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K76T point mutation of chloroquine resistance transporter gene: Is it a potential molecular marker for chloroquine resistance in Sri Lankan *Plasmodium falciparum* isolates?

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Current evidence suggests that K76T mutation of chloroquine resistance transporter (*Pfcrt*) gene may be used as a molecular marker for chloroquine (CQ) resistance of *P. falciparum*. This study was carried out to determine the frequency of K76T mutation of *Pfcrt* gene in Sri Lankan *P. falciparum* isolates collected from Mannar district in the Northern Province. Mutation patterns were compared with *in vitro* and *in vivo* CQ failure rates for this parasite population to analyze its association with resistance to CQ and to calculate the genotype-resistance (GRI) and genotype-failure (GFI) indices for K76T mutation. *P. falciparum* DNA was extracted from dried blood spots using a QiaAmp DNA Blood Mini Kit. Mutation patterns at 76 codon of *Pfcrt* of field isolates were detected using a polymerase chain reaction – restriction fragment length polymorphism assay. Parasite isolates were categorized into wild (sensitive) and mutant (resistant) types based on the banding patterns of digested products on 2% agarose gels. GRI and GFI indices were calculated for this parasite population. Of 38 CQ resistant isolates, 86.8% (N = 33) showed the mutant allele (K76T) at codon 76 of *Pfcrt*. There was a statistically significant association between the presence of K76T mutation and *in vivo* resistance to CQ (x^2 = 5.11, p = 0.02). Of 33 sensitive isolates, 39.4% (N = 20) possessed the wild type allele at the same codon position. The calculated GRI and GFI indices were 1.13 and 1.38 respectively for this area. Even though results show a statistically significant association between the presence of K76T allele and CQ treatment failure of *P. falciparum* isolates in the study population, its mere presence alone does not seem to correlate with resistance to CQ. Therefore, mutations at other codons of *Pfcrt* shown to accompany K76T mutation as well as those in *P. falciparum* multi drug resistance 1 (*Pfmdr1*) gene need to be analyzed to determine whether other mutations play a role together with K76T in clinically resistant Sri Lankan parasite isolates. More studies are required to validate the calculated GRI and GFI values, which may be used to predict the therapeutic failure of CQ in a particular area in Sri Lanka in the future.

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