THE EFFECT OF MALARIA DISEASE ON LIVER FUNCTION IN CHILDREN BELOW 5 YEARS OF AGE

ABSTRACT

Malaria continues to be a major global health concern in tropical regions, especially affecting children between the ages of 1 and 5. The aim of this study is to assess the influence of malaria on hepatocellular function in this vulnerable age group. The enrollment of 582 randomly selected children was approved ethically, and parental consent was obtained. Of these, 396 were in the test group (who tested positive for malaria), and 186 were in the control group (apparently healthy). Giemsa-stained thin and thick films were used to confirm the diagnosis of malaria, and serum markers such as SGOT, SGPT, ALP, and gamma glutamyl transferase were used to assess hepatocellular function while the malaria diagnosis was made. As further markers of liver health, albumin and protein levels were evaluated. The findings showed that, in comparison to the control group, children with malaria parasitemia had statistical significantly higher levels of ALP, SGOT, SGPT, and Gamma Glutamyl Transferase as well as lower levels of total protein and albumin ($p < 0.05$). This suggests a significant effect on liver function in children with malaria, ages 1 to 5. Finally, our research highlights the connection between liver impairment in young children and malaria parasitemia. To improve early detection and management of liver-related complications in affected children, we recommend adding hepatic function assessments to routine evaluations, especially in malaria-endemic areas.

Keywords: *Serum glutamic-oxaloacetic transaminase; serum glutamic-pyruvic transaminase; alkaline phosphatase; gamma-glutamyl transferase*

1. INTRODUCTION

Malaria is still a health problem in several tropical and populated areas of the world [1]. Malaria in humans is caused by the following *Plasmodium* species; *Plasmodium falciparum, P. vivax, P. malaria, and P. ovale* but it has been postulated that a new species, *P. knowlesi* also infects humans [2, 24]. The transmission of malaria is well aided by its vectors of which some species of female Anopheles mosquitoes are involved [3, 25]. When blood is affected by malaria, it undergoes some biochemical changes and complications are bound to occur as a result of the disease as shown in some studies [4, 26].

One of the functions of the liver is to carry out carbohydrate, proteins and fats metabolism. During these metabolic pathways, some of the enzymes and the end products released are highly sensitive to the abnormalities that occur in the liver and these abnormalities can be measured and considered as biomarkers of liver dysfunction.

Liver cells are infected by the malaria sporozoites and this causes the organ to be congested and can also lead to sinus obstruction and inflammation of the cells. As a result of these changes in the hepatocytes, there may be leakage of parenchymal enzymes and membranous enzymes into the general stream [5, 27]. Therefore, the increment in hepatic SGOT, SGPT and ALT in malaria patients further suggests that the serum levels of these liver markers increase with increasing *Plasmodium* density.

According to [6, 28], this change suggests that the pre-erythrocytic stage (liver) of the parasite's life cycle in the human host is associated with profound disruption of hepatocyte membranes and hepatic parenchyma, resulting in the release of hepatic enzymes into the blood. It may indicate that there is a possibility of leakage.

During severe malaria attack, hepatic cells are usually involved in the pathophysiology of the disease and most times show in form of jaundice which occurs when bilirubin is raised, liver enlargement and when the enzymes associated with the hepatic cells are elevated [7]. Raised bilirubin in the blood primarily unconjugated is seen in malaria caused by *Plasmodium falciparum* and it is mainly as a result of haemolysis of erythrocytes that are parasitized and non-parasitized ones and sometimes as a result of liver damage.

The present study is concerned with an attempt to ascertain the changes in the hepatic functions of malaria infected children in the study area which will be valuable in the establishment of a reliable diagnosis and therapeutic interventions.

2. METHODOLOGY

Study area

The study was conducted among 1-5 years old children attending Rivers State University Teaching Hospital (RSUTH), Omega Children Hospital, and Palmers Hospital and Schools (Early Breed Group of Schools, St Francis Nursery and Primary school, and Staff Nursery and Primary school) all in Port Harcourt, Rivers State. Port Harcourt is situated at latitude 4º 47´ 21´´ N and longitude 6º 59´ 54´´

Study design

This was a cross-sectional study conducted among randomly selected children between the ages of 1-5 years. A total of five hundred and Eighty-two (582) children were involved in this study. Three hundred and ninety-six (396) children had malaria and were regarded as the test group while one hundred and eighty-six (186) children who were not infected with malaria and were regarded as the control group.

Eligibility

Inclusion criteria

The children included in the study include those within the age range of 1-5 years who had malaria with no history of hepatic disorders and were not on any anti-malarial drug. The control group had children who were not infected with 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

Those whose parents did not give consent, children above ten (10) years of age, had any other underlining health issues, and children on anti-malaria treatments/drugs were excluded from the study**.**

Sample collection and analysis

About 10 ml of venous blood samples were collected aseptically with a disposable hypodermic syringe. About 4ml of which was dispensed into an ethylene diethyl tetra acetic acid (EDTA) sample container for malaria parasite analysis using thin and thick blood film technique to detect malaria presence [8-9] while Quantitative buffy coat used for estimation of parasitic densities [10]. While the remaining 6ml dispensed into heparin bottle and was used for liver function tests; total protein, albumin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyl transferase as parameters using Jendransik and Groff method, Biuret method, Amstrong method, Reitman and Frankel method and Rate method respectively [11-12].

Statistical analysis

Data obtained were subjected to statistical analysis using *t*-test and data were expressed as mean ±SD. This analysis was performed using Graphpad Prism 3.0 Package. The test was considered significant when $p<0.05$.

3. RESULTS

Table 1. below is on the Comparative Means (±SEM) of the Parameters of the Test and Control groups of 1-5years of age. The result revealed that children with malaria had significantly higher

levels (P<0.05) of serum glutamic-oxaloacetic transferase (SGOT), serum glutamic-pyruvic transferase (SGPT), alkaline phosphatase (ALP), and gamma-glutamyltransferase (GGT) than the control group.

Table 1.: Comparative Means (±SEM) of Liver Function Test Parameters of the Test and Control.

Parameters	Test n=396	Control n=186	P-value
SGOT (iu/l)	18.29 ± 0.44	5.68 ± 0.15	P < 0.05
SGPT (iu/l)	8.71± 0.10	4.66 ± 0.13	P < 0.05
ALP (iu/l)	70.38 ± 0.80	17.29 ± 0.55	P < 0.05
GGT (iu/l)	21.86 ± 0.28	15.98 ± 0.25	P < 0.05
Protein (g/l)	42.71 ± 0.43	63.86 ± 0.82	P < 0.05
Albumin (g/l)	31.49 ± 0.35	53.50 ± 0.80	P < 0.05

P-Values $\leq$0.05 is statistically significant

Age Range: 1-5 years.

4. DISCUSSION

Results obtained in the present study showed noticeable increment in activities of enzymes serum glutamic oxaloacetic-transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), and alkaline phosphatase (ALP), and a reduction in protein and albumin levels among children infected with malaria.

Thus, the findings confirmed that children aged 1 to 5 years are the most vulnerable, which is in line with the reports of [13, 14, 15]among others (2021). This could be due to a developing organ (liver), a developing immune system, a lack of protection from mosquito bites, high exposure rates, and nutritional factors [16].

Studies showed that increment in serum levels of liver enzymes, glutamic-oxaloacetic transaminase/glutamic-pyruvic transaminase (GOT/GPT), and alkaline phosphatase are used as

markers of liver damage. The majority of the test subjects had elevated levels of liver enzymes, serum glutamic-oxaloacetic transaminases/serum glutamic-pyruvic transaminase (SGOT/SGPT), and alkaline phosphatase, indicating liver disease. The leakage of hepatic enzymes into the blood is directly proportional to the density of malaria parasites [17-18].

Raised bilirubin is usually caused by parasitized and non-parasitized RBC hemolysis and/or hepatocyte injury in uncomplicated malaria [19]. According to [20], although severe jaundice can occur, the condition is typically accompanied by a slight increase in hepatic enzymes and is more likely to be brought on by hemolysis than by hepatic injury. Previous research has shown that intravascular hemolysis and hepatic dysfunction were the primary causes of jaundice (42.1%) in the current study. Albumin levels were shown to be lower [21].

When comparing malaria-infected children to non-infected children, lower levels of albumin and protein were found. This is in agreement with [22] findings, who observed that participants infected with malaria had a 15% decrease in serum albumin levels. However, a reduction in albumin level could indicate an acute-phase reaction and aid in assessing prognosis at the time of admission. It was unsurprising to find that lower parasitemia individuals had higher albumin levels than those with moderate parasitemia, which was statistically significant ($p<0.05$).

The non-severity of the fever and other symptoms of malaria at such level could be attributed to the increased albumin levels. This finding is in consonance with [23] findings, who demonstrated that there was a drop in albumin level at high parasitemia when compared to low and moderate parasitemia, but that the difference was not statistically significant ($P>0.05$).

5. CONCLUSION

Malaria infection in Sub Saharan Africa has resisted approaches geared towards combating it, however, in the event of malaria infection, a high index of suspicion, prompt diagnosis, and prompt treatment are essential to avoid the morbidity and mortality associated with disease progression, especially in children. The significant decrease in serum albumin and protein levels, as well as an increase in ALP, SGOT, SGPT, and GGT, which are liver function parameters, suggest that high malaria parasitemia has a negative impact on the integrity and functions of the liver in children, which could lead to mortality if not treated.

6. RECOMMENDATIONS

The study recommends several strategies to address the implications of malaria on hepatocellular function in children aged 1 to 5 years. First and foremost, there is a pressing need to integrate routine hepatic function assessments into the standard evaluations for this vulnerable age group in malaria-endemic areas. This proactive approach aims to facilitate the early detection and effective management of liver-related complications associated with malaria. Additionally,

collaborative efforts with healthcare practitioners and policymakers are essential to develop or update protocols and guidelines that explicitly include hepatic function assessments as part of the standard care for pediatric malaria cases. To ensure the proficiency of healthcare providers in conducting and interpreting these assessments, the implementation of targeted training programs is recommended. Concurrently, public health awareness campaigns should be launched to educate parents, caregivers, and communities about the evident correlation between malaria and impaired liver function in young children. Emphasis should be placed on the importance of regular health check-ups, which should include hepatic function assessments as a preventive measure.

Furthermore, the study underscores the necessity for ongoing research initiatives to delve deeper into the specific mechanisms through which malaria impacts hepatocellular function in children. These endeavors should extend to investigating potential interventions and treatments that could effectively mitigate the adverse effects on the liver. International collaboration is encouraged to facilitate the sharing of findings and best practices in managing malaria-related complications in pediatric populations. Advocacy efforts should also be directed towards the inclusion of hepatic function assessments in national and international malaria control policies. Lastly, policymakers are urged to allocate resources for the implementation of routine hepatic function assessments, ensuring that healthcare facilities in malaria-endemic areas are adequately equipped. Establishing a system for ongoing monitoring and evaluation of the impact of these assessments on early detection and management of liver-related complications in children with malaria will contribute to the overall success of these recommendations.

Consent

Written informal consent was obtained from the parents of the children and the institutional authorities.

References

1. Park, K. (2011) . Park's Textbook of Preventive and Social Medicine. 21st. Jabalpur, India: Banarsidas Bhanot
2. Midega, J. T., Mbogo, C. M., Mwambi, H, W., Ojwang, G., Wangang, J. M., Nzovu, J. G., Githune, J., Yan, G. & Beler, J. C. (2007). Estimating dispersal and survival of Anopheles recapture method. *Journal of Medical Entomology*, 44(6),923-929.
3. Nwalozie, R., Onosakponome, E. O., Nnokam, B. A. & Lenox-Prince, T. (2022). Evaluation of Malaria Parasitaemia among COVID-19 Patients in Rivers State, Nigeria. *Journal of Applied Life Sciences International*, 25(4), 12-18.

4. Wokem, G. N, Okafor, R. A & Nwachukwu, B. C. (2008). Some haematologicalprofilesss of children with malaria parasitaemia in Port Harcourt, Nigeria. *Nigerian Journal of Parasitology*,29(2), 92-97.

5. Al-Salahy, M., Shnawa, B., Abed, G., Mandour, A. & Al-Ezzi, A. (2016). Parasitaemia and its relation to hematological parameters and liver function among patients malaria in Abs, Hajjah, Northwest Yemen. *Interdisciplinary Perspective on Infectious Disease,*2016
6. Burtis, C., Ashwood, E., Border, B. (2001). Tietz Fundamentals of Clinical Chemistry. Liver functions. 5th ed. Philadelphia, Pa, USA: Saunders Company.
7. Anand, A. C. & Puri, P. (2005). Jaundice in malaria. *Journal of Gastroenterology and Hepatology*, 20(9), 1322-1332.
8. Michael, W. & Evelyn, O. E. (2021). Evaluating Prevalence and Misdiagnosis of Plasmodium Using Microscopy Compared With Polymerase Chain Reaction Technique in Two Tertiary Care Hospitals in Rivers State, Nigeria. *International journal of infection*, 8(1):e109411.
9. Okafor, R.A., Amadi, F. C.., Okolonkwo, B. N., Nyenke, C. U. & Okeke, C. U. (2022). Implication of Malaria on Liver Health. *Merit Journal of Microbiology and Biological Sciences*, 10(4), 40-45
10. Cheesbrough M. (2006). Transmission, Lifecycle and Analysis of malaria parasite. District Laboratory Practice in Tropical Countries:2nd ed. Cambridge University Press.
11. Okolonkwo, B. N., Chukwubike, U. O. Amadi, C. F. &Nyenke, C. U. (2022a). Therapeutic Effects of Vitamin E on Paraquat Induced Liver Toxicity in Male Albino Rats (*Rattus Norvegicus*). *Journal of Advances in Medicine and Medical Research*, 34(17),1-7

12. Okolonkwo, B. N., Amadi, C. F., Chikwubike, U. O. &Nyenke, C. U. (2022b). The Comparative Effect of Vitamin E + C on the Chronic Toxicity of Paraquat in Albino Rats (*Rattus norvegicus*). *European Journal of Medicinal Plants*, 33(6), 7-13
13. Wokem, G. N., Nnadi, E., Azuonwa, O. & Okafor. A. (2018). Effects of Malaria on Selected Liver Function Effects of Malaria on Selected Liver Function Profiles of Children in Port Harcourt, Rivers State. *International Journal of Tropical Disease and Health*, 31(4), 1-8.
14. Tsegaye, A. T., Ayele, A. & Birhanu, S. (2021) Prevalence and associated factors of malaria in children under the age of five years in Wogera district, northwest Ethiopia: A cross-sectional study. *Public Library of Science*, 16(10).
15. Dao, F., Djonor, S. K., Ayin, C. T. M., Adu, G.A., Sarfo, B., Nortey, P., et al (2021). Burden of malaria in children under five and caregivers' health-seeking behaviour for malaria-related symptoms in artisanal mining communities in Ghana. ParasitesVectors 14, 418.
16. Kafai, N. M. & Odom-John, A. R. (2018). Malaria in Children. *Infectious disease clinics of North America*, 32(1), 189–200.
17. Bisht, R., Mishra, M. & Mishra, S. (2017). Study of Malaria Parasite with Special Reference to Liver Function Test of the Patient Attending at TMU Hospital Moradabad (U.P). *International Archives of BioMedical Clinical Research*, 3(1), 33-37.
18. Ignatius, C. M., Emeka, E. N. & Blessing, N. E. (2008). Effect of malaria parasitaemia on liver enzyme tests. *International Journal of Tropical Medicine*, 3(3), 49–52.
19. Abro, A. H., Ustadi, A. M., Abro, H. A., Abdou, A. S., Younis, N. J. & Akaila S. I. (2009). Jaundice with hepatic dysfunction in *P. falciparum* malaria. *Journal of the College of Physicians and Surgeons Pakistan*, 19(6), 363–366
20. Molyneux, M. E., Looareesuwan, S., Menzies, I. S., Grainger, S. L., Philips, R. E., Wattanagoo, Y. et al. (1989). Reduced hepatic blood flow and intestinal malabsorption in severe *falciparum* malaria. *The American Journal of Tropical Medicine and Hygiene*, 40(5), 470–476.
21. Singh R., Kaur M., Arora D. A. (2010). Prospective study of hepatic involvement in *Plasmodium falciparum* malaria. JournalofClinicalandDiagnosticResearch. 4(2), 2190–2197.
22. Ahsan, T., Ahmad, N., Shaheer, A., Mahmood, T., Ali, H., Farooq, M.U. et al. (2008). Jaundice in *falciparum malaria.* Changing trends in presentation, need for awareness.*Journal Pakistan Medical Association*, 58(11), 616-621.
23. Akech, S., Gwe, S., Idro, R., Fegan, G., Eziefula, A.C. & Charles, R. J. (2006). Volume expansion with albumin compared to gelofusine in children with severe malaria. Result of a controlled trial. Public Library of Science Clinical Trials, 1(5):21.

24. Conroy, A.L., Datta, D. & John, C.C. (2019). What causes severe malaria and its complications in children? Lessons learned over the past 15 years. BMC Medicine, 17(1), 521.

25. Kibret, S., Alemu, M., Teklu, T., & Beyene, B. (2019). Prevalence of malaria and associated factors among febrile children under five years in Adama, Ethiopia: a cross-sectional study. BMC Research Notes, 12(1), 1-62.

26. World Health Organization. (2019). World malaria report 2019.

27. Okeke, T. A., Uzochukwu, B. S., Okafor, H. U., & Ani, O. E. (2020). Assessment of the quality of malaria treatment among febrile under-five children presenting to primary healthcare facilities in Anambra State, Nigeria. PloS one, 15(1), e02278734.

28. Nkumama, I. N., O'Meara, W. P., Osier, F. H., & Newton, C. R. (2022). Factors associated with malaria parasitaemia in children under 5 years in sub-Saharan Africa: a systematic review and meta-analysis. The Lancet Global Health, 10(1), e103-e1155.