International Journal of Pathogen Research

Volume 12, Issue 6, Page 179-184, 2023; Article no.IJPR.110595
ISSN: 2582-3876

Case Study for Hepatic Involvement of Children with Malaria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJPR/2023/v12i6267

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/110595

Original Research Article

Received: 20/10/2023
Accepted: 27/12/2023
Published: 28/12/2023

ABSTRACT

Background: Malaria has a significant impact on public health and economic development in affected regions such as Sub-Saharan Africa. It is a global problem affecting people every year leading to a substantial number of deaths especially among children under the age of 5.
Aim: A cross sectional study of Evaluation of hepatic involvement of children with malaria among the middle age children (6-10years) attending some hospitals and schools in South South region of Nigeria was conducted.
Methodology: Following ethical approval from the institutions as well as concrete consent from the children's families, 418 randomly selected children aged 6 to 10 years participated in the study. Out of this number, 298 children had malaria and 120 children who had no malaria were taken to be the

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control. Blood was collected through the vein using syringe into ethylene diaminetetracetic acid and lithium bottles. Giemsa stain was used to stain the blood films. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyltransferase (GGT), albumin and total protein were analysed with the conventional biochemical methods.
Results: Analysis of the data obtained showed that Aspartate aminotransferase (AST) 18.12±0.47, alanine aminotransferase (ALT) 8.56±0.12, alkaline phosphatase (ALP) 69.55± 0.87 and gamma glutamyltransferase (GGT) 21.41±0.29 values increased (P<0.05) in malaria subjects significantly when compared with the control 5.58±18, 4.62±0.17, 16.58±0.57 and 16.64±0.29 respectively. The study equally revealed that the test group showed significant (P<0.5) decrease of albumin 30.40±0.37 values when compared with the control group54.87±0.90.
Conclusion: The changes in these liver parameters go on to suggest that plasmodiasis might have adverse effect on the hepatic functionality (integrity) as well as the function. Therefore, this should not be neglected as such neglect might result to mortality.

Keywords: Children; liver; malaria; evaluation; albumin; aminotransferase.

1. INTRODUCTION

Malaria remains a major public health problem and cause of suffering and premature death of millions of people in tropical and sub-tropical countries. Malaria-causing parasites, which kills nearly one million people each year [1,2] and is one of the most important causes of morbidity in Africa occurs mostly in tropical regions and rarely in temperate regions. Women and children in malaria endemic areas are more vulnerable to malarial infection. This is due to weak immunity in children and during pregnancy, making women and children more susceptible to malarial infection, increasing the risk of illness, causing severe anemia, neurologic problems and death.

Malaria and its complications cause severe devastating effects on the population thereby compromising the health and growth of millions of children throughout the tropics [3,4]. Malarial infection in humans is caused by the species of the Plasmodium namely *Plasmodium falciparum*, *Plasmodium vivax, Plasmodium ovale* and *Plasmodium malariae,* with *Plasmodium falciparum* as the most common and responsible for most death in Africa. The parasites are transmitted by the bite of female Anopheles mosquitoes, which act as a primary host in the parasite life cycle. The remainder of the cycle continues in the human host, specifically the hepatocytes and erythrocytes causing significant organs dysfunction.

Malaria is endemic in 91 countries with about 40 of the world's population at risk of frequent episodes of malaria especially children. Each year there are 300 million clinical cases of malaria globally with about 90% in Africa resulting in 1.5 to 2.7 million deaths, mostly children under 5 years [5,6]. Malaria is transmitted all over Nigeria with 76% of the population living in high transmission areas while 24% lives in low transmission areas. The transmission season can last all year round in the south and is about 3 months or less in the northern part of the country.

The prevalence of malaria has been reported in Nigeria. According to Wokem et al. [7], the prevalence rate was 67.2% in Ataba and 65. 5% in Port Harcourt, Rivers state, Nigeria while 80.4% prevalence rate was recorded in Ota by Olasehinde et al. [8]; Mmbando et al. [9]. In Aba, Abia State, there was a prevalence rate of 80.4 % reported by Kalu et al. [10]; Oyibo et al. [11] but Enugu State had the lowest prevalence rate of 35.8%.

Malaria has serious impairment in organ function as it interferes with some organs such as the brain, liver, kidney and other organs especially when it is not treated in a timely manner. The liver is mostly affected when individuals have severe malaria and this is always accompanied with increased serum bilirubin and elevated liver enzymes according to the reports by Ignatius et al. [12] and Wokem et al. [13]; Alemu et al. [14]. Several studies revealed that the activities of liver enzymes and the level of parasitaemia correlate positively.

The effect of malaria on the liver cells has been studied extensively without much information on its effect on children who are possibly in their middle years of 6 to 10 years. To this effect, in this study, malaria and its effect on the liver on children who are in the middle years will be studied.

2. METHODOLOGY

2.1 Study Area

This cross-sectional study of hepatic involvement of middle age children with malaria was done among children attending some hospitals and schools in South South region of Nigeria. The city is located at latitude 4º 47´ 21´´ North and 6º 59´ 54´´ longitude.

2.2 Study Design

A total of four hundred and eighteen (418) children were randomly recruited and two hundred and ninety-eight (298) children with malaria were the treatment group while one hundred and twenty (120) children without malaria were the control

2.3 Eligibility Criteria

Inclusion criteria: The children recruited for this study were those within the age range of 6 to10 years who had malaria parasitaemia and no history of liver disease, and were not on any anti-malarial drug. Controls group were children who were not infected by malaria parasite and who had no history of any liver disease after laboratory trials by subjecting them to hepatitis B and C screening.

Exclusion criteria: The subjects that were excluded in this study were all adults and individuals below 6 years and above 10 years of age regardless of their health status, all malaria infected children on anti-malaria medication prior to commencement of this study and hepatitis free subjects.

2.4 Sample Collection and Analysis

A sample of 10 ml venous blood was drawn with syringe. Approximately 5ml of which was dispensed into ethylene diethyl tetracetic acid (EDTA) bottle for malaria parasite test using both thin and thick film techniques [15,16] and quantitative buffy coat for malaria density determination [17]. The remaining 5 ml was used for liver function tests using Reitman and Frankel method for aspartate aminotransferase and alanine aminotransferase and, Rate method for gamma glutamyl transferase [18,19]. Biuret method for total protein, Bromocresol green for albumin and Amstrong method for alkaline phosphatase.

2.5 Statistical Analysis

The various data generated from the analysis were statistically analyzed using SPSS version 23.0 for descriptive and inferential statistics. The descriptive statistics were presented as Mean±SD while T-test was done for inferential statistics. The significance of the test was set at $p<0.05$.

3. RESULTS

Table 1 shows Comparatives Means (±SD) of the Parameters of the Treatment and the Control groups of age group 6 to10 years. From the statistical analysis, Aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyltransferase (GGT) levels were significantly higher ($P<0.05$) in the treatment group which is the malaria-infected group than in the control group which represented those without malaria.

4. DISCUSSION

This work revealed that there was an increase in aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma glutamyltransferase (GGT) levels in those who were malaria positive when compared with those who were not infected (control). This result obtained tallied with the results obtained by Wokem et al. [13]

The rise in liver enzymes might imply an element of hepatic dysfunction, suggesting malarial infection as the major factor as such middle aged children studied were not associated to the many factors that can cause liver derangement in adult such as alcoholism; this now suggests that any derangement in the liver function may be associated with malaria.

Dysfunction in the liver capillaries during malaria attack is primarily due to sequestration of parasite-infected erythrocytes leading to ischemia [20]. Malarial drug toxicity may also be an underlying factor in hepatocyte damage as well as enzyme leakage [21] and the children who were included in this study were not on any anti- malarial drug suggesting that increase in the liver enzymes detected could be traced back malaria infection.

Table 1. Comparative mean values (±SD) of liver function test parameters between treatment and control groups

Parameters	Test n=298	Control n=120	P-value
AST (iu/l)	18.12 ± 0.47	5.58 ± 0.18	P < 0.05
ALT (iu/l)	8.56 ± 0.12	4.62 ± 0.17	P < 0.05
ALP (iu/l)	69.55 ± 0.87	16.58 ± 0.57	P < 0.05
GGT (iu/l)	21.41 ± 0.29	16.64 ± 0.29	P < 0.05
Protein (g/l)	42.45 ± 0.49	65.61 ± 1.04	P < 0.05
Albumin (g/l)	30.40 ± 0.37	54.84 ± 0.90	P < 0.05

Age Range 6-10 years

The study revealed that total protein levels decreased in malaria infected children when compared with non-infected children. This observation was consistent with the reports given by Wokem et al. [9]; Devi et al. [22].

During immune responses, proteins are known to be very important. This suggests that reduced protein levels may be as a result of acute phase responses of infection. In the present study, the decrease in total plasma protein seen in malaria-infected children could be as a result of reduced protein synthesis and falciparum malaria infection could cause destruction of cells responsible for protein synthesis. This finding is in good accordance with previous reports by Christian et al. [23] which showed that chronic infection can cause decreased albumin and total protein levels.

Comparing malaria infected children with the controls, decreased albumin levels were seen in malaria infected children. This finding is in accordance with the study of Wokem et al. [13]; Devi et al. [22]. The severity of malaria depends on an individual's initial immunity. As previously reported, lower albumin levels were seen in severe parasitemia compared to moderate and low parasitemia [13,21,24] and this low albumin levels may be responsible for the severity of fever and other malaria symptoms.

5. CONCLUSION

The levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT) were significantly elevated, and the liver function parameters, total protein and albumin levels was shown to decrease as shown in this study. Therefore, it shows evidence of a positive correlation between increased levels of malaria parasitemia and hepatocellular damage in middle-aged children, which can be fatal if not taken care of adequately.

CONSENT AND ETHICAL APPROVAL

Ethical clearance for the study was obtained from the Ethics Committee, Rivers State Ministry of Health. Informal consent was obtained from the parents and guardians of the children.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/110595