A new study identifies possible biomarkers of severe malaria in African children

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The levels of small molecules called microRNAs (miRNAs) circulating in blood could help identify early on children with life-threatening forms of malaria, according to a study led by the Barcelona Institute for Global Health, an institution supported by 'la Caixa' Foundation, in collaboration with the Manhiça Health Research Center (CISM) in Mozambique. The results, published in *Emerging Infectious Diseases* journal, could also help better understand the mechanisms underlying severe malaria.

Malaria mortality among young African children remains unacceptably high. To improve the outcome, it is important to rapidly identify and treat children with severe forms of the disease. However, at the beginning of the infection, it is not always easy to distinguish early on between uncomplicated and life-threatening disease symptoms. One characteristic of severe malaria is the sequestration of red blood cells infected with the malaria parasite (P. falciparum) in vital organs such as the lungs, kidneys or brain. This leads to organ damage, which in turn results in the release of small molecules called microRNAs (miRNAs) into body fluids, including blood.

"We hypothesized that miRNA levels in plasma would be differently expressed in children with severe and uncomplicated malaria, due to parasite sequestration in vital organs," explains ISGlobal researcher Alfredo Mayor, who coordinated the study. To test this hypothesis, he and his team first used an advanced sequencing technique to identify miRNAs released by human brain endothelial cells when exposed to red blood cells infected by P. falciparum in a dish. They then measured expression of these miRNAs in blood samples from Mozambican children with severe or uncomplicated malaria. They found that six of the identified miRNAs were higher in children with severe malaria. One of these miRNAs, which is expressed by a variety of tissues, was also positively related with the amount of a parasite-derived protein named HRP2. "This suggests that increasing amounts of parasite associated with parasite sequestration may lead to higher levels of secretion of this miRNA by damaged tissues," explains Himanshu Gupta, first author of the study.

"Our results indicate that the different pathological events in severe and uncomplicated malaria lead to differential expression of miRNAs in plasma," says Mayor. "These miRNAs could be used as prognostic biomarkers of disease, but we need larger studies to validate this," he adds. The findings also provide a ground for better understanding the mechanisms underlying severe malaria.

More information: Himanshu Gupta et al, Plasma MicroRNA Profiling of Plasmodium falciparum Biomass and Association with Severity of Malaria Disease, *Emerging Infectious Diseases* (2021). DOI: 10.3201/eid2702.191795

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