Review Article

Tuberculosis Risk in Health Care Workers

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ABSTRACT

Risk to health care workers (HCW) is of paramount importance in the global fight against tuberculosis (TB). There is mounting evidence that they are at increased risk of contracting TB infection as well as developing the disease. This occupational risk is at alarming proportions in the low- and middle-income countries (LMIC), because of increased exposure and lack of preventive measures. Although tuberculin skin test has been used for a long time to detect latent TB infection (LTBI), it has significant drawbacks. Interferon-gamma release assays arrived with a lot of promise, but the expected benefit of more specific diagnosis has not yet been proved. The treatment of LTBI is an area, which is not well studied in LMIC. Effective environmental and personal protective measures along with education to the patients and the HCW needs to be carried out expeditiously, to reduce the occupational risk of TB. **[Indian J Chest Dis Allied Sci 2013;55:149-154]**

Key words: Tuberculosis, Nosocomial transmission, Health care workers.

GENERAL AND HISTORICAL ASPECTS

Tuberculosis (TB) is one of the worst killers in the world, from the time immemorial. It is communicable by the inhalation of airborne particles. When patients with TB visit health care facilities (HCF), they are likely to transmit the disease to the health care workers (HCW). This aspect of occupational risk is largely understudied and preventive measures are frequently not in place. This problem is more in the low- to middle-income countries (LMIC), due to increased prevalence of TB and lack of effective control programmes.

With increasing incidence of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) this problem has been further compounded, with the risk of HCW contracting more severe forms of the disease, which are difficult or sometimes impossible to treat successfully. These patients with MDR-TB and XDR-TB have relatively higher morbidity and visit the HCF more frequently. We had reported the first health care worker death in India due to XDR-TB.[1] The subject was a nurse in the respiratory ward and had received the best medical and surgical treatments possible, and yet succumbed to the illness.[1] The grim reality is that we live and practice medicine in an era of potentially incurable TB, where palliative and end-of-life care are being considered.[2] It is necessary that drastic steps are taken to protect the health of HCW to win the battle against TB.[3]

Another aspect of transmission is that which occurs from HCW to patients. Centers for Disease Control and Prevention (CDC) recently reported the transmission of *Mycobacterium tuberculosis* from a health care worker to patients in New York City.[4]

DATA FROM LOW- AND MIDDLE-INCOME COUNTRIES

Approximately one-third of the world population harbors latent TB infection (LTBI), based on tuberculin skin testing (TST).[5] In a systematic review[6] assessing the incidence of LTBI among HCW in LMIC, based on 51 studies, the estimated annual risk of LTBI ranged from 0.5% to 14.3% and the annual risk of TB disease ranged from 69 to 5,780 per 100,000.[6] Attributable risk for TB disease in HCW, compared to the risk in the general population ranged from 25 to 5,361 per 100,000 per year.[6] India alone accounts for an estimated one quarter (26%) of all TB cases worldwide with China and India combined accounting for 38%.[5] HCF in LMIC had a median of 36 HCW per 100 TB patients treated at the facility, which is much lower than facilities in high-income countries, which have a median of 6,450 HCW per 100 TB patients.[6,7] Thus, HCWs in low-income countries are likely to have significantly higher TB exposure.

Some studies[8,9] have established the grim reality of nosocomial transmission of TB in India. The annual risk of TB infection is about 5% per year in HCW in

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comparison to the national average of 1.5%.[10-12] The excess of 3.5% can be attributed to nosocomial transmission.[8] In a prospective study[13] conducted in our institution among nursing students, the annual risk of TB infection as measured by TST conversion was 7.8%, which was 5-folds higher that the national average. In the same cohort, using interferon-gamma release assays (IGRAs), the annual risk of TB infection was even higher (11%).[14]

In a study from North India,[15] TB developed in 2% of the resident doctors already working in the hospitals, giving an incidence of 11.2 new cases per 1000 person-years of exposure. The estimated incidence of TB among resident doctors was 10-fold higher than the incidence for the country. Extra-pulmonary TB was more common and accounted for two-thirds of the cases.

In a retrospective review of HCW who underwent anti-TB treatment in a referral hospital in southern India,[16] 125 HCW who had active TB were identified between 1992 and 2001. The annual incidence of pulmonary TB was 0.35 to 1.80 per 1000 HCW. The annual incidence of extra-pulmonary TB was 0.34 to 1.57 per 1000 HCW.

Molecular epidemiological study[17] at a TB hospital in Delhi by deoxyribonucleic acid fingerprinting in mycobacterial isolates from patients showed that nosocomial transmission of mycobacteria was likely to have occurred.[17] The predominance of mostly pleural disease among HCW indicates that the disease was from newly acquired primary infection, rather than reactivation of previous LTBI. Molecular epidemiological studies have shown that pleural TB is associated with the highest fingerprint-clustering rate of all forms of TB, suggesting that pleural TB is an early manifestation of recent infection.[18,8]

RISK GROUPS AMONG HEALTH CARE WORKERS

It is logical to assume that the risk of LTBI and TB disease are proportionate to the level of patient contact and exposure to contact with infectious TB cases. The prevalence of LTBI in nurses has been found to be 1.3% to 35.6% times higher than other HCW.[19,20] Higher level of clinical training, nursing occupation and recent exposure to TB have been found to be the independent risk factors for TST conversion.[21,22]

There is a considerable heterogeneity regarding the risk of developing TB disease. The risk as compared with general population is highest among workers in TB in-patient facilities, laboratories, general medicine wards, and emergency rooms.[6] Workers in out-patient medical facilities have an intermediate risk, while workers in surgery, obstetrics, administration and operating theaters have the lowest risk.[6]

Levels of training and age were associated with the prevalence of LTBI in most studies. Studies from Brazil[23,24] have proved that the prevalence of LTBI in senior years was two to three times higher compared with junior years. A study from India[11] has shown a 4-fold higher prevalence in medical students who were more than 23 years of age than in medical students aged 18-20 years, which could be attributed to additional 3-5 years spent in training, and thus patient contact.[11] This could also reflect the increasing patient contact in the clinical years; compared to the initial years of training as pre-clinical students, where patient contact is minimal.

Each additional year of occupation increased the prevalence of LTBI in HCW.[25,20] The risk increased by 1.5 [95% confidence intervals (CI) 1.0 to 2.2][26] to 2.4 (95% CI 1.1 to 5.0) times with employment duration of more than one year.[20] There was a 3-fold higher prevalence of LTBI with more than 10 years of employment.[11] In a prospective study[27] conducted in our institution among nursing students, TST positivity was strongly associated with time spent in health care after adjusting for age at entry into healthcare. In our institution, HCW with frequent patient contact and those with a body mass index (BMI; kg/m^2) less than 19 were at increased risk of acquiring active TB.[28] Nosocomial transmission of TB was prominent in locations, such as medical wards and microbiology laboratories.[28]

Procedures like sputum collection, sputum induction, nebulisation, sputum processing, bronchoscopy, endotracheal intubation are deemed high risk for exposure to bacteria laden aerosols. In our cohort, involvement with sputum collection and caring for pulmonary TB patients were both associated with TST conversions among nursing students.[13]

SCREENING OF STAFF

Given the increased risk, there is no doubt that there needs to be effective screening of HCW for LTBI and active TB. However, there is no consensus on the "gold standard" test for diagnosing LTBI. Conversion in test regardless of the testing method used is usually considered as presumptive evidence of new *Mycobacterium tuberculosis* infection, which is associated with an increased risk for progression to TB disease. The TST has been in use for a very long time. TST conversion is defined as an increase in the size of the induration of 10mm or more during a 2-year period in a HCW with a documented negative (<10mm) baseline two-step TST result.[29] But it has many drawbacks, including low specificity due to cross-reactivity to environmental mycobacteria and previous vaccination with bacille Calmette-Guerin

(BCG). Also there is controversy regarding the optimum dose of the reagent and the cut-off value for positive test in various risk groups. The test itself is highly operator dependent. There is a potential booster effect by repeated testing.

IGRAs were introduced about a decade ago with great enthusiasm to overcome the problems associated with TST. IGRAs measure interferon-γ released by sensitised T-cells after stimulation with *Mycobacterium tuberculosis* antigens. IGRAs have been found to have higher specificity and positive predictive value in comparison to TST in high income and low TB burden diseases.[30-32] Serial testing with IGRAs has the advantage of avoiding subjective measurement and eliminates multiple visits. According to Centers for Disease Control and Prevention (CDC) guidelines published in the year 2005,[33] IGRAs were expected to replace TST in all instances, where TSTs are currently used, including serial testing.[33]

However, the initial enthusiasm has died down. The recent 2010 CDC guidelines[34] suggested more caution and called for more research regarding serial testing with IGRAs. The measurement values of IGRAs are highly dynamic, with changes over time from biologic variability and an inherent tendency for conversions (negative to positive test) and reversions (positive to negative test).[35,36] This has been our experience also, when we evaluated serial IGRAs responses over a 2-year period in nursing students at a tertiary care hospital in South India.[37] We found IGRAs results to be negatively associated with successive visits suggesting responses may decrease over time within individuals independent of exposure, although this effect was small. We also identified a small random effect for student (variance=1.76), after accounting for known LTBI risk factors and TB exposure, suggesting that there may be unknown factors contributing to differences in baseline interferon-gamma response across students. Salient differences between TST and IGRAs are given in table 1.

Once LTBI is suspected, a general screening needs to be done to rule out active TB disease. There is no consensus regarding optimal drugs used and the duration of treatment of LTBI in LMIC.[38]

INFECTION CONTROL METHODS

Multi-pronged strategy needs to be taken to reduce the nosocomial transmission of TB (Table 2). World Health Organization (WHO) and Government of India have published guidelines regarding detailed technical and operational measures that can be implemented to reduce the transmission of TB in HCF.[39,40] Education of the HCW as well as the patients is of paramount importance in controlling the spread of TB. There are large gaps in the knowledge and attitudes of HCW on TB.[41] In a survey in Delhi,[42] only 12% of the private practitioners request sputum investigations for suspected TB,[42] thereby increasing the probability of missing infectious TB patients. In another study[43] among nurses, only 67% reported *Mycobacterium tuberculosis* as the causative organism of TB, and only 22% reported sputum microscopy as the most appropriate way to diagnose pulmonary TB.[43] The patients need to be educated on cough etiquette to minimise the generation of infectious droplet nuclei.

Early detection of patients with infectious TB and segregating them can help in preventing the hospital spread. All TB suspects should be provided separate waiting area and consideration should be given to provide expedited priority service to decrease exposure for other patients and HCW.[44] In a pilot study[45] at our hospital, all new patients who registered at the hospital were screened using a TB screening questionnaire at the new patient triage area over a one-month period. For all those who had cough with sputum for more than two weeks, a sputum smear test for microscopy for detecting acid-fast bacilli was done and the results were obtained the same day. Out of 81 patients who fulfilled the

Table 1. Comparison of tests for diagnosing LTBI[29-37]

	TST	IGRAs
Technology	Simple	Complicated
Cost	Less	High
Operator dependence	High	Less
Ease of doing	Difficult	Easy
No. of visits	2	1
Influence of exposure to environmental mycobacteria on test results	Significant	Nil
Effect of previous BCG vaccination	Controversial	Nil
Cut-offs of conversion	Well described	Not clear
Biological variability in serial testing	Less	High

LTBI=Latent tuberculosis infection; TST=Tuberculin skin test; IGRAs=Interferon-gamma release assays; BCG=Bacillus Calmette-Guerin

Table 2. Prevention of tuberculosis among health care workers

Situations for Transmission	Preventive Measures
Infectious TB patients in community	Prompt/effective treatment
	Teach infection control measures
	Recommend leave of absence from work/school till non-infectious
	As far as possible, avoid hospitalisation
Known cases and TB suspects in health care facility	Identify symptomatics at triage/reception
	Quick testing and diagnosis — AFB smear/Xpert MTB/RIF
	Prompt initiation of treatment
	Segregation/isolation
	Reduce time spent by TB cases in hospital premises
	Environmental measures
	Personal protective measures
Health care workers at risk	Periodic screening
	Treatment of LTBI
Symptomatic health care workers	Annual screening for disease/infection
	Sensitisation and a high index of suspicion
	Early diagnosis by AFB smear/Xpert MTB-RIF
	Prompt initiation of treatment
	No patient/co-worker contact till non-infectious

TB=Tuberculosis; AFB=Acid-fast bacilli; MTB=*Mycobacterium tuberculosis*; RIF=Rifampicin; LTBI=Latent TB infection

entry criteria, 19 patients (23.4%) were found to have a positive sputum smear. Five of them ultimately were found to have MDR-TB. All those diagnosed were taught cough etiquette and their appointment with other departments was fast tracked. Such fast tracking of TB suspects effectively reduces the duration and the risk of exposure to other patients and other HCW.

Once detected, the patients should be isolated and effective anti-TB treatment should be started with measures to improve compliance. Polymerase chain reaction (PCR) based nucleic acid amplification (NAA) tests for *Mycobacterium tuberculosis* can decrease diagnostic delay and reduce the duration of infectiousness.[29] The Xpert MTB-Rif, which is an automated assay employing automated nucleic acid amplification to detect *Mycobacterium tuberculosis* appears to be a promising tool.[46,47] This test facilitates confirmation of the diagnosis of TB in a couple of hours and also helps in detecting mutations causing rifampicin resistance, which are surrogate markers for MDR-TB.

Patients with proven TB should not be admitted in hospital, unless otherwise clinically indicated; like, for management of complications or drug intolerance. If they need to be hospitalised, they should be admitted in isolation rooms; which should be separate for TB suspects, drug-sensitive and drug-resistant TB patients. Efforts should be taken to reduce the concentration of droplet nuclei in the air by increasing natural ventilation or mechanical ventilation by exhaust fans.[44] WHO recommends more than 12 air changes per hour (ACH) in areas where infectious patients are kept.[40] In resource-limited settings, natural ventilation may be the only measure that can be implemented. But such rooms should have openings in opposite sides of the room that can be left open on all climates.[39] The openings should constitute more than 20% of floor area. If assisted ventilation is being used (e.g., exhaust fans) to maintain the adequate ACH it should be ensured that these are kept switched on at all times. Additional air-cleaning methods to prevent airborne spread include room-air recirculation units containing HEPA filters or ultraviolet germicidal irradiation.[44] The disadvantage of these air-cleaning methods is their high cost and the need for meticulous maintenance.

Patients need to wear surgical mask, which may reduce the spread of droplet nuclei. Infectious patients should be provided with sputum container with lids containing 5% phenol.[39] HCW need to wear N-95 respirator masks, while entering the room to attend to these patients. By rotating the staff who are posted in the high risk areas, the risk of exposure can be reduced.

CONCLUSIONS

In the fight against TB, protecting the health of HCW is important. TB control programmes should highlight this important need. Efforts should be taken to implement control strategies to prevent nosocomial transmission of TB and make the health care centers safer for both patients and HCW.

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