Loss of Protective Humoral and Cellular Immunity to Invasive Nontyphoidal *Salmonella* during *Plasmodium falciparum* Malaria Infection in Malawian Children

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Background: In malaria endemic settings, invasive nontyphoidal *Salmonella* (iNTS) infections are commonly associated with *Plasmodium falciparum (P. falciparum)* malaria infections, but the immunologic basis for this linkage is poorly understood. We hypothesized that *P. falciparum* malaria infection compromises humoral and cellular immunity to NTS which consequently increases susceptibility to iNTS infection.

Methods: We prospectively recruited Malawian children aged between 6 to 60 months at Zingwangwa Community Health Centre, which were placed in the following groups; febrile with uncomplicated malaria (n=59), febrile malaria-negative (n=50), non-febrile malaria-negative (n=47). Only malaria-infected children were followed up for examination at days 14 and 30 in convalescence. Participants were clinically examined and sampled 3ml venous blood for analyses to investigate STmspecific serum or whole blood bactericidal activities, and neutrophil respiratory burst activity.

Results: We found that serum bactericidal activity (SBA) to STm was significantly reduced in acute malaria-infected children (Median -0.201og10, IQR [-1.85, 0.32]) and at day 14 in convalescence (Median -0.49, IQR [-2, 0.49]) compared to febrile malaria-negative children (Median -1.85log10, IQR [-2.85,-1.24]). Both acute malaria-infected (Median 8.8% IQR [3.7, 20]) and febrile malaria-negative children (Median 9.4% IQR [4.4, 19.5]) had reduced STm-specific neutrophil respiratory burst activity compared to non-febrile malaria-negative children (Median 40.5% IQR [33, 65.8]).

Conclusions: *P. falciparum* malaria infection abrogates protective humoral immunity to STm in children through a mechanism that is not fully understood. Reduction in both humoral and cellular immunity to STm during malaria episodes underscores the malaria-related risk of iNTS in children from malaria endemic settings.