Latent Tuberculosis in Healthcare Workers: Time to Act

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Reactivation of Latent Tuberculosis is an important source of active infection with *Mycobacterium tuberculosis*. Thus, testing for latent TB is one of the important steps in the control of TB disease around the world. Healthcare workers (HCWs) are at risk of acquiring TB from contact with infected patients they care for in the case of nurses and physicians or from exposure to infected specimens in the case of laboratory workers. This article aims to highlight the possibility of testing HCWs in Oman for latent TB and offering them prophylactic treatment to reduce their risk of developing active disease in the future.

Tuberculosis (TB) remains an important infectious disease that claims a great number of mortalities around the world despite progress in medical knowledge and management. In Oman, the National TB program was started in 1981 and was initially aimed at controlling TB and more recently, to eliminate the disease from the country.[1] As part of the national vaccination program, Bacillus Calmette-Guerin (BCG) vaccination is given at birth to all newborns.

Latent TB Infection (LTBI) is diagnosed when the patient has evidence of TB infection either by positive Mantoux Tuberculin skin test (TST) or more recently by a positive interferon gamma release assays (IGRAs) with no clinical or radiological evidence for active disease.[2] Patients are usually asymptomatic and they tend not to be contagious. Reactivation of LTBI is one of the major causes of the development of new cases of active TB in low prevalence countries like Oman.[3,4] Hence, it is important to identify and treat LTBI if we aim to attain total control of TB in the country.[4] To date, there are no national guidelines for screening or management of LTBI in Oman. Currently, treatment for LTBI is only offered for contacts of open pulmonary TB cases.

Healthcare workers (HCWs) are at risk of infection with TB in view of their constant exposure to infected patients.[5] Inadequate use of preventative measures like N95 masks, poor ventilation at the work place, exposure during procedures like sputum induction and bronchoscopy are other risk factors.[6] One of the aims of testing for latent TB is to raise HCWs awareness about the possibility of acquiring infection from patients if proper precautions are not taken, it is presumed that HCWs who test positive for LTBI will become more careful and adhere more to infection control measures. Prophylaxis will not prevent HCWs from acquiring TB disease due to new extrinsic infection if they are exposed to an open case for a long period of time, but rather prevent the reactivation of the intrinsic latent infection (studies have shown that in non-HIV patients, a course of preventive therapy was strongly protective for at least a decade). Re-exposure can be assessed by re-doing the TST; if there is a significant increase in the size of TST reaction (>9 mm), then re-treatment may be considered depending on individual case scenario and risk benefit assessment.

The exact prevalence of active TB cases among HCWs in Oman is unknown as there is no data to record this in detail. TB remains a social stigma and this might contribute to the low levels of reporting active cases, as well as the policy of repatriation of expatriates with open TB. Hence, it is difficult to formulate a policy without evidence from Oman's Ministry of Health records, which show only four cases in 2010 (Personal communication). This probably does not reflect true numbers; partly due to the fact that many HCWs are expatriates and hence might not report to government health facilities due to the fear of repatriation according to the current policy for positive cases.[7] Many, particularly those with extra pulmonary TB, would probably travel home to start treatment and then come back.[1]

The prevalence of LTBI in the general population in Oman is not known as surveys assessing LTBI have not been done. Screening for LTBI has also not been done for medical staff, neither Omani's or expatriates; hence, the prevalence of LTBI amongst them is also unknown. Studies from various parts of the world have shown a high prevalence of LTBI among HCWs. A study from Poland showed that the prevalence among TB ward clinicians was 34%, 30% among nurses and 50% among TB lab workers.[8] In a recent study from Thailand, the risk of TST conversion indicating recent onset LTBI was significantly greater in HCWs working in outpatient and inpatient departments compared to those working in intensive care and operating rooms.[9] Being of age >30 years and employment for more than 5 years were risk factors for having positive TST.[10,11] While place of work was an additional risk factor, with administrative and pharmacy staff exhibiting the lowest prevalence of LTBI.[12] Prevalence of LTBI among HCWs in countries with low incidence ranges from 7-14% in Germany to 7.6% in Switzerland.[10] In countries with intermediate incidence like Japan, the prevalence was 9.9%.[13] LTBI was diagnosed using interferon gamma release assays (IGRAs) in these studies. However, the rates would probably be higher if TST was used.

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In most parts of the world, TST remains the most popular test for latent TB.[14] The main problem with TST is its low specificity. It cannot discriminate between infection with *Mycobacterium tuberculosis* (MTB), prior BCG vaccination or infection with Non-tuberculous Mycobacteria (NTM).[15] This means that a significant number of uninfected individuals will be exposed to chemoprophylaxis unnecessarily.[2]

Recently, new *in vitro* immune assays called interferon gamma release assays (IGRAs) have been introduced as an alternative tests for diagnosis of LTBI.[16] Two interferon gamma (INF-γ) tests are now available, Quantiferon-TB and T-Spot TB. The production of INF-γ after *in vitro* stimulation of T cells with MTB specific antigens (EAST-6, CFP 10, TB 7.7) is measured.[15] These tests reduce the risk of overestimation of latent TB that result from cross reactivity to BCG vaccine or environmental mycobacterial exposure.[17] IGRAs have a very high negative predictive value (NPV) of approximately 99%, meaning that when an individual has negative IGRAs, they are very unlikely to develop tuberculosis in the future.[16] The progression rate for positive IGRA is 14%, while that for positive TST is only 2.3%.[18] The use of IGRAs in serial testing of HCWs has not been thoroughly studied.[19,20] Using a two step approach in screening HCW for LTBI with the use of TST as an initial screening test and performing IGRA for those who had positive TST, was found to reduce the cost of screening by 50%.[21]

Nosocomial transmission of TB is an important occupational health problem among HCWs. Reduction of this risk should be a priority.[12] Administrative and infection control measures appear to be most important in preventing nosocomial transmission; however, control measures against TB infection remain inadequate in most healthcare facilities in the developing world. This means that the risk of TB transmission from patients to HCWs is high. The first outbreak of Multi Drug Resistant (MDR) TB was thought to have started from a healthcare facility in South Africa.[12] The lifetime risk of developing active TB (in HCW with recent LTBI) is 10 - 20%,[22] this is reduced to half when prophylactic therapy is taken. Systematic screening for LTBI reduced the rate of active TB cases.[22] HCWs are essential in the fight against TB and their health should be protected. Occupational TB can lead to loss of skilled HCWs and may lead to the avoidance of working in high risk clinical areas. Pre employment screening chest X-ray for HCWs and annual TST followed by IGRA for those who are positive, installation of ultraviolet lights on consultation and X-ray rooms as well as the use of N95 masks are important measures for minimizing the nosocomial transmission of TB and should be strengthened in Oman.[12]

Obtaining baseline data on LTBI and establishing a surveillance program for HCWs is important. In United Kingdom (UK), National Health Services (NHS) guidelines recommend that all new NHS employees who are going to be in contact with patients or clinical materials, be offered Mantoux test followed by IGRA (for those who are TST positive). Those from countries of high incidence should be offered IGRA testing, while positive workers should be offered treatment for LTBI.[23] We suggest that all HCWs in Oman be screened for LTBI using the two step approach. Screening will increase the awareness of HCWs about the disease, improve the use of precautions to prevent infection, and lead to early detection of active cases. The question of how to gain consent for screening and using latent TB treatment among HCWs is a challenge, in view of the length of the treatment course and the possibility of serious drug side effects. This issue will be solved as new studies show efficacy of shorter courses of preventive therapy.[24]

Acknowledgements

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