Molecular studies on clinically severe \textit{Plasmodium vivax} infections

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Severe clinical cases exclusively associated with \textit{Plasmodium vivax} are increasingly being reported worldwide with complications like renal failure, jaundice, acute respiratory distress syndrome, cerebral malaria, seizures, anemia, thrombocytopenia, pulmonary edema, splenic rupture and death. Emergence of \textit{P. falciparum} like severity in \textit{P. vivax} and its pathogenesis has been speculated to be linked to increasing chloroquine resistance (CQR). Two main transporters studied with regard to CQR in \textit{P. vivax} are \textit{P. vivax} chloroquine resistance transporter, \textit{pvcrt-o}; and the \textit{P. vivax} multidrug resistance transporter, \textit{pvmdr1} which are orthologous to the \textit{pfcrt} and \textit{pfmdr1} genes respectively. Even though these transporters are not established as molecular markers for CQR, they have a speculated role in CQR of \textit{P. vivax}. Further, it has been demonstrated that the clinical severity in \textit{P. vivax} could be associated with increased expression levels of parasite transporter genes likely to be involved in CQR i.e. \textit{pvcrt-o} and \textit{pvmdr1}. In this study, relative expression levels of \textit{pvcrt-o} and \textit{pvmdr1} genes were analyzed in severe and non-severe \textit{P. vivax} cases compared to a non-severe control group. \textit{P. vivax} positive isolates were classified as severe and non-severe according to the WHO guidelines for severe malaria. Transcription analysis of drug resistance genes was carried out for severe and non-severe \textit{P. vivax} isolates by real-time PCR normalized to \textit{β}-tubulin; the endogenous gene. The severe \textit{P. vivax} isolates were found to have higher expression levels of the drug resistance genes (\textit{pvcrt-o} and \textit{pvmdr1}) as compared to the non-severe \textit{P. vivax} infections. Increased expression levels of CQR transporters in severe infections indicate their role in the changing pathogenesis of \textit{P. vivax} that can no longer be considered benign. It brings to light how genes linked to the emerging CQR in \textit{P. vivax} might impart virulence to vivax malaria making them excellent genetic markers for disease severity.

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