EMERGENCE OF PLASMEPSIN MUTATIONS IN *Plasmodium falciparum* ISOLATES FROM SOUTH AMERICA AND IMPLICATIONS FOR GENOMIC SURVEILLANCE

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Background *Plasmodium falciparum* infections in Brazil initially decreased with the introduction of artemisinin-based combination therapy (ACTs). However, in 2020, cases surged by 39%, with a 45% increase in mining areas. *P. falciparum*, responsible for about 90% of global malaria cases and severe outcomes, is resurging, particularly among mobile miners whose border crossings complicate diagnosis and treatment. Understanding how different populations, including miners, metabolize antimalarial drugs is vital for enhancing treatment effectiveness and monitoring ACT-resistant parasites. This research will guide the Ministry of Health on drug dosages and resistance management strategies. **Objective** This study aims to genetically characterize genes involved in metabolizing drugs used in ACTs for *P. falciparum* infections. **Methods** We analyzed samples from 99 patients with *P. falciparum* malaria in Roraima, Brazil's area with the highest number of imported cases.[1] The isolates were from Guyana, French Guiana, Venezuela, Brazil (Roraima) and Suriname. We investigated mutations in genes linked to resistance, including *pfcrt* (chloroquine [CQ] resistance) using PCR, *pfpm2/pfpm3* (piperaquine [PPQ]) and *pfmdr1* (mefloquine [MQ] and artemether-lumefantrine [AT-LU]) copy number variations using qPCR, and performed Sanger sequencing for *pfk13* (artemisinin [ART]), *pfmdr1*, and *pfcrt*. We are also developing a 50-gene panel for Next Generation Sequencing to profile gene mutations in these isolates. **Results** Preliminary results show no mutations for *pfcrt* C350R, *pfk13*, or *pfmdr1* N86Y. However, 98% (n = 97) of samples exhibited *pfcrt* mutations at K76T and I356L. We also identified the Y184F mutation in *pfmdr1*. All isolates had a single copy of *pfmdr1*, but 4% (n = 4) had two copies of *pfpm3* or *pfpm2*, and 3% (n = 3) had two copies of both. **Conclusion** CQ resistance markers in this region highlight the need for alternative therapies. While no *pfmdr1* N86Y mutations were found, the wild type is linked to tolerance to ART and LU. The presence of PPQ-resistant markers suggests caution with dihydroartemisinin-PPQ (DHA-PPQ), given recent resistance increases in the Guianan Shield. AT-LU is recommended as the first-line treatment for *P. falciparum* in the Amazon, as DHA-PPQ may select for resistant parasites since gold miners self-medicate with DHA-PPQ. Understanding resistance patterns, especially among transient populations like miners, is crucial or optimizing therapies, shaping health policies, and improving treatment outcomes, thus enhancing malaria control and public health.

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