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Submicroscopic gametocytemia and malaria in Malawi: Molecular identification and implications for transmission

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Background: Asymptomatic *Plasmodium* parasite infections occur frequently in people where malaria is endemic, and, if gametocytemic, represent a source of “silent” transmission that is not associated with malaria disease. Microscopy is insufficient to detect most gametocyte infections, which occur at low densities relative to asexual parasite stages. A novel, highly sensitive and specific quantitative reverse transcription polymerase chain reaction (qRT-PCR) assay was recently created that uses five markers to distinguish developing and mature *P. falciparum* gametocytes from asexual stages at submicroscopic densities.

Methods & Materials: We evaluated this assay using human blood samples collected during October 2012 in a cross-sectional, all-ages, household-level study of the International Center of Excellence for Malaria Research (ICEMR) project in Malawi. We aimed to define potential infectious reservoirs by assessing prevalence and predictors of submicroscopic gametocyte infection in three settings representing urban/low (Blantyre), semi-rural/mountainous (Thyolo), and rural/high (Chikhwawa) transmission. Of 2,795 people who were surveyed and sampled for *Plasmodium* microscopy, additional blood from a subset of 628 people was collected into RNAProtect for qRT-PCR testing. Samples that tested positive for *P. falciparum* lactate dehydrogenase DNA by PCR were further tested using the qRT-PCR assay to assess relative stage distribution.

Results: While microscopy detected only one sample with gametocytes, qRT-PCR identified 31 gametocytemic samples, including 7 with only developing gametocytes, 7 with mature gametocytes, and 17 with both developing and mature gametocytes. We present data on the predictors of gametocytemia and compare these results with microscopic and molecular results for asexual parasites. Age category was strongly associated with gametocytemia ($p < 0.0001$), with 2.1% of children under 5 years, 9.1% of children 5 to 15 years, and 1.1% of adults carrying mature gametocytes in this dry season sample.

Conclusion: The use of a new molecular assay enabled us to identify a large number of submicroscopic gametocyte infections, most of which were asymptomatic in this cross-sectional sample.

School-aged children represent an important potentially infectious reservoir that may require a targeted control approach. A better understanding of which humans may be unrecognized sources of parasite transmission is critical in order to enhance malaria interventions, particularly in areas approaching elimination.

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Typhoid fever surveillance in Africa program: Carriers of invasive *Salmonella* in Africa survey (CISAS)

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Background: Studies investigating the prevalence of *Salmonella* carriers are lacking, especially from African countries, and to date, little research has been dedicated to investigating the role of chronic carriers in *Salmonella* infection and transmission in endemic regions.

Methods & Materials: This study utilizes stool culture diagnostics to identify the prevalence of *Salmonella* Typhi, non-typhoidal *Salmonella* (NTS), and *Salmonella* ParaTyphi carriers within the general populations in two sites, located in Guinea-Bissau and Senegal, respectively. Conducted along side the Typhoid Fever Surveillance in Africa Program (TSAP), CISAS will additionally identify potential carriers within households of confirmed acute *Salmonella* cases. Study participants of all ages and both sexes from randomly selected households within the TSAP catchment areas are considered for inclusion. Bacterial pathogens are isolated from positive stool culture and confirmed using biochemical and agglutination reactions. Thirty-day follow-up of patients with positive stool culture will help track periodicity of bacterial shedding, and subsequent monthly follow-up will bear light on clearance patterns. Antibiotic resistance is assessed and genetic analyses of isolated *Salmonellae* will be carried out to investigate phylogenetic relatedness of strains and to understand possible transmission pathways.

Results: A total of 1,313 stool cultures from participants in 164 households have been processed in Guinea-Bissau with 27 (2.6%) cultures positive for *Salmonella* spp. from individuals ranging from 5 to 40 years. A total of 555 stool cultures from participants in 90 households have been investigated in Senegal with 7 (1.3%) positive for salmonellae from individuals ranging from 3 to 55 years. All identified isolates from both sites have been confirmed as NTS and 6 patients from Guinea Bissau have shown repeat positive cultures from within 30 days of identification. Resistance was found against chloramphenicol (1/22), nalidixic acid (1/21), and trimethoprim/sulfamethoxazole (1/23) in Guinea Bissau, and in Senegal, isolates showed resistance to ciprofloxacin (1/7) and nalidixic acid (2/7).