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Tuberculosis Diagnostic Challenge

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Editorial

Tuberculosis is an infectious disease causing a major global health problem. According to the WHO fact sheet, in 2015, 10.4 million people fell ill with TB and 1.8 million died from the disease (including 0.4 million among people with HIV), over 95% of deaths due to TB occurs in countries with low or middle income.

The disease is caused by the bacterium, *Mycobacterium tuberculosis*, which has the characteristic of being "aerobic, non-spore forming, non-motile and acid fast". *M. tuberculosis* is transferred by in airborne transmission; where the bacilli are held within the minute droplet nuclei of 1-5 micron diameter expelled from open pulmonary or laryngeal TB patients. What makes this bacterium highly infectious is that these minute nuclei can stay suspended for many hours in air and can be carried for long distances.

The consequences of inhalation of the droplet nuclei depends on the immune status of the exposed person, he can either develop latent tuberculous infection or active TB disease. Latent infection occurs when the bacilli are controlled by the immune cells isolating them within granulomas.

Failure of achieving that is followed by rapid multiplication of TB bacilli leading to active infection in different organs as lungs, bone, lymph nodes or kidneys.

In spite of the improvement in TB research, diagnosis of latent tuberculous infection and active TB disease remains a challenge.

An approach called "Targeted testing" was applied for the control of TB. It aims at diagnosis and treatment of persons with latent TB infection who are at high risk to exposure to infection and those who are at high risk of developing TB disease when infected. The diagnostic tools used for screening of such individuals are; "Tuberculin skin testing" TST and "Interferon γ release assay" IGRA.

TST detects T-cell mediated delayed-type hypersensitivity reaction if the person has been infected with *M. tuberculosis* but that takes 2 to 8 weeks after initial infection with M. tuberculosis. A TST cannot tell how long the patient has been infected with TB. It also cannot tell if the infection is latent or active and it is affected by BCG vaccination. IGRA has the same disadvantages except that it is not affected by BCG vaccination.

As regard diagnosis of TB disease, systems that depend wholly on detection of the *Mycobacteria* in stained smears or culture face the challenge that the bacterial load must at least be 5,000 to 10,000 per ml in the sample to be detected microscopically and 10 to 100 bacteria for detection by culture based methods. The time factor for positivity by culture methods, the impact of the immune status and the appropriate sample quality should also be considered. Approaches which indirectly detect the organism by its biochemical reactions, by-products or host immune mechanisms are still developing.

Direct detection of *M. tuberculosis* in clinical specimens Using Nucleic Acid Amplification (NAA) tests are used to amplify DNA and RNA segments to rapidly identify the microorganisms in a specimen. Possible benefits of using NAA tests are the earlier laboratory confirmation of TB disease, earlier treatment initiation, improved patient outcomes and interruption of transmission by early diagnosis. However, the molecular methods are of high cost inappropriate for monitoring treatment progress.

There is still an urgent need for a highly sensitive and specific diagnostic method to diagnose both LTBI and active *M. tuberculosis* disease that can be performed at the point of care.

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