

The impact of helminth infection and anthelmintic treatment on *P. falciparum* specific antibody responses in school and preschool children in Magu district, Tanzania

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A study was conducted to examine possible interactions between schistosome and STH infections and the effect of an antihelmintic intervention on *P. falciparum* specific antibody responses among school and pre-school children in Magu district, Mwanza region, Northwestern Tanzania. A total of 2822 serum samples were prepared from blood collected from 1572 children (baseline survey), 658 children (first follow up survey) and 592 children (second follow up survey). The immune response against *P. falciparum* infection was measured by determination of the level of IgG3 against *P. falciparum* schizont antigen (PfSE-IgG3) using the Enzyme Linked Immunosorbent Assay (ELISA) method. Out of 1505 children with complete baseline information, 1247 (82.9%) were seropositive for PfSE-IgG3. The seroprevalence of PfSE-IgG3 increased with age ($\chi^2 = 37.59$, $p < 0.001$) and differed significantly among schools ($\chi^2 = 70.30$, $p < 0.001$). Geometric mean PfSE-IgG3 levels increased with age ($F = 35.92$, $p = 0.001$) and differed significantly among schools ($F = 25.72$, $p < 0.001$). The seroprevalence of PfSE-IgG3 was significantly higher in children infected with *P. falciparum* ($\chi^2 = 41.92$, $p < 0.001$), *S. haematobium* ($\chi^2 = 8.74$, $p < 0.01$) and hookworm ($\chi^2 = 23.10$, $p < 0.001$) compared to children without any infection. Children with co-infections of *P. falciparum* and *S. haematobium* had significantly higher levels of PfSE-IgG3 responses compared to uninfected children ($t = 5.52$, $p < 0.001$) or children with *P. falciparum* infection only ($t = 2.67$, $p < 0.01$). Children co-infected with *P. falciparum* and hookworm had significantly higher levels of PfSE-IgG3 responses compared to uninfected children ($t = 6.93$, $p < 0.001$) or children with *P. falciparum* infection only ($t = 2.75$, $p < 0.01$). The seroprevalence and levels of PfSE-IgG3 were not associated with sex or *S. mansoni* infection. In a multivariate linear regression analysis, age group, *P. falciparum*, *S. haematobium* and hookworm infections were significant predictors of PfSE-IgG3 levels after adjusting for sex. PfSE-IgG3 levels were positively correlated with infection intensities of *P. falciparum*, *S. haematobium* and hookworm. For each parasite infection, PfSE-IgG3 levels increased with increasing infection intensity indicating possible interactions between PfSE-IgG3 and *P. falciparum*, *S. haematobium* and hookworm infections. PfSE-IgG3 levels were significantly associated with splenomegaly and hepatosplenomegaly. Levels of PfSE-IgG3 were higher in children with splenomegaly compared to those without splenomegaly ($t = 12.78$, $p < 0.001$). Likewise, children with hepatosplenomegaly had significantly higher PfSE-IgG3 levels compared to children without hepatosplenomegaly ($t = 24.24$, $p < 0.001$). In a multivariate logistic regression analysis PfSE-IgG3 was an important predictor of both splenomegaly and hepatosplenomegaly. Overall, there was a significant increase ($t = 2.23$, $p = 0.027$) in post-treatment geometric mean PfSE-IgG3 levels particularly for children with baseline age of 9 -13 years in the intervention group. In conclusion, this study has demonstrated that *P. falciparum* and *S. haematobium* co-infection and *P. falciparum* and hookworm co-infections are positively correlated with PfSE-IgG3 levels indicating positive interactions of *S. haematobium* and hookworm infections on anti-*P. falciparum* immune responses. Further, anthelmintic treatment of schistosome and hookworm infections was associated with increased levels of PfSE-IgG3 indicating a positive impact on anti-*P. falciparum* immune responses. However, it was not clear if this increase was associated with improved protection against *P. falciparum* infection and disease.

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