Diagnostics and biomarkers

PO - (8607) - DETECTION OF PLASMODIUM FALCIPARUM HISTIDINE-RICH PROTEIN 2/3(PFHRP-2/PFHRP-3)GENES DELETION AND AMINO ACID NUCLEOTIDE SEQUENCE VARIABILITY IN NIGERIA

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Background
Prompt diagnosis and appropriate treatment remain the hallmark for reducing malaria-related mortality in high transmission areas. Rapid diagnostic tests (RDTs) that targets the Pfhrp-2 gene are essential in resource limited settings where microscopy is not available. However, Pfhrp-2 gene deletion are implicated in limiting RDT sensitivity. Studies evaluating Pfhrp-2 and Pfhrp-3 deletion and the amino acid sequence diversity has not been investigated in Nigeria. We therefore hypothesized that malaria parasites in Nigeria are lacking Pfhrp-2/Pfhrp-3 genes with variable amino acid repeats sequences.

Methods
The study was part of a prospective cohort study evaluating RDTs performance. We pooled 66 samples comprising false negative (n = 31) and true positive (n = 35) to elucidate Pfhrp-2/Pfhrp-3 gene deletion, RDT cross reactivity with Pfhrp-3 antigen and amino acid sequence diversity. The 18SrRNA, msp 1, msp2 and glurp genes were amplified to establish active Plasmodium falciparum infection and the exon-2 regions of Pfhrp-2 and Pfhrp-3 genes were amplified to determine the presence or absence of Pfhrp-2 and Pfhrp-3 genes. Isolates with conserved Pfhrp-2/Pfhrp-3 were sequenced.

Results
All 66 samples were positive for 18SrRNA, msp1, msp2 and glurp, indicating active P. falciparum infection. However, 16.7% and 6.0% of the samples were lacking Pfhrp-2 and Pfhrp-3 genes. Of the false negative samples, 25.8% and 12.9% has Pfhrp-2 and Pfhrp-3 deletions. Three Pfhrp-3 conserved antigens cross reacted to give RDT positive results. An extensive diversity in the amino acid sequence was observed.

Conclusion
Plasmodium falciparum parasites in Nigeria lacks Pfhrp-2 and Pfhrp-3 genes. However, the proportion of deletions is low compared to reports from other malaria endemic regions. In addition, a high amino acid tandem repeats was observed. A combination of pLDH and Pfhrp-2 based RDTs is recommended for accurate malaria diagnosis.

Keywords: Malaria, Pfhrp-2/Pfhrp-3, Gene Deletion, RDTs, Nigeria.