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Beyond the Skin Test: Unlocking Tuberculosis Clues Hidden in the Blood

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Tuberculosis (TB) is a centuries-old disease, yet it remains one of the world's deadliest infectious diseases today. According to the World Health Organization (WHO), an estimated 10.6 million people fell ill with TB in 2021, and 1.6 million died making it the second leading cause of death from a single infectious agent after COVID-19 (WHO, 2022a). What's even more alarming is the fact that about one-quarter of the global population nearly 2 billion people carry the TB bacteria in a latent form, where the bacteria remain alive but inactive within the body, causing no symptoms and not being contagious, yet still carrying the risk of reactivation and progression to active disease if the immune system weakens (Houben & Dodd, 2016).

In Sri Lanka, TB is still a significant public health concern. The country reported 8,342 new and relapse TB cases in 2022, a rise from previous years affected by COVID-19-related disruptions (WHO, 2022b). While Sri Lanka is considered a low-burden country, around 4,000–5,000 cases go undiagnosed or unreported each year, making TB a silent threat in many communities. Latent TB infection (LTB), which affects an estimated 23% of the global population, is particularly difficult to detect and monitor (Knight et al., 2019).

Traditionally, TB in Sri Lanka is diagnosed using methods like the Mantoux skin test and chest X-rays. However, these methods have limitations especially for detecting latent infections. The Mantoux test, for example, often produces false-positive results in individuals who have received the Bacille Calmette-Guérin (BCG) vaccine (which includes over 99% of Sri Lankan children) and may miss infections in immuno-compromised individuals, such as those with HIV or recovering from COVID-19.

To address these challenges, researchers at the National Institute of Fundamental Studies (NIFS) have explored a cutting-edge, non-invasive approach using extracellular vesicles (EVs) (tiny particles) naturally released by cells into the bloodstream. These EVs carry fragments of genetic material and proteins, which have recently gained global attention as potential diagnostic tools in diseases such as cancer, Alzheimer's, and infectious diseases like TB.

In the recent NIFS study, EVs were isolated from the blood serum of TB patients and healthy individuals using a simple, low-cost method involving polyethylene glycol (PEG). The goal was to see if these vesicles carried traces of the tuberculosis-causing bacterium, Mycobacterium tuberculosis, and if so, whether they could be used to detect latent or active TB infections. The study successfully found specific M. tuberculosis gene fragments in the EVs of patients with latent TB, marking an important step forward in non-invasive diagnostics.

What makes this approach especially promising is that a simple blood sample could, in the future, help distinguish between individuals with active TB, latent TB, and healthy controls. Additionally, this method could reduce the need for repeated chest X-rays or invasive procedures, making it accessible for rural and underserved populations.

Globally, researchers are turning to artificial intelligence (AI) and machine learning to help analyze complex genetic data like those found in EVs. At NIFS, this approach was used to compare TB-related gene expression in both blood and exosome samples, revealing key differences that could improve diagnostic precision (Magana-Arachchi et al., 2024) Importantly, this study included RNA-sequencing data from Sri Lankan patients, adding critical value to local healthcare efforts.

As Sri Lanka strives to eliminate TB by 2035 in line with global targets, early detection and community awareness will be crucial. People who have been in close contact with TB patients especially within families should be tested and monitored even if they show no symptoms. This is particularly important given the findings of a recent study from Kandy, showing significant TB exposure among family contacts, especially in households with chronic illness or poor living conditions (Bandara et al., 2024).

The message is clear: TB is preventable and curable, but only if it's detected early. Innovations such as EV-based diagnostics could become game-changers in this fight. By combining modern molecular biology, machine learning, and a strong public health approach, Sri Lanka has a real opportunity to lead in TB control and prevention not only through treatment, but through innovation and foresight.