Mycobacterium Tuberculosis Thymidylate Kinase is A Potential 2 Diagnostic Biomarker for Pulmonary Tuberculosis

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Abstract

Diagnosis of pulmonary tuberculosis (PTB) in context of HIV infection remains challenging due to the paucibacillary nature of the disease. Mycobacterium tuberculosis thymidylate kinase 26 (TMKmt) has been validated as a novel biomarker with high detection limits for PTB in sputum. We aimed to clinically test TMKmt as a diagnostic biomarker for pulmonary tuberculosis among HIV positive individuals at Makerere University Joint AIDS Program Immuno Suppression Syndrome clinic. Methods A total of 120 participants with presumptive PTB were enrolled in a cross-sectional study between January and September 2018. Venous blood and expectorated spot sputum was obtained from 116 consenting participants. Tuberculosis culture was performed on sputum as the gold standard to confirm PTB status while direct ELISAs were performed on sputum and serum to determine the level of TMKmt antigen. Sensitivity, specificity and receiver operator characteristic curves were used to assess the precision of TMKmt in diagnosing PTB. Results Of the 116 participants, only 22 (19%) were PTB positive based on either Lowenstein Jensen or Mycobacterial growth inhibition tube culture. The mean sputum TMKmt levels were significantly higher in PTB positive individuals (4.889 ± 0.135) ng/ml as compared to PTB negative individuals (4.303 ± 0.07295) ng/ml (t-test, $P < 0.0005$). At a cut off value of > 4.683 ng/ml, the test had a sensitivity of 73% (95% CI, 49.78% - 89.27%) and a specificity of 72% (95% CI, 62.15% - 81.07%). These results were supported by a receiver operator analysis which showed an area under the curve of 0.75 (95% CI, 0.63 - 0.86). Conclusion Sputum TMKmt is a potential diagnostic biomarker for active pulmonary tuberculosis. This forms an alternate test that would replace smear microscopy and overcome the current TB diagnostic challenges.

Full Text

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Figures

Figure 1

TMKmt levels(ng/ml) in serum of TB negative and TB positive individuals. The boxes show mean and standard deviation, whiskers are defined as 5th and 95th percentiles. Dots define the outliers.

Figure 2

TMKmt levels (ng/ml) in sputum of TB negative and TB positive individuals. The boxes show mean and standard deviation, whiskers are defined as 5th and 95th percentiles. Dots define the outliers.

Figure 3

putum TMKmt levels (ng/ml) between males and females (Fig 3A). Shows the sputum TMKmt levels between the different age groups (Fig 3B). The boxes show mean and standard deviation, whiskers are defined as 5th and 95th percentiles. Dots define outliers. Asterisk (*) indicate significant results (t-test, $P < 0.05$)

Figure 4

Shows the ROC curves for sputum TMKmt as a diagnostic biomarker for pulmonary tuberculosis (fig 4A).
Shows the ROC curves for serum TMKmt as a diagnostic biomarker for pulmonary tuberculosis (fig 4B).

Supplementary Files

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