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Genetic evidence of emerging sulfadoxine-pyrimethamine resistance of *Plasmodium falciparum* isolates in an operational area in the Northern Province of Sri Lanka

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Sulfadoxine-pyrimethamine (S-P) is currently being used as the treatment of choice for chloroquine resistant, uncomplicated *Plasmodium falciparum* infections in Sri Lanka. The use of S-P has increased in the country because of increasing chloroquine resistance. The point mutations of *P. falciparum* dihydrofolate reductase (Dhfr) and dihydropteroate synthase (Dhps) genes that confer resistance to S-P tend to accumulate more rapidly with increasing drug pressure. This study was designed to determine the frequency of mutations at codons 108, 51, 59 and 164 of Dhfr and 436, 437 and 540 of Dhps of *P. falciparum* using a PCR-RFLP method. Samples were collected in an operational area of the Northern Province where more than 50% of *P.falciparum* infections were found to be chloroquine resistant during a previous study. Those who received S-P were followed up for 42 days to determine its *in vivo* efficacy. Laboratory results showed that 86.7% of the 30 isolates studied (all chloroquine-resistant infections) were double mutants at codons 108 (Ser to Asn) and 59 (Cys to Arg) of the Dhfr gene. None had mutant alleles at either 51 or 164 codon positions. With regard to the Dhps gene, 73.3% and 83.8% of isolates showed wild type alleles at codons 436 and 437; all had wild type allele at codon 540. However, none of the patients showed clinical evidence of resistance to S-P. Our results showed that the majority of *P. falciparum* isolates in this sample have established the initial genetic change in developing S-P resistance, namely Ser to Asn at 108. They also suggest an active propagation of additional genetic changes that will lead to clinical failures. This emphasizes the need for a surveillance method to monitor further genetic changes combined with *in vivo* efficacy trials for S-P.

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