Role of the *pfcrt* codon 76 mutation as a molecular marker for population-based surveillance of chloroquine (CQ)-resistant *Plasmodium falciparum* malaria in Ugandan sentinel sites with high CQ resistance

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Abstract

The mutant genotype at codon 76 of the *pfcrt* gene (T76) has been proposed as a molecular marker for surveillance of chloroquine (CQ)-resistant *Plasmodium falciparum* malaria but this proposal has not been validated by population-based surveys. In 1998–1999, in 6 Ugandan sentinel sites, the prevalence of *P. falciparum* infections with the T76 genotype and the level of CQ use were measured by community surveys, and CQ resistance was determined by in-vivo tests on 6–59-month-old children with clinical malaria. The prevalence of T76 was not related to the overall clinical (early and late treatment failure: ETF+LTF; $r = 0 \cdot 14$, $P = 0 \cdot 78$) or parasitological (RI+RII+RIII; $r = 0 \cdot 17$, $P = 0 \cdot 73$) CQ resistance. However, the percentage of individuals carrying only infections with the T76 genotype (T76 alone) increased with increasing ETF ($r = 0 \cdot 76$, $P = 0 \cdot 07$) and type RIII parasitological failure ($r = 0 \cdot 69$, $P = 0 \cdot 12$). Similarly, the ratio between T76 and K76 (the wild type) prevalences (T76/K76) was strongly and positively correlated with ETF ($r = 0 \cdot 85$, $P = 0 \cdot 03$) and RIII ($r = 0 \cdot 82$, $P = 0 \cdot 04$). Moreover, T76 alone ($r = 0 \cdot 90$, $P = 0 \cdot 01$) as well as T76/K76 ($r = 0 \cdot 90$, $P = 0 \cdot 01$) significantly increased with increasing community CQ use. T76 alone and T76/K76 can be useful markers to estimate the ETF and RIII prevalence as well as the amount of CQ use in the community.

Keyword: *Plasmodium falciparum*, gene mutation, genes, *pfcrt*, drug resistance, chloroquine, Uganda