Associations between Total Body Parasite Burden and Malarial Retinopathy in Paediatric Cerebral Malaria

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INTRODUCTION

Malaria, the most prevalent mosquito-borne infectious disease worldwide, remains a significant contributor to death and disability. In 2022, there were an estimated 249 million cases worldwide, with 95% of them in Sub-Saharan Africa. Of the severe malaria syndromes caused by *Plasmodium falciparum* infection, cerebral malaria (CM) carries the highest risk for mortality. About two-thirds of children with clinical CM develop retinal abnormalities termed malarial retinopathy, comprising macular whitening, vessel colour changes or haemorrhages. The presence of malarial retinopathy confers a higher risk of mortality in children with CM. The pathogenesis of malarial retinopathy remains poorly understood but sequestration of parasitised erythrocytes in retinal vasculature has been previously hypothesised to produce vessel colour changes observed on ophthalmoscopy. Therefore, our study aimed to investigate the association between the individual components of malarial retinopathy and sequestration of parasitised erythrocytes in retinal vasculature of children with CM.

METHODS

Patients aged 6 months to 13 years with a clinical diagnosis of cerebral malaria, diagnosed as Blantyre Coma Scale <2, Plasmodium falciparum parasitaemia and no other identifiable cause of coma.

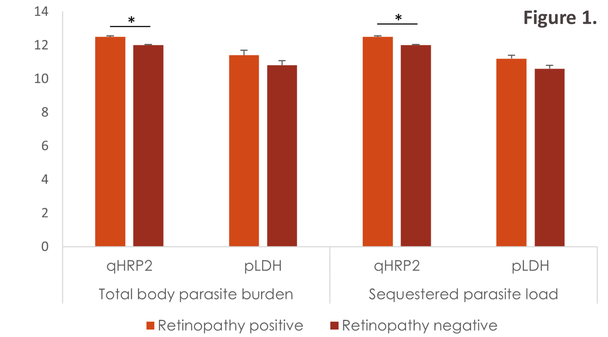
Admitted to Queen Elizabeth Central Hospital, Blantyre, Malawi between January 2010 and March 2023.

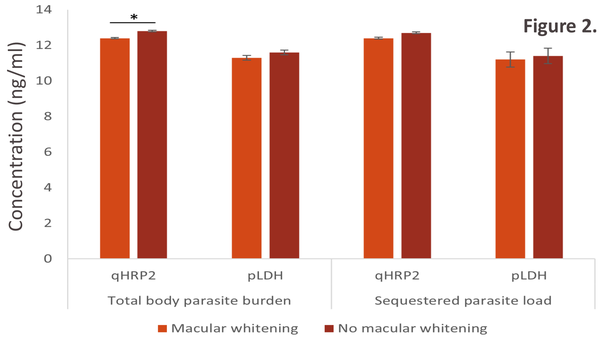
Total body parasite burden using parasitic lactate dehydrogenase (pLDH) and quantitative histidine-rich protein 2 (qHRP2) was determined from plasma samples collected upon admission.

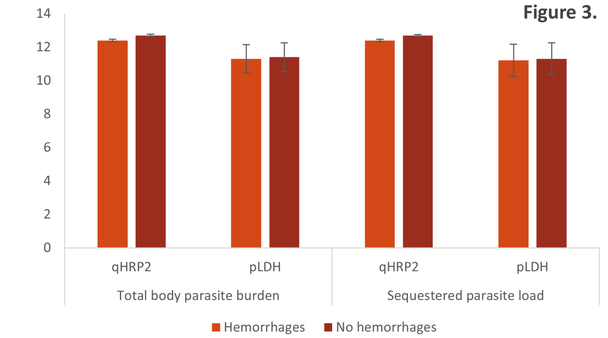
RESULTS

	Retinopathy positive (n = 91)	Retinopathy negative (n = 14)	P-value for difference between groups
Age (months)	52.8 (30.6)	66.7 (31.5)	0.118
Sex (% male)	49 (54%)	7 (50%)	0.788
Weight (kg)	14.0 (5.1)	16.9 (8.1)	0.212
Blantyre Coma Score			
0	9 (9%)	2 (14%)	0.644
1	33 (36%)	6 (43%)	
2	49 (54%)	6 (43%)	
3	0 (0%)	0 (0%)	
Parasitemia [log (parasites/ µl)]	9.2 (2.7) N=89	8.5 (2.9) N=13	0.464
Hemactocrit,	22.1 (7.6)	24.2 (2.9)	0.078
Glucose (mmol/l)	5.9 (2.2) N=80	5.6 (2.5) N=13	0.669
Lactate (mmol/l)	6.0 (5.3) N=90	4.7 (4.5) N=13	0.258
Outcomes			
Died	14 (15%)	3 (21%)	0.805
Survived and Normal	74 (81%)	11 (79%)	
Survived with neurologic sequelae	3 (3%)	0 (0%)	

Table 1. Demographic characteristics of participants included in all analyses (complete retinopathy data and no pre-treatment with broad spectrum antimalarials)

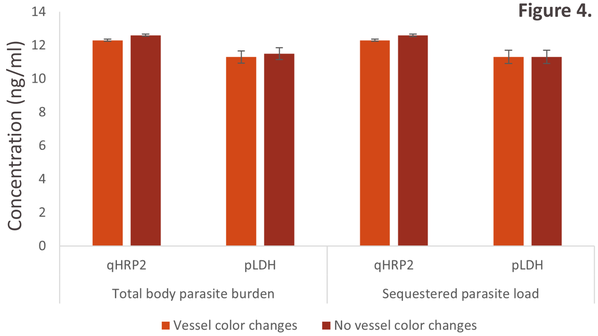






Figures 1-4. Intensity of Sequestration and Malarial Retinopathy in Paediatric Cerebral Malaria

RESULTS



CONCLUSIONS

Patients with malarial retinopathy had a significantly higher total body parasite burden and sequestered parasite load, as measured by qHRP2, than patients without malarial retinopathy.

When assessing the correlation between the individual components of malarial retinopathy, patients with macular whitening exhibited higher levels of total body parasite burden as measured by qHRP2 but not by pLDH.

Higher intensity of sequestration, as measured by qHRP2, is associated with malarial retinopathy in children with CM but not with the individual components of malarial retinopathy : macular whitening, haemorrhages and vessel colour changes.

Our results suggest that qHRP2 may be a more accurate marker of severe disease in cerebral malaria than pLDH.

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