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Commentary

Clinical Predictors of Pulmonary Tuberculosis

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DESCRIPTION

In 2019, there were an estimated 209,000 tuberculosis (TB) cases among South Africa's 75 million people living with HIV (PLHIV). Many of these cases go undiagnosed and untreated (treatment coverage rate of 58%), resulting in a 17% case fatality rate. Current active case-finding strategies for tuberculosis rely on symptomatology, but recent TB prevalence surveys in Africa and Asia show that a large proportion (36%-80%) of TB cases are asymptomatic, including 44% of TB cases in South Africa with a known HIV positive status. Recent evidence also suggests that *Mycobacterium tuberculosis* can be aerosolized by tidal breathing in tuberculosis patients, even in the absence of coughing. *Mycobacterium tuberculosis* transmission may be perpetuated if subclinical TB cases are missed through symptom screening. Innovative active case-finding approaches that do not rely on the presence of symptoms are required. Chest radiography has been used successfully in prevalence surveys as a screening tool to guide confirmatory sputum microbiological testing and for subclinical TB diagnosis, and computer-aided detection holds promise for cost-effective mass screening. Additionally blood-based tools such as C-Reactive Protein (CRP) and host-blood transcriptomics are being investigated.

Simple clinical prediction models are appealing as triage tools for TB suspects to determine the need for further investigations or to guide empiric TB preventive therapy, and they provide a pragmatic solution in resource-limited settings. Clinical prediction scores that include such variables have been developed as triage tools to prioritize TB investigation among PLHIV (People Living with HIV) at routine clinic visits, for empiric diagnosis of TB disease in patients presenting to clinics, and for prognosis of incident TB in low transmission settings. The majority of clinical predictive tools rely on Tuberculin Skin Testing (TST), Interferon-Release Assay (IGRA), or radiography results. TST and IGRA positivity indicate *Mycobacterium tuberculosis* specific T-cell sensitization that is linked to an increased risk of TB disease. These tests, however, cannot distinguish between cleared and persistent *Mycobacterium tuberculosis* infection. Understanding *Mycobacterium tuberculosis* sensitization risk factors may help elucidate risk factors associated with prior *Mycobacterium tuberculosis* infection and guide efforts to reduce transmission.

The TB was studied in a cohort of mostly ART-experienced South African adults with HIV who had no clinical suspicion of TB and were not seeking care, and it was determined whether they were useful for clinical prediction of disease in this setting. A multi-center prospective observational cohort study was used to examine the relationship between socio-demographic, clinical, immunological, and virological factors and baseline risk of *Mycobacterium tuberculosis* sensitization (IGRA positivity), prevalent pulmonary TB, and progression to incident pulmonary TB. The diagnostic and prognostic utility of clinical prediction models for pulmonary TB were then determined and compared with published clinical TB triage tools, with and without the addition of IGRA or RISK11, a transcriptomic signature of TB risk.

The diagnostic or prognostic clinical tuberculosis prediction rules are not entirely dependent on the presence of TB symptoms. Several scoring systems could not be validated because variables such as chest radiographs and TST results were not included in the dataset. Using ROC analysis and Area Under the Curve (AUC) with 95% confidence intervals, the diagnostic and prognostic performance clinical prediction tools was evaluated.

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