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Biochemical and Haematological Changes in Malaria-Infected Children Under Five at Ahmadu Bello University Teaching Hospital, Zaria, Nigeria

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Abstract
Significant alterations in biochemical and haematological markers primarily characterise the development of malaria. The objective of this study was to analyse the serum lipid and protein profiles, as well as some haematological markers, in children under the age of five who are infected with the malaria parasite. This cross-sectional study was conducted at the Department of Paediatrics, Ahmadu Bello University Teaching Hospital, Zaria, Kaduna State, on a sample of 316 children with malaria and 100 children who were seemingly healthy and under the age of five. Among the 316 patients, 50 (15.8%) tested positive for malaria, while 20 samples from persons who appeared to be in good health were examined. Significant reductions ($p<0.05$) in cholesterol (mean±SD: 0.450±0.026 mmol/L vs. 0.907±0.069 mmol/L), triglycerides (mean±SD: 0.326±0.058 mmol/L vs. 0.461±0.123 mmol/L), and albumin (mean±SD: 5.23±2.82 g/L vs. 2.82±2.18 g/L) were observed in malaria-positive children compared to healthy controls, indicating potential biomarkers for malaria severity.
Keywords: Biochemical changes, child-health, haematological changes, malaria parasites, under-five children

INTRODUCTION

Malaria is caused by a parasitic organism that undergoes part of its life cycle in people and the remaining portion in mosquitoes. Malaria continues to be a prominent cause of death worldwide, endangering the lives of almost a third of the global population (WHO, 2024). A significant proportion of children residing in malaria-endemic regions of Africa experience at least one episode of severe malaria throughout their early years of life (Goncalves *et al.*, 2014). Globally, the burden of malaria in the WHO African Region remains disproportionately high. Approximately 78% of all malaria-related fatalities in the region occurred in children under the age of 5 (WHO, 2024). Cerebral malaria and severe anaemia are the most prevalent and consequential consequences of *Plasmodium falciparum* malaria in children (Luzolo and Ngoyi, 2019).

The liver, which is the main location where Plasmodium infection occurs, produces cholesterol. This has led to investigations into the possible relationship between the liver's cholesterol synthesis and the infection of the liver by *Plasmodium* (Akanbi *et al.*, 2012). The liver maintains the balance of lipid and lipoprotein metabolism to ensure homeostasis. Hepatocellular injury, a frequent occurrence in severe and acute *P. falciparum* infections, hinders these processes and alters the composition of plasma lipids and lipoproteins (Sibmooh *et al.*, 2004).

The alterations in the lipid profile found in the blood serum can be ascribed to the degree of haemolysis caused by malaria, which is directly related to the intensity of the infection (Abdulazeez *et al.*, 2017). Elevated cholesterol levels, resulting from malaria and reduced levels of endogenous antioxidants, increase the likelihood of reactive oxygen species (ROS) production. Reactive oxygen species (ROS) can interact with various biological molecules, including DNA, lipids, proteins, and carbohydrates, resulting in damage to cellular components (Checa and Aran, 2020).

Despite advancements in malaria control, it remains a leading cause of morbidity and mortality in sub-Saharan Africa, particularly among children under five (WHO, 2024). Recent statistics indicate over 200 million cases and approximately 400,000 deaths annually (Adegunloye, 2018), implying the need for further research into biochemical and haematological changes associated with malaria infection in under five children.

METHODOLOGY

This research was carried out at the Department of Paediatrics, Ahmadu Bello Teaching Hospital (ABUTH), Shika, Zaria, Kaduna State, Nigeria.

This cross-sectional study enrolled 316 malaria-positive and 100 healthy children under five. The sample size was calculated based on an expected prevalence of biochemical changes of 20%, with a confidence level of 95% and power of 80%. Participants were randomly selected from the Paediatrics Department.

This study obtained ethical approval (NHREC/10/12/2015) from the Ethics Review Committee of Ahmadu Bello University Teaching Hospital. Participation in the study was entirely optional and dependent upon parents or caregivers providing written informed consent.

The participants' socio-demographic data were obtained after obtaining written informed consent from their parents or carers, with the assurance of confidentiality and anonymity. Every participant provided 3 mL of whole blood. Giemsa staining was used to detect, identify, and estimate parasites in both thick and thin blood films, following the methods described by Chessbrough (2009). Capillary tubes were employed for the detection of PCV and Hb. The serum was stored in a refrigerator until it was required for additional analysis.

The levels of cholesterol, low-density lipoproteins, triglycerides, albumin, globulin, and proteins were measured using the methods and principles outlined by Friedewald *et al.* (1972), Tietz (1986), Doumas *et al.* (1971), and Berne and Levy (1975)f accordingly.

In addition, the packed cell volume (PCV) and haemoglobin (Hb) were measured using the Jain (1986) technique.

Data were analyzed using ANOVA and post hoc Tukey□s tests for multiple comparisons.

RESULTS

Among the 316 patients showing symptoms of malaria and the 100 apparently healthy children serving as controls, 50 individuals (15.8%) were diagnosed with malaria. Additionally, 20 of the control children were selected for additional study of their biochemical and haematological profiles.

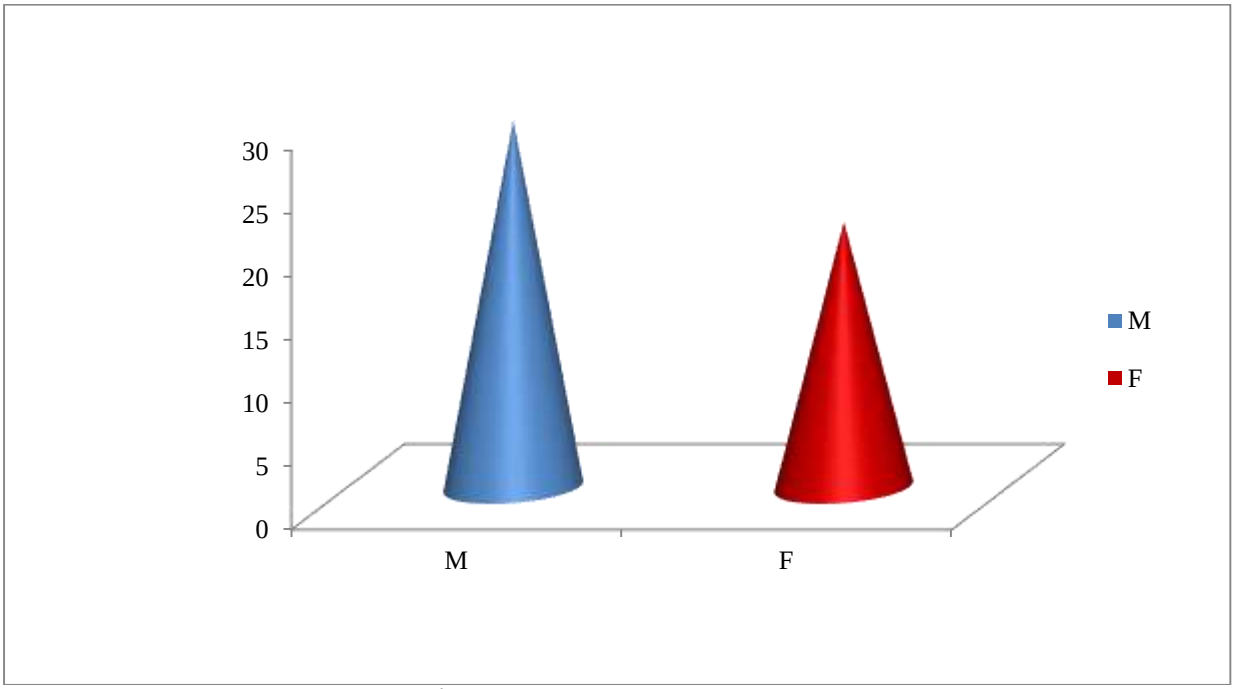

Figure 1. The prevalence of *P. falciparum* malaria parasite infection based on gender distribution

Figure 1 illustrates a higher incidence of malaria in males (58%) compared to females (42%), suggesting potential sex-based susceptibility differences. Table 1 shows significant reductions in cholesterol (p=0.000), LDL (p=0.000), and albumin (p=0.003) levels in malaria-positive children, highlighting the potential use of these markers in assessing malaria severity. However, there is no statistically significant difference between malaria patients and the negative control group in terms of packed cell volume (p-1. 750) and haemoglobin (p-0.139), as shown in Table 2.

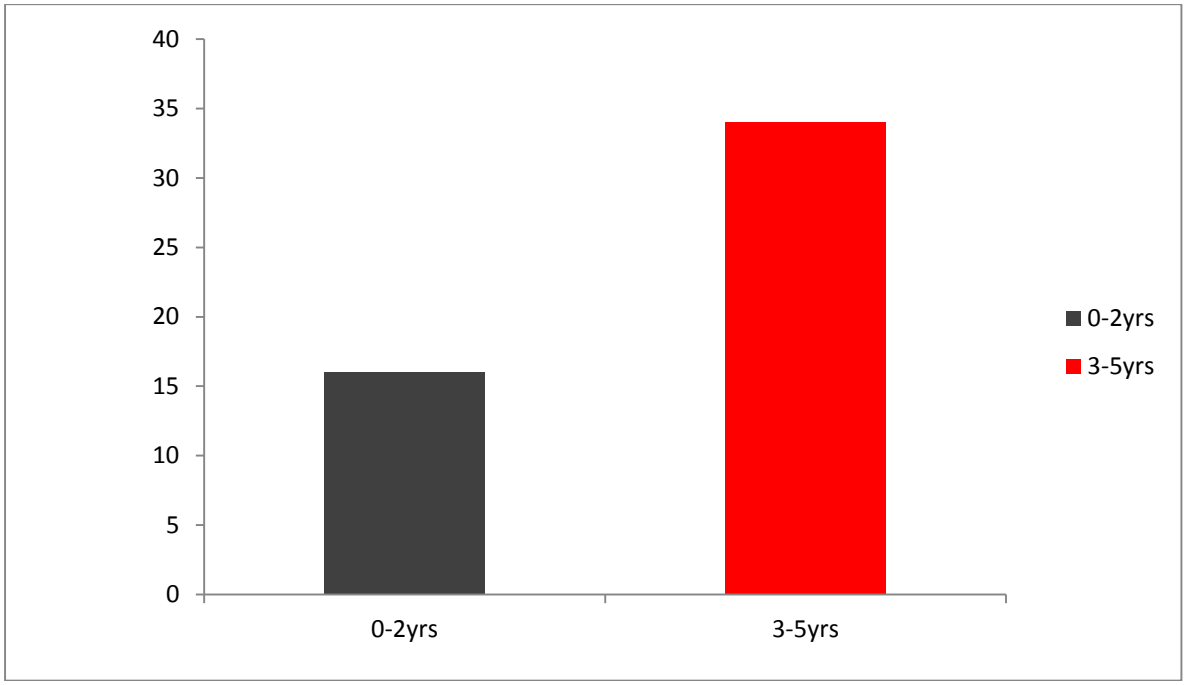

Figure 2. The prevalence of *P. falciparum* malaria parasite infection according to age distribution

Table 1. Serum estimation of biochemical parameters in malaria positive and control in under five children attending Department of Paediatrics, Ahmadu Bello University Teaching Hospital, Shika, Zaria, Kaduna state

Biochemical parameters	Malaria Positive (SD)	Malaria Negative Control (SD)	p-value
Cholesterol (mmol/L)	.45026	.90698	0.000
High density lipoprotein (mmol/L)	.48969	.48653	0.005
Low density lipoprotein (mmol/L)	.23702	.64911	0.000
Triglyceride (mmol/L)	.32579	.46123	0.000
Albumin (g/L)	5.23259	2.81864	0.003
Globulin (g/L)	6.71486	3.25212	0.042
Protein (g/L)	6.61726	3.54520	0.829

Table 2. Estimation of haematological parameters in malaria positive and control in under five children attending Department of Paediatrics, Ahmadu Bello University Teaching Hospital, Shika, Zaria, Kaduna state

Haematological parameters	Malaria Positive (SD)	Malaria Negative Control (SD)	p-value
Packed cell volume (%)	7.00790	5.49521	1.750
Haemoglobin (g/dL)	2.33289	1.83148	0.139

DISCUSSION

This study indicates that males are more vulnerable to malaria infection than females. This finding is consistent with the findings of Akanbi *et al.* (2010). Furthermore, research findings suggest that genetic and hormonal variables have a role in females having a stronger immune response to parasite infections (Zuk *et al.*, 1996).

Moreover, the findings indicate a greater quantity of children between the ages of 3 and 5 in comparison to those between the ages of 0 and 2. The reason for this is that the majority of children admitted to the Department of Paediatric, Ahmadu Bello University Teaching Hospital, Zaria fall between the age range of 5 to 10, with a larger proportion falling between 2 and 5 years old. The World Health Organisation (WHO, 2007) agrees with the findings of this study about the association between malaria infection and age.

The blood lipid profile results obtained in this study were lower than those of the control group, including high-density lipoprotein, low-density lipoprotein, triglycerides, and total cholesterol. However, all values were within the normal range. In line with this research, Chikezie and Okpara (1996) found that individuals with moderate malaria infection had decreased serum levels of low-density lipoprotein and high-density lipoprotein compared to the control group.

Furthermore, the findings of this research correlate with the results of Baptisa *et al.* (1996), which indicated that children residing in regions susceptible to malaria exhibited notably reduced levels of cholesterol, triglycerides, HDLc, and LDLc in their plasma. Ogbodo *et al.* (2008) saw noteworthy reductions in both total cholesterol and HDL levels when comparing them to the control group's results. They stated that the decrease in overall cholesterol levels could be attributed to a substantial decrease in HDL, likely caused by oxidative modification.

Mohanty *et al.* (1992) examined alterations in plasma lipids induced by *Plasmodium falciparum* malaria in a sample of 83 individuals who were in good health, 60 individuals with severe malaria, and 23 individuals with mild malaria. The researchers quantified the concentrations of high-density lipoproteins, low-density lipoproteins, total cholesterol, and triglycerides in the plasma. The patients exhibited lower triglyceride levels compared to the controls, which agrees with the findings of this study. In their study, Al-Omar *et al.* (2010) observed a significant negative correlation between the number of parasites and the level of cholesterol in the blood serum of 200 malaria patients and 200 healthy blood donors of the same age. Increased parasitemia correlated with decreased serum cholesterol levels.

Parola *et al.* (2013) conducted a study that found that reduced HDL and potentially LDL levels are the main factors contributing to the low cholesterol levels observed in malaria. Undoubtedly, a parasitic element connects the reduction in cholesterol transport, esterification by lecithin cholesterol acyl transferase, and/or liver enzyme inhibition to the diminished levels of HDL. Hypocholesterolemia is primarily caused by the parasite's absorption of cholesterol and phospholipids from the host and the negative impact on enzymes responsible for creating HDL. These factors contribute to the development of hypocholesterolemia. In contrast, malaria can rapidly decrease HDL levels due to the accelerated removal of the substance from cells, surpassing its production rate (Mohanty *et al.*, 1992; Nilsson-Ehle and Nilsson-Ehle, 1990).

In this study, the malaria patients exhibited significantly lower total protein, albumin, and globulin levels compared to the controls. This finding correlates with the assertions put forth by McKenzie *et al.* (2005) and Adebisi *et al.* (2002). Albumin has various physiological effects. For instance, it directly affects the vascular endothelium by binding to the endothelial glycocalyx, which helps maintain normal permeability (Curry *et al.*, 1993). Additionally, it has complex effects on erythrocytes (Reinheart *et al.*, 1995). These characteristics suggest that albumin may have a role in the pathophysiology of malaria, particularly cerebral malaria. The albumin molecule's strong negative charge influences the adherence of parasitised red cells to the endothelium, the aggregation of red cells, and the loss of red cell deformability (Emmerson, 1989).

Haematological parameters, such as packed cell volume (PCV) and haemoglobin levels, play a crucial role in the treatment of individuals with malaria. The results obtained from this study show that the PCV value is slightly lower in malaria-infected subjects than in the control group. The decrease in PCV level, sometimes known as anaemia, in malaria-infected individuals, may be attributed to a certain level of haemolysis (Hoffbrand *et al.*, 2005). Another possible cause could be normocytic or normochromic anaemia, namely the type associated with chronic illness, which has been observed in individuals infected with malaria (Hoffbrand *et al.*, 2006).

Similarly, in Ibadan, in south-western Nigeria, Igbeneghu (2005) recorded a prevalence rate of 66.3% for anaemia among children who were infected with malaria. Furthermore, studies conducted in other African countries discovered a prevalence rate of 83.6% and 56.3%, respectively (Valerian *et al.*, 2013). Also, the data obtained indicate a significant decrease in the haemoglobin level among the infected individuals compared to the control group, corresponding to the findings reported by Rosenthal *et al.* (2004).

CONCLUSION

The findings of this study establish the relationship between malaria, biochemical and some haematological parameters. Similarly, significant differences were observed in those parameters relative to age and gender.

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