

Role of the *pfcr* 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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Received 22 January 2002, Revised 11 March 2002, Accepted 11 March 2002, Available online 8 April 2004.

[https://doi.org/10.1016/S0035-9203\(02\)90439-6](https://doi.org/10.1016/S0035-9203(02)90439-6)

Abstract

The mutant genotype at codon 76 of the *pfcr* 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; $r = 0.14$, $P = 0.78$) or parasitological (RI+RII+RIII; $r = 0.17$, $P = 0.73$) CQ resistance. However, the percentage of individuals carrying only infections with the T76 genotype (T76 alone) increased with increasing ETF ($r = 0.76$, $P = 0.07$) and type RIII parasitological failure ($r = 0.69$, $P = 0.12$). Similarly, the ratio between T76 and K76 (the wild type) prevalences (T76/K76) was strongly and positively correlated with ETF ($r = 0.85$, $P = 0.03$) and RIII ($r = 0.82$, $P = 0.04$). Moreover, T76 alone ($r = 0.90$, $P = 0.01$) as well as T76/K76 ($r = 0.90$, $P = 0.01$) 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.

Keywords

Malaria *Plasmodium falciparum*; gene mutation; *pfcr* drug resistance; chloroquine Uganda