

Abstract

MALARIA IN ENDEMIC REGIONS OF GUYANA: A STUDY OF PREVALENCE, RISK FACTORS AND PATTERNS OF TREATMENT-SEEKING AND PLASMODIUM FALCIPARUM RESISTANCE TO CHLOROQUINE, QUININE AND MEFLOQUINE.

Wallis Sherry-Lee Best Plummer

Since blanket national treatment protocols lead to inept management of malaria in communities of diverse epidemiologies, community-based cross-sectional surveys in six endemic communities sought to determine the epidemiology and factors influencing malaria in Guyana. Despite the low (<8%) parasite rate, 61% of participants gave a 12-month history of malaria. Bed-net use, the most commonly-applied vector avoidance measure (VAM), was the only VAM associated overall with a lower likelihood of having malaria ($p = 0.012$). At least 66% respondents took responsibility for malaria-screening and treatment-seeking, but only 34% complied with the recommended recheck-smear at the end of therapy to confirm clearance of parasitaemia. Quinine, as the (current) first-line

schizontocide, was studied to determine its therapeutic (*in vivo*) and parasitological efficacy. Responses of *P. falciparum* isolates to quinine, mefloquine and chloroquine, were also studied *in vitro* using the WHO Mark III test-system. One therapeutic failure (day-14) and 2-R1 infections were identified *in vivo* and resistance to chloroquine (73%), quinine (43%), and mefloquine (20%) was observed *in vitro*. Although *pfcr* K76T was a good population-marker of chloroquine resistance, *pfmdr1* mutations failed to predict quinine response *in vivo* or *in vitro*. This dissertation calls attention for the first time to the general ineffectiveness of irregularly-practiced VAMs, and identifies the presence of *P. falciparum* resistance to quinine and mefloquine in Guyana. The value of the *pfcr*, *pfmdr1* and *cg2* mutations as predictors of chloroquine or quinine response in this low-transmission environment is also discussed. Recommendations include further population-studies to determine the reliability of *pfmdr1* mutations as population-markers of quinine resistance in Guyana, vectorial studies of *Anopheles* transmission and a revision of the current treatment protocols to contain the spread of *P. falciparum* resistance.

Key words: *P. falciparum*, antimalarial resistance, vector-avoidance measures