Urine Outperforms Serum: *Fasciola* Worm Antigen as a High-Accuracy Capture Antigen for *S. haematobium* Immunodiagnosis

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Abstract

Accurate diagnosis of urogenital schistosomiasis remains constrained by the poor sensitivity of microscopy in low-intensity and chronic infections and the absence of reliable point-of-care tools for *Schistosoma haematobium*. We evaluated alternative antigen sources and antigen combinations to improve serological detection using urine and serum in endemic (NE) and non-endemic (NNE) populations.

Methods Crude *Fasciola gigantica* worm antigen (FWA) and egg antigen (FEA) were assessed as capture antigens in indirect ELISA for anti-*S. haematobium* IgG. FWA-serum demonstrated excellent discrimination in NNE samples with an AUC of 0.957, sensitivity of 93.75%, and specificity of 85.42%. Notably, FWA-urine showed superior performance across both NE and NNE categories, achieving AUC values >0.95, sensitivity >97%, and specificity >85%, highlighting its potential as a non-invasive diagnostic marker. In contrast, FEA-urine showed inconsistent performance, while FEA-serum achieved sensitivity >90% and AUC of 0.968 only in NNE samples.

In a complementary approach, admixtures of *S. mansoni* and *S. haematobium* soluble egg antigens (SEA) and worm antigens (SWA) were evaluated. SEA admixtures performed best in urine from positive vs negative endemic samples (sensitivity 91.67%; specificity 66.67%). Conversely, SWA admixtures showed superior performance with sera from positive vs negative non-endemic samples (sensitivity 93.75%; specificity 72.92%). ROC analyses revealed that SEA admixtures in sera often performed no better than chance (AUC 0.5–0.6), whereas SWA mixtures produced clearer discrimination patterns in NNE sera.

These findings demonstrate that diagnostic performance is strongly influenced by antigen source, antigen combination, biological sample, and endemicity context. Cross-reactive trematode antigens from *Fasciola* provide a sustainable and highly sensitive alternative to scarce *S. haematobium* materials, particularly for urine-based testing. Strategic antigen admixtures further enhance detection depending on epidemiological setting.

This work provides quantitative evidence for a context-adapted, non-invasive immunodiagnostic strategy for urogenital schistosomiasis suitable for deployment in resource-limited primary health care settings and offers a scalable pathway toward pan-trematode diagnostic platforms.