Title

Interferon-γ assay sensitivity for diagnosing active pulmonary tuberculosis is affected by HIV and immune status.

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ABSTRACT

Objective: To evaluate the sensitivity of the QuantiFERON-TB Gold In-tube (QFT-G IT) test and the IP10 biomarker in HIV-positive and HIV–negative patients with pulmonary tuberculosis (TB).

Background: In HIV negative TB patients, we have shown that an *M.tuberculosis* specific IP-10 response could be used as a marker for immuno-diagnosis of TB.

Materials and methods: Through the National Tuberculosis and Leprosy Programme of Tanzania 157 pulmonary TB patients with positive sputum culture were recruited for the study. All participants were subjected to HIV-testing and measurement of CD4-cell count as well as immune assay testing using both the QFT-G IT and the IP10 immunoassay.
IFN-γ and IP-10 were determined in supernatants from whole blood stimulated with *M.tuberculosis*-specific antigens using the QuantiFERON Gold In-Tube system. IFN-γ was determined according to the manufacturer and IP-10 using xMAP technology. In previous studies the IP-10 cut-off was established based on ROC curve analysis and a potential IP-10 test was defined based on a diagnostic test algorithm with positive, negative and indeterminate results.

Results: The overall sensitivity was 73% (36/157) for the QFT-G IT and 77% (42/157) for the IP10 test. Sensitivity was lower in HIV-positive than in HIV-negative for both the QFT-G IT (63 vs. 80%, p=0.01) and the IP10 test (66 vs. 85%, p=0.01). When using a combined biomarker approach the overall sensitivity was 85% (95% CI: 79-90%) ranging from 95% (95% CI: 88-99%) in HIV-negative to 72% (95% CI: 61-83%) in HIV-positive patients. In HIV-positive patients, increasing CD4 cell count was associated with a decreasing proportion of QFT-G IT indeterminate results (p=0.03) although not all indeterminate results could be explained by low CD4 cell count. Interestingly we found no such trend for the IP-10 response and CD4 cell count (p=0.61). IP-10 is released by macrophages and our finding suggests that the IP-10 response may be independent of the T-cells.

Conclusions: QFT-G IT test performance is impaired in HIV-positive patients with low CD4 cell count. Other biomarkers, such as the IP-10 alone or in combination with IFN-γ, may play an important role in improving immuno-diagnosis of TB infection.