COMBINED SPECIFIC IGG – AND IGA-BASED DIAGNOSIS OF TUBERCULOSIS IN AFRICAN PRIMARY HEALTHCARE CLINIC ATTENDEES WITH SIGNS AND SYMPTOMS SUGGESTIVE OF TUBERCULOSIS

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Background IgG-based tests for the diagnosis of active tuberculosis disease (TB) often show a lack of specificity in TB endemic regions, which is mainly due to a high background prevalence of latent TB infection (LTBI). Here, we investigate the combined performance of the responses of different Ig classes to selected mycobacterial antigens in primary healthcare clinic attendees with signs and symptoms suggestive of TB.

Methods We evaluated the sensitivity and specificity of serologic IgA, IgG and/or IgM to LAM, 7 mycobacterial protein antigens (ESAT-6, Tpx, PstS1, AlaDH, MPT64, 16 kDa and 19 kDa) and 2 antigen combinations (TUB, TB-LTBI) in the plasma of 42 individuals with other respiratory diseases (separated into 21 LTBI controls and 21 uninfected healthy controls), and 21 active TB patients at baseline, of whom 19 were followed up at month 6 at the end of TB treatment.

Results The leading single serodiagnostic markers were anti-16 kDa IgA, anti-MPT64 IgA, anti-LAM IgG and anti-TB-LTBI IgG. IgA responses to MPT64 and 16 kDa had the highest sensitivity/speciﬁcity of 95%/95% and 95%/90% in differentiating active TB from other respiratory diseases and active TB from LTBI controls, respectively. The combined use of 3 or 4 antibodies further improved this performance to accuracies above 95%. After successful completion of anti-TB treatment at month 6, only particularly anti-TUB IgG showed distinctively decreased levels.

Conclusions These results show the potential of combining IgG and IgA responses against selected protein and non-protein antigens in differentiating active TB from other respiratory diseases in TB endemic settings, and may provide a benchmark for vaccines.