Journal of Diagnostics
2018 Vol. 5, No. 1, pp. 1-5
ISSN(e): 2409-322X
ISSN(p): 2413-8371
DOI: 10.18488/journal.98.2018.51.1.5

EFFECT OF PLASMODIUM FALCIPARUM ON LIVER FUNCTION PARAMETERS OF CHILDREN IN AKOKO AREA OF ONDO STATE, NIGERIA

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Article History
Received: 22 May 2018
Revised: 20 June 2018
Accepted: 4 July 2018
Published: 10 July 2018

Keywords
Plasmodium falciparum
Children
Serum enzymes
Liver function.

ABSTRACT

Background: Malaria remains one of the most important causes of morbidity and mortality in endemic areas, primarily affecting children under five years of age. The highest death burden occurs in young children who have not yet developed protective immune mechanisms against the parasite. Objective: This study was undertaken to investigate the effect of Plasmodium falciparum infection on liver function in malaria patients in Ikare Akoko, Ondo State Nigeria. Methods: Blood samples taken from 101 patients (children between the ages of 6 months – 5years) at the State Specialist Hospital Ikare Akoko Ondo State Nigeria between August to October, 2012 were examined. After screening, the patients were grouped into two. Group 1, the test group (those who tested positive to falciparum malaria) and a total of 101 children were selected into this group while 101 children who tested negative to malaria were selected into group 2 (control group). Changes in the activities of serum enzymes were determined in both groups using normal range values as baseline. Results: In falciparum malaria patients, the serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) activities respectively were 63.10+2.76, 138.46+5.04, 70.50±4.33 and those of the non infected patients respectively were 62.39+2.96, 131.46+4.38 and 65.57 ±2.39. This indicates the serum levels of ALT, AST and ALP in infected patients were significantly (P = 0.05) elevated relative to their non-infected counterparts, an indication of defective liver function. Conclusion: This study suggests that malaria parasites could be responsible for derangement of the liver functions in patients and could therefore contribute to organ damage in affected individuals if not treated.

Contribution/Originality: This is an original article. It has not been submitted to any other journal for publication. The major contribution to knowledge by this research work is that it suggest malaria parasites could be responsible for derangement of the liver functions in patients and could therefore contribute to organ damage in affected individuals if not treated.

1. INTRODUCTION

Malaria, a disease caused by *Plasmodium species*, is one of the oldest and greatest health challenges affecting 40% of the world's population. It is the most common vector borne disease and a major public health problem in more than 100 countries around the globe with more than 2.5 billion people at risk and affecting 300 – 500 million people annually [1-4] killing between 1-3 million people, with 90 % of such cases occurring in sub-Saharan Africa [5-7] Malaria remains the single most important infection causing morbidity and mortality in the world and is second

only to Mycobacterium tuberculosis as the single most important infectious agent [8]. In endemic countries of Africa, children under the age of five and pregnant women bear the brunt of the burden of malaria disease. This is because they have lower immunity to the disease compared to other people in the same environment [9, 10]. In certain locations, the malaria situation is deteriorating as a result of environmental changes including global warming, civil disturbances, travel and increasing drug resistance [8].

Malaria parasite interferes with 3 major organs in the body namely brain, kidney and liver [11]. The invasion of malaria parasite can cause organ congestion, sinusoidal blockage and cellular inflammation [12] leading to the leakage of the parenchyma and membranous enzymes into the circulation [13] The disease affects almost all organ systems but acute kidney and liver injury are the most dreaded complications of severe malaria. Renal involvement varies from mild protenuria to severe ozotemia associated with metabolic acidosis. The most common renal lesion of malaria is acute renal failure due to acute tubular necrosis and mild proliferative glumerulo-nephropathy [14] Various authors have reported close relationship between incidence of severe malaria and liver damage characterized by jaundice [15-17] Jaundice results from intravascular hemolysis of paralyzed erythrocytes, hepatic dysfunctioning and possibly an element of micro angiopathic hemolysis associated with intravascular coagulation [18]. As mentioned earlier, liver dysfunction has been recognized in malaria infection but information on correlation between malarial infection and hepatic dysfunction in children in Nigeria is scanty. This research therefore, was undertaken to investigate the effect of *Plasmodium falciparum* on the liver function parameters of Nigerian children.

2. METHODS

2.1. Study Location

The study was conducted both at the research laboratory, Department of Biochemistry, Adekunle Ajasin University, Akungba Akoko, Ondo state, Nigeria, where the biochemical analyses were carried out and the pediatric section of the State Specialist Hospital, Ikare Akoko, Ondo state, Nigeria, where the blood samples were collected at the children out-patient unit between August and October, 2012.

2.2. Subjects

The study subjects consisted of 202 children who attended the pediatric clinic section of the general hospital Ikare, Akoko, Ondo State, Nigeria. These subjects were children between the ages of 6 months to 5 years who took ill with fever (temperature >37.5°C), headache, vomiting, diarrhea, respiratory distress and other clinical signs and symptoms of malaria as previously documented [2]. Those children who did not fall into this group were excluded from the study. Apparently healthy children who were symptomatic but tested negative to *P. falciparum* in their peripheral blood were used as control individuals. The scope, nature and objectives of the study were thoroughly explained to the parents or guardians of the children for their consent which was sought and obtained.

2.3. Collection of Blood Specimen

Venous blood samples were obtained from the subjects using a syringe. 2 ml of blood was obtained from each patient by venipuncture into a clean blood container. Each sample was immediately screened for malaria parasite. Plasma was obtained by centrifuging the whole blood samples at 3000 rpm for 10 min at room temperature. The serum was decanted into plain bottles and kept at 4 ^{0}C until required for analyses. Analyses were done within 48 hours in all cases.

2.4. Experimental Design

After the level of parasitaemia was determined, samples were selected for biochemical analyses and grouped into two (2) *inter alia*:

- Group 1 (control group), comprised apparently healthy children who tested negative to the parasite.
- Group 2 (infected group), consisted of children who tested positive with *Plasmodium falciparum.*

2.5. Biochemical Assay Protocols

Alanine aminotransferases (ALT), Aspartate aminotransferases (AST) and Alkaline phosphatase (ALP) activities were determined using standard assay kits obtained from Randox Laboratories, UK. The methods are as described in the users' manuals/leaflets.

2.6. Statistical Analysis

The data obtained were subjected to standard statistical analysis of variance (ANOVA) using the SAS software [19] treatment means were compared using the Duncan procedure of the same software. The significance level was set at P = 0.05.

3. RESULTS

Table 1 shows the effects of P. falciparum on the serum levels of AST, ALT and ALP. Relative to control, the AST and ALT levels of the infected group were significantly elevated (P = 0.05). ALP activity was also elevated but this was not statistically significant (p = 0.05).

Table-1. The effect of P. falciparum on the levels of serum enzymes in children

Groups	AST (U/I)	ALP (U/I)	ALT (U/I)
1(control)	131.46 ± 4.38[a]	65.57 ± 2.39[a]	62.39 ± 2.96[a]
2(infected)	138.46 ± 5.04[b]	70.50±4.33[b]	63.10 ± 2.76[a]

Results are represented as mean ± standard error of mean (SEM). Values carrying different superscripts are significantly different (P<0.05) from each another while those with the same superscript are not significantly different (P>0.05) from one another.

4. DISCUSSION

The observed increase in serum liver enzymes could be due to leakage from hepatic cells that were damaged by the auto immune response and, or by abnormal cell activation induced by the parasites [20]. Previous report showed increased but statistically insignificant levels of alkaline phosphatase (ALP) in experimental mice. It also suggested the elevation indicated that the hepatic stage of the parasite's life cycle in the host, usually accompanied by significant perturbation of the hepatocyte membrane, leads to leakage of the enzyme out of the liver cells [21]. As indicated by alterations in the levels of the liver function markers, there appears to be a measure of liver dysfunction and compromise in *P. falciparum* malaria infected patients, which seems to be more severe. The changes in liver function markers induced by other forms of human malaria parasites (*P. vivax*, *P. malariae* and *P. ovale*) have been observed to be mild and usually reversible after few weeks of anti malaria treatment, but the changes induced by *P. falciparum*, the commonest form of malaria infection have been reported to be complicated [22].

Elevation in serum activities of the three enzymes (ALP, ALT and AST) indicates liver damage. Elevation of serum ALP activity has been attributed to hepatobiliary diseases [23] while increase in serum ALT and AST activity has been reported in conditions involving necrosis of hepatocytes [24].

The observed derangement in liver function in malaria patients in this study may result from alteration in blood flow through the organs as parasitized red blood cells adhere to endothelia cells, blocking the sinusoids and obstructing the intrahepatic blood flow. Histopathological changes have been reported in malaria patients, which include hepatocyte necrosis, cholestasis, and bile stasis [15, 25, 26] The bile stasis might result due to impairment

of bilirubin transport which may lead to reticulo-endothelial blockage and disturbance of hepatocyte microvilli [25, 27, 28] investigated histopathological changes of the liver in malaria patients and observed kupffer cell hyperplasia, malaria pigmentation, portal infiltration and liver cell necrosis all of which are indications of hepatic cell alteration.

5. CONCLUSION

This study shows that malaria infection caused derangement in liver function characterized by significant elevations in the activities of ALT, ASP and ALP. Therefore, adequate prevention and control measures should be employed for management of *falciparum* malaria so as to reduce incidence of tissue damage arising from malaria infection. Use of antioxidants and protease inhibitor may offer clinical benefit by preventing organ complications due to endothelial apoptosis.

Funding: This study received no specific financial support.
Competing Interests: The authors declare that they have no competing interests.
Contributors/Acknowledgement: We are grateful to the management of the State Specialist Hospital, Ikare Akoko, Ondo State, Nigeria under the leadership of Dr Yemi Akinwande and his successor, Dr Olatunde for giving us access to their facilities. We are also grateful to the parents of the children volunteers in this work for their understanding and cooperation. Finally, our gratitude goes to our project students (2011/2012 session), too many to mention here for their robust contributions.

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