. Sensitivity and specificity were also calculated for cut-off values of TST ≥ 15mm and IGRA ≥ 0.35 IU/ml, and the sensitivity was 100% and specificity was 91.67%. This showed that during serial testing, for detection of conversions and reversions, threshold of TST ≥ 15mm and IGRA ≥ 0.35 IU/ml had greater sensitivity and specificity.

Screening of HCWs for TB is an important component of infection control programs (Menzies *et al*., 1995; Blumberg, 2004; Centers for Disease Control and Prevention, 2005; World Health Organization, 1999). Routine TST and IGRA of HCWs with patient contact should be part of the screening program and should be conducted on an

annual basis, with a major effort to institute treatment for LTBI. IGRAs are more specific than TST, and have characteristics suited for serial testing (Pai *et al*., 2006). To fully evaluate the use of IFN-γ assays, long-term cohort studies to determine the association between positive IFN-γ assay results and the subsequent risk of active tuberculosis are required in diverse settings (Pai *et al*., 2004). If such studies demonstrate a strong consistent association, IFN-γ assay might have the potential to replace TST.

There is a greater need of improved infection control programme and providing necessary treatment facilities and support to the HCWs who are the occupational risk group. Combination of TST and IFN-γ assay serially done with a gap of 12 to 18 months is more reliable than a single test. An intensive and committed campaign globally against TB is the only solution to reach the WHO goal of 1 TB patient per 100,000 population by the year 2050. Research and development in the form of providing the latest diagnostic equipments to medical colleges helps in maintaining a national data with regard to TBI and LTBI in HCWs.

Acknowledgement

This work was supported by nursing and medical students. I offer my sincere thanks to all the students who participated in the study.

References

American Thoracic Society. 2000. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am. J. Respir. Crit. Care Med.*, 161: S 221- S 247.

Andersen, P., Munk, M.E., Pollock, J.M., Doherty, T.M. 2000. Specific immune-based diagnosis of tuberculosis. *Lancet*, 356: 1099 - 1104.

Basu, S., Andrews, J.R., Poolman, E.M., Gandhi, N.R., Shah, N.S., *et al*. 2007. Prevention of nosocomial transmission of extensively drug-resistant tuberculosis in rural South African district hospitals: an epidemiological modelling study. *Lancet*, 370: 1500–1507.

Basu, S., Friedland, G.H., Medlock, J., Andrews, J.R., Shah, N.S., *et al*. 2009. Averting epidemics of extensively drug-resistant tuberculosis. *Proc. Natl. Acad. Sci. U S A.*, 106: 7672–7677.

Blumberg, H. 2004. *M. tuberculosis* infection control in health care settings. In: Lautenbach E, Woeltje K. Practical handbook for health- care epidemiologists. Thorofare, NJ: Slack Incorporated, 259–273.

Centers for Disease Control and Prevention. Guidelines for preventing the transmission of Mycobacterium tuberculosis in health-care settings, 2005. *MMWR*, 54: 1–141.

Chadha, V.K. 2003. Epidemiological situation of tuberculosis in India. *J. Indian Med. Assoc.*, 101: 144 - 147.

Chadha, V.K., Kumar, P., Jagannatha, P.S., Vaidyanathan, P.S., Unnikrishnan, K.P. 2005. Average annual risk of tuberculous infection in India. *Int. J. Tuberc. Lung Dis.*, 9: 116–118.

Devasahayam, J., Christopher, Peter Daley, Lois Armstrong, Prince James, Richa Gupta, Beulah Premkumar, *et al*. 2010. Tuberculosis Infection among Young Nursing Trainees in South India. *PLoS One*, 5(4): e10408

Huebner, R.E., Schein, M.F., Bass, J.B. Jr. 1993. The tuberculin skin test. *Clin. Infect. Dis.*, 17: 968 - 975.

Joshi, R., Reingold, A.L., Menzies, D., Pai. 2006. *M. tuberculosis* among health-care workers in low- and middle-

income countries: a systematic review. *PLoS Med*., 3(12): 2376 – 2391.

Khatri, G.R., Frieden, T.R. 2002. Controlling tuberculosis in India. *N. Engl. J. Med.*, 347: 1420 – 1425

Lalvani, A. 2003. Spotting latent infection: the path to better tuberculosis control. *Thorax*, 58: 916 - 918.

Mack, U., Milgori, G.B., Sester, M., Rieder, H.L., *et al*. 2009. LTBI: latent tuberculosis infection or lasting immune response to *M. tuberculosis* A TBNET consensus statement. *Eur. Respir. J.*, 33(5): 956 – 973.

Menzies, D., Fanning, A., Yuan, L., Fitzgerald.995. *M. tuberculosis* among health care workers. *N. Engl. J. Med.*, 332: 92–98.

Pai, M., Riley, L.W., Colford, J.M., Jr. 2004. Interferon-γ assays in the immuno-diagnosis of tuberculosis: a systematic review. *Lancet Infect. Dis.*, 4: 761–776.

Veriko Mirtskhulava, Russell Kempker, Katherine, L., Shields, Michael, K. Leonard, Tengiz Tsertsvadze, Carlos del Rio *et al*. 2008. Prevalence and Risk Factors for Latent Tuberculosis Infection among Health-care Workers in the Country of Georgia. *Int. J. Tuberc. Lung Dis.*, 12(5): 513–519.

Pai, M., Gokhale, K., Joshi, R., Dogra, S., Kalantri, S., *et al*. 2005. ycobacterium tuberculosis infection in health care workers in rural India: comparison of a whole-blood interferon gamma assay with tuberculin skin testing. *JAMA*, 93: 2746–2755.

Pai, M., Joshi, R., Dogra, S., Mendiratta, D.K., Narang, P., *et al*. 2006. Serial testing of health care workers for tuberculosis using interferon-γ assay. *Am. J. Respir. Crit. Care Med.*, 174: 349–355.

Pai, M., Kalantri, S., Dheda, K. 2006. New tools and emerging technologies for the diagnosis of tuberculosis: Part 1. Latent tuberculosis. *Expert Rev. Mol. Diagn.*, 6: 413–422.

World Health Organization. 1999. Guidelines for the prevention of tuberculosis in health care facilities in resource-limited settings. Geneva: World Health Organization.

How to cite this article:

Reshmi Gopalakrishnan and Vijay Kumar, G.S. 2017. Interferon Gamma Release Assay and Tuberculin Skin Test in the Diagnosis of Latent Tuberculosis among Health Care Workers – A Comparative Study. *Int.J.Curr.Microbiol.App.Sci.* 6(6): 2360-2368.
doi: https://doi.org/10.20546/ijcmas.2017.606.280