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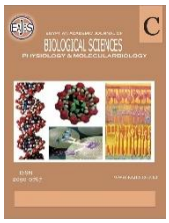

Hepatic Dysfunctions in Malaria-Infected Children: Analyzing the Impact of *Plasmodium falciparum* on the Liver Function Parameters in Sub-Saharan Africa

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ABSTRACT

This study investigated hepatic dysfunctions in children courtesy of malaria infection. Liver function parameters of the infected and non-infected individuals were determined and compared. Serum alanine transaminase (ALT) and aspartate transaminase (AST) were determined by the method described by Reitman and Frankel. Biuret method was used to estimate the serum total protein (TP) and Bromocresol green method was used to estimate the serum albumin (ALB). The concentrations of both AST and ALT of the test subjects were significantly higher ($p<0.05$) when compared with the control groups. There were also some differences between the concentrations of both AST and ALT of female and male patients. The results of the study further show that children between the ages of 0-5 years were more impacted compared to those at the ages of 6-12 years. There were low levels of total protein and albumin in the infected children compared to non-infected children. The study reveals that malaria parasites were shown to make some damages to the liver cells of the infected individuals by increasing the plasma concentrations of ALT and AST and decreasing the hepatic synthesis of proteins and albumin. Findings of this study may be used to make effective intervention and elimination against malaria parasites especially in children living in malaria endemic regions.

INTRODUCTION

Malaria is a disease affecting almost all African and some Asian countries. Malaria is very common in tropical areas of Asia, Central and South America, killing millions of people (De Castro *et al*., 2004; Bomblies *et al.,* 2008; Cohen *et al*., 2009). Malaria is a disease caused by female *Anopheles* mosquitoes, killing millions of people worldwide. However, the majority of people dying from malaria are sub-Saharan Africans, especially children under five years, with *Plasmodium falciparum* being the deadliest and most common in Africa (Snow et al., 2017; WHO, 2023). Each year, millions of people contract malaria leading to estimated deaths of 1 to 2.7 million people (Gallup and Sachs, 2001). Around 90% of people dying from this estimated figure are sub-Sahara Africans, mostly children under five years (Sherman, 1998; Philip, 2011). For instance, in 2019, globally, around 229 million people were infected with malaria with over 409,000 deaths. However, children under the age of 5 years were the most vulnerable group from these deaths (WHO, 2021). Malaria is caused by a protozoon, called *Plasmodium.*

Plasmodium species comprises *Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae and Plasmodium knowlesi* (Walker *et al*., 2017). Among these species, *P. falciparum* is the most lethal and common among African patients. As parasites of malaria are found in red blood cells, the disease can also be transmitted when a contaminated blood is donated to another person, the sharing of used needles or syringes, or through organ transplant (Kileen *et al.,* 2006). The release of malaria parasite materials into the host leads to triggering of host's responses thereby causing various clinical symptoms such as fever, back pain, chills, and headache (Dondorp *et al.,* 2009).

Due to its increasing morbidity and mortality rates, and challenges of antimalarial resistance in most developing countries, malaria remains a public health concern (Jain *et al*., 2016). Malaria infection has been reported to have multi-organ complications (Dondorp *et al.,* 2004). Although reported to have multi-organ complications, liver is the major affected organ during malaria parasite invasion. The infection can lead to compromised hepatic functions through the effects of malaria parasites on synthesis of some important biochemical compounds produced by the liver. Malaria parasites can also cause Kupffer cell hyperplasia, hemozoin loading, and monocytic infiltration (McCarthy *et al*., 2017). Even though some abnormalities in liver function parameters as a result of malaria parasites invasion had been investigated, to the best of our knowledge, no study was performed on the impact of malaria parasites on important parameters such as alanine transaminase (ALT), and aspartate transaminase (AST), total protein, and albumin on the liver of malaria infected children. This study is therefore aimed at investigating the hepatic dysfunction in malaria-infected children in Sub-Saharan Africa.

MATERIALS AND METHODS

1-Study Design/Study Site:

The study was carried out in Federal Medical Centre Gusau. The Medical Centre is located in Gusau, headquarters of Zamfara state, Northwestern Nigeria. Gusau has three (3) seasons, dry, wet (rain), and harmattan. The dry season is partially cloudy and hot throughout, while the wet (rain) is cloudy and rainy. The dry season starts from February to May; the rain season starts from June to October. The harmattan season starts from November to January. Gusau has an area of 3,364 km (2,090 mi)^2 and a population of 383,162 as of the 2006 census, with temperatures ranging from 30°C to 34°C. The study was carried out between May and December, 2024. Two hundred (0-12) children were considered in this study. The hospital is visited by almost everyone regardless of their identity. The second phase of the study, testing of liver marker enzymes was done at Biochemistry Laboratory, Federal University Gusau, Zamfara State.

2-Blood Sample Collection and Malaria Parasite Screening:

At federal medical centre Gusau, left over blood samples of two (2) groups of people (0-5 and 6-12 years) were collected; fifty (50) female and fifty (50) male patients tested positive for malaria. A total of 100 hundred individuals were used for control subjects. The collected samples were analyzed for malaria parasites at hematology laboratory of the health center by a technologist after which the samples were obtained for the analyses.

3-Laboratory Analyses:

3.1 Liver Function Test:

Samples for liver function test were obtained from EDTA anti coagulated blood after centrifugation for 3 minutes at 1000 revolution per minute. The plasma was transferred into clean plain tubes. The samples were frozen at-20 C and batches were run weekly. The analysis was performed using Selectra Pro S Chemistry (ELITech Group Company, Germany). Samples were thawed and placed in paediatric cups. Results displayed on the monitor of this equipment included: ALT, AST, total protein (TP), and albumin (ALB).

RESULTS

3.1 Demographic characteristics of the participating subjects

Table 1 below shows the demographic characteristics of the participating subjects. Volunteers were both males and females. A total of 100 hundred individuals were used for control subjects. This comprises fifty (50) healthy male volunteers and fifty (50) healthy female volunteers. The infected subjects were also fifty (50) males and fifty (50) females. With regards to the ages of the participants, 50 were between 0-5 years and 50 were between 6-12 years in the control groups. Also, 50 were between 0-5 years and 50 were between 6-12 years in the infected group.

Table 1: The Demographic characteristics of the participating subjects.

Features	Number
Total number of test groups	
Female patients	50
Male patients	50
Total number of control groups	
Female patients	50
Male patients	50
Age ranges	
0-5 years	50
6-12 years	50

Table showing number of participating individuals: 50 female patients; 50 male patients; 50 male controls; and 50 female controls; age range: 0-5 and 6-12 years old.

3.2 Liver Enzymes and Protein Levels of Infected Female Children:

The liver enzymes of the infected female subjects showed some levels of derangement from the control group. Generally, the values of biochemical parameters such as AST and ALT were significantly increased ($p < 0.05$) among the children infected with malaria compared with the control (Table 2). However, the levels of Albumin (ALB) and total protein (TP) were significantly decreased ($p > 0.05$) in malaria infected children than values recorded in control, all these observations were made in the female children's participants.

Table 2: Liver enzymes and proteins levels of infected female children.

Subjects	AST (U/L)	ALT (U/L)	ALB (g/L)	TP (g/L)
Control Females No=50	8.50 ± 0.477^{a}	6.00 ± 0.894^{a}	29.53 ± 2.46^{a}	75.256 ± 2.131^{a}
Infected Females No=50	14.36 ± 1.39^{b}	10.71 ± 0.801^{b}	16.920 ± 1.718^{b}	50.63 ± 1.473^{b}

Values are mean$\pm$SEM. Values with different superscripts down the columns are significantly different at ($p<0.05$). AST-Aspartateaminotransferase, ALT-Alanineaminotransferase, ALB-Albumin, TP-Total Protein.

3.3 Liver Enzymes and Protein Levels of Infected Male Children:

The liver enzymes of the infected male subjects displayed some degree of disparity compared with the control groups. The biochemical indices, AST and ALT were significantly raised ($p < 0.05$) in the male children infected with malaria when compared with normal group (Table 3). Meanwhile, the values of ALB and TP were significantly decreased in male children infected with malaria. The results of both test subjects and control groups of all the parameters are shown in the table below.

Table 3: The liver enzymes and proteins levels of infected male children

Subjects	AST (IU/L)	ALT (IU/L)	ALB (g/L)	TP (g/L)
Control Males No=50	8.50±1.716[a]	8.40±0.933[a]	39.40±2.06[a]	75.95±3.53[a]
Infected Males No=50	15.56±1.200[b]	11.56±1.010[b]	18.27 ± 1.082[b]	52.53±1.42[b]

Values are mean±SEM. Values with different superscripts down the columns are significantly different at ($p<0.05$). AST-Aspartateaminotransferase, ALT-Alanineaminotransferase, ALB-Albumin, TP-Total Protein.

3.4 Liver Enzymes and Protein Levels of Infected Children Aggregated by Age:

The liver enzymes of the infected subjects of both age groups showed some derangements from the control groups. There were significant differences in liver enzymes of AST and ALT in the infected subjects of both groups of 0-5 years and 6-12 year-participants compared to the control groups (Table 4). For other parameters of albumin and total protein, there is a wide difference between the control groups and the test subjects (Table 4).

Table 4: Liver enzymes and protein levels of infected children aggregated by age.

Subject	AST (IU/L)	ALT (IU/L)	ALB (g/L)	TP (g/L)
Control (No=100)	9.70±0.620[a]	5.60±0.535[a]	34.45±1.93[a]	75.60±2.00[a]
0-5years (No=50)	17.40±1.189[b]	13.80±1.21[b]	17.44±1.29[b]	51.98±1.31[b]
6-12years (No=50)	16.92±1.406[b]	12.67±1.04[b]	18.075±1.56[b]	51.22±1.70[b]

Values are mean±SEM. Values with different superscripts down the columns are significantly different at ($p<0.05$). AST-Aspartateaminotransferase, ALT-Alanineaminotransferase, ALB-Albumin, TP-Total Protein.

3.5 Liver Enzymes and Protein Levels of Infected Children Aggregated by Sex:

The liver enzymes of the infected subjects of both male and female groups showed some derangements from the control group. There were significant differences in liver enzymes of AST and ALT in the infected subjects of male and female compared to the control groups (Table 5). The same is true in other parameters of albumin and total protein, where there is a wide difference between the control group and the test subjects (Table 5).

Table 5: Liver enzymes and protein levels of infected children aggregated by sex.

Subjects	AST (IU/L)	ALT (IU/L)	ALB (g/L)	TP (g/L)
Control Females No=50	8.50±0.477[a]	6.00±0.894[a]	29.53±2.46[a]	75.256±2.131[a]
Infected Females No=50	14.36±1.39[b]	10.71±0.801[b]	16.920±1.718[b]	50.63±1.473[b]
Control Males No=50	8.50±1.716[a]	8.40±0.933[a]	39.40±2.06[a]	75.95±3.53[a]
Infected Males No=50	15.56±1.200[b]	11.56±1.010[b]	18.27 ± 1.082[b]	52.53±1.42[b]

Values are mean±SEM. Values with different superscripts down the columns are significantly different at ($p<0.05$). AST-Aspartateaminotransferase, ALT-Alanineaminotransferase, ALB-Albumin, TP-Total Protein.

DISCUSSION

Malaria is a disease affecting many developing countries including sub-Sahara African countries, killing hundreds of millions of people especially small children, although caused by many species of *Plasmodium* (Walker *et. al*., 2017), the most lethal and prominent in Africa is *Plasmodium falciparum.* In humans, invasion of malaria parasites leads to compromised hepatic functions (Anand and Puri, 2005). Therefore, assessment of hepatic functions especially during severe malarial attacks can play an important role in effective intervention and elimination of malaria infection. In this study, the activities of important liver enzymes such as AST and ALT as well as total protein and albumin among patients with malaria and those without malaria were assessed. The results of the study indicated that the concentrations of both aspartate transaminase (AST) and alanine transaminase (ALT) were significantly higher ($p<0.05$) when compared with the control groups (Tables 2 and 3) with some slight differences in the concentrations of both AST and ALT between female and male patients.

Differences in the concentrations of AST and ALT of the test subjects and the control groups might be connected to the increased leakages of these liver marker enzymes into the systemic circulation as a result of the damage caused by malaria parasites. Malaria parasites are reported to cause increase in these liver marker enzymes depending on the density of the parasites in the blood (Elnoman *et al.,* 2012). Invasion of hepatocytes by the malaria parasites can lead to sinusoidal blockage, organ congestion, and cellular inflammation which in turn caused the leakage of AST, alkaline phosphatase, and ALT (Burtis *et al.,* 2001; Jarike *et al.,* 2002). From our findings, both AST and ALT of the infected individuals were found to be higher compared to non-infected individuals. This finding agrees with other studies carried out by Enemchukwu *et al.,* (2014) and [19] Mieebi *et al.,* (2020). In both studies, increased levels of ALT and AST in patients with untreated malaria parasites reported by Mosab *et al.,* (2008) and Guthrow *et al.,* (2007) also corroborated these findings.

Also, the results of the study show that children between the ages of 0-5 years were more impacted compared to those at the ages of 6-12 years (Table 4). The issue of age-specific immunity against malaria in malaria endemic regions has been previously reported (Zuk and McKean, 1996; Klein, 2004; Roberts *et al.,* 2001). Vulnerability of children under 0-5 years compared to those at the ages of 6-12 years may be connected to their low level of immunity against pathogens especially in malaria endemic regions. The results of the study also show that male patients were more impacted than their female counterparts (Table 5). Generally, biological sex has been reported to have an effect on responses against pathogens (Fish, 2008; Nhamoyebonde and Leslie, 2014; Bernin and Lotter, 2014; Fischer *et al.,* 2015). Higher occurrence of malaria in male patients compared to female patients had been reported by (Camargo *et al.,* 1996; Abdalla *et al.,* 2007; Mulu *et al.,* 2013). According to the authors, the difference may be due to difference in the exposure between males and females. Our findings also correlate with Briggs *e. al.,* (2020), who also reported a higher prevalence of malaria in males compared to females. According to the authors, the difference was not as a result of lower rates of infections in females, but rather as a result of faster clearance of asymptomatic infections.

Many important blood plasma proteins such as albumin are synthesized by the liver. Albumin among many other functions plays a role in transporting vitamins, drugs, and steroid hormones, as well as tissue growth and healing. Lower than normal levels of albumin and total protein required by the body may signal damage caused to the liver (AFP, 2005). Our study shows low levels of total protein and albumin in the infected children compared to non-infected children. The concentrations of total protein and albumin were significantly lower

in the infected subjects ($p<0.05$) when compared with those of the control groups (Tables 2 and 3). This finding is corroborated by Kayode *et al*., 2011; Ebrahim *et al.,* 2019; Balogun *et al.,* 2021, who reported a decrease albumin levels in malaria patients. Decrease in albumin levels and total proteins in our study may indicate damage to the liver as the blood level of albumin is an indication of liver functions and is ultimately used to assess the degree of severity of many health conditions such as renal diseases (Friedman and Fadem, 2010; Wiedermann *et al.,* 2017) and cardiovascular disease (Chien *et al.,* 2017; Arques, 2020). Therefore, liver being the site of malaria parasite multiplication could have its functions for the synthesis of total albumin and other proteins hampered as such the relationship between malaria and albumin.

CONCLUSION

In this study, malaria infection in children was shown to disrupt liver cells thereby increasing the plasma concentrations of ALT and AST. However, the hepatic synthesis of proteins and albumin was reduced, indicating some levels of damage to the liver, courtesy of malaria parasites. The severity of both cases is higher in male patients compared to female patients and more pronounced in children under the ages of 0-5 years compared to those at the ages of 6-12 years. Hence, this study provides information about the effects of malaria on liver parameters as this will help to differentiate the characteristics pattern of complications from that of viral hepatitis as well as providing effective intervention and elimination of malaria infection especially in children living in malaria endemic areas.

Declarations:

Ethical Approval: Written informed consent was obtained from all the caregivers of the participants. The ethical approval was granted by the Centre of Research and Ethics Committee with reference number FMC/2021/985/008/NHREC/TR/19/03/2016 and permission to carry out the clinical examination of subjects was given by the institution authorities.

Competing interests: Authors of this work have declared that no competing interest exists.

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Availability of Data and Materials: The data presented in this study are available on request from the corresponding author.

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REFERENCES

Abdalla, S.I., Malik, E.M., Ali, K.M. (2007). The burden of malaria in Sudan: incidence, mortality and disability–adjusted life–years. *Malaria Journal* 6:97. DOI: https://doi.org/10.1186/1475-2875-6-97, PMID: 17662153.

American Family Physician. (2005). Evaluation of Abnormal Liver Function Tests. www.aafp.org/afp/2005/0401/p1605.html.

Anand, A.C, Puri, P. (2005). Jaundice in malaria. *Journal of Gastroenterology and Hepatology*, 20 (9):1322-1332.

Arques, S. (2020). Serum albumin and cardiovascular disease: State-of-the-art review. *Annals of Cardiology and Angeology* 69(4): 192–200.

Balogun, J. B., Muhammad, S. S., Dogara, M. M. (2021). Effect of malaria infection on hepatic and renal functions in pregnant women attending antenatal clinic at General Hospital Dutse, Jigawa-Nigeria. *Fudma Journal of Sciences* 5(2): 526–530.

Bernin, H., Lotter, H. (2014). Sex Bias in the outcome of human tropical infectious diseases: influence of steroid hormones. *Journal of Infectious Diseases*, *209 Suppl*.

3:S107–S113. DOI: https://doi.org/ 10.1093/infdis/jit610, PMID: 24966190.

Bomblies, A., Duchemin, J.B., Eltahir, E.A.B. (2008). Hydrology of malaria: Model development and application to a Sahelian village. *Water Resources Research* 44: 12445.

Burtis, C. E., Ashwood, A., Border, B. (2001). Liver Function: Tietz Fundamentals of Clinical Chemistry. 5th Edition. Saunders Company, Philadelphia. 748-770.

Camargo, L.M., dal, Colletto, G.M., Ferreira, M.U., Gurgel, S.M, Escobar, A.L., Marques, A., Krieger, H, Camargo, EP, da Silva LH. (1996). Hypoendemic malaria in Rondonia (Brazil, western Amazon region): seasonal variation and risk groups in an urban locality. *American Journal of Tropical Medicine and Hygiene*, 55:32–38. DOI: https:// doi.org/ 10.4269/ajtmh.1996.55.32, PMID: 8702019.

Chien, S. C., Chen, C. Y., Lin, C. F., Yeh, H. I. (2017). Critical appraisal of the role of serum albumin in cardiovascular disease. *Biomarker Research* 5:(31) 1-9. DOI:10. 1186/ s40364-017-0111-x.

Cohen, J.M., Smith, D.L., Vallely, A., Taleo, G., Malefoasi, G., Sabot, O. (2009). Holding the Line. In Shrinking the Malaria Map: A Prospectus on Malaria Elimination. Edited by: Feachem, R.G.A., A.A. Phillips, G.A. Targett, M.E. Group. San Francisco: The Global Health Group: UCSF Global Health Sciences, 40-60.

De Castro, M.C., Y. Yamagata, D. Mtasiwa, M. Tanner, J. Utzinger, J. Keiser and B. H. Singer (2004). Integrated urban malaria control: a case study in Dar Es Salaam, Tanzania. *American Journal of Tropical Medicine and Hygiene* 71:103-117.

Dondorp, A. M., Lee, S. J., Faiz, M.A. (2004). The role of the host in the pathogenesis of severe malaria. *New England Journal of Medicine*, 351 (17): 1740-1748. Doi: 10.1056/ NEJMoa040123

Dondorp, A. M., Nosten, F., and Yi, P. (2009). Artemisinin resistance in *Plamsodium falciparum* malaria. *New England Journal of Medicine*, 361 (5): 455-467.

Ebrahim, A., Gnanasekaran, N., Genet, S. (2019). Oxidative stress and diminished total antioxidant capacity in malaria patients correspond to increased parasitemia and severity of the disease. *Reactive Oxygen Species* 8(23): 287–296.

Elnoman, A., Elbadawi, N. E., Mohamed, M. I., Elzaki, H., Elimam, N., Ounsa, M. A. A. G., Mohamed, E. Y. (2012). The Effects of Diet and Exercise on Weight-loss - When 2 Plus 2 Could Add Up To 22. *Journal of Physiobiochemical Metabolism*, 1:2.

Enemchukwu, B. N., Ibe, C. C., Udedi, S. C. Iroha, A. Ubaoji, K. I. and Ogundapo S. S. (2014). Liver Function Assessment in Malaria, Typhoid and Malaria-Typhoid Co-Infection in Aba, Abia State, Nigeria. *Pakistan Journal of Biological Sciences*, 17(6): 860-863.

Fischer J, Jung N, Robinson N, Lehmann C. (2015). Sex differences in immune responses to infectious diseases. *Infection* 43:399–403. DOI: https:// doi.org/10.1007/s15010-015-0791-9, PMID: 25956991.

Fish EN. 2008. The X-files in immunity: sex-based differences predispose immune responses. *Nature Reviews Immunology,* 8:737–744. DOI: https:// doi.org/ 10. 1038/ nri2394, PMID: 18728636.

Friedman, A. N., Fadem, S. Z. (2010). Reassessment of albumin as a nutritional marker in kidney disease. *Journal of the American Society of Nephrology* 21(2): 223–230

Gallup, J.L., J. D. Sachs (2001). The

Economic Burden of Malaria. *American Journal of Tropical Medicine and Hygiene* 64(1-2):85-96.

Guthrow, C. E., Morris, J. F., Day, J. W. (2007). Enhanced noneenzymatic of human serum albumin. *Procure National Academic Science United State of America,* 76(9): 4258-4261.

Jain A, Kaushik R, Kaushik R.M. (2016). Malarial hepatopathy: clinical profile and association with other malarial complications. *Acta Tropical;* 159(1): 95–105.

Jarike, A. E., Emuveyon, E. E., Idogun, S. F. (2002). Pitfalls in the interpretation of liver parenchymal and membranous enzyme results. Pre-clinical *P. falciparum* malaria in the Nigerian environment. *Nigerian Journal of Clinical Medicine*, 10: 21-27.

Jessica Briggs, Noam Teyssier, Joaniter I Nankabirwa, John Rek, Prasanna Jagannathan, Emmanuel Arinaitwe, Teun Bousema,Chris Drakeley, Margaret Murray, Emily Crawford, Nicholas Hathaway, Sarah G Staedke, David Smith, Phillip J Rosenthal, Moses Kamya, Grant Dorsey, Isabel Rodriguez-Barraquer, Bryan Greenhouse. (2020). Sex-based differences in clearance of chronic *Plasmodium falciparum* infection. *Epidemiology and Global Health Microbiology and Infectious Disease*. DOI: https://doi.org/10.7554/eLife.59872.

Kayode, O. T., Kayode, A. A. A, Awonuga, O. O. (2011). Status of selected hematological and biochemical parameters in malaria and malaria-typhoid co-infection. *Journal of Biological Sciences* 11(5): 367–373.

Killeen, G.F., Ross, A., Smith, T. (2006). Infectiousness of malaria-endemic human populations to vectors. *American Journal of Tropical Medicine and Hygiene*, 75:38-4.

Klein, S.L. (2004). Hormonal and immunological mechanisms mediating sex differences in parasite infection. *Parasite Immunology;* 26:247–264. DOI: https://doi.org/10.1111/j.0141-9838.2004. 00710.x, PMID: 15541029.

McCarthy (2017). A phase II pilot trial to evaluate safety and efficacy of ferroquine against early *Plasmodium falciparum* in an induced blood-stage malaria infection study. *Malarial Journal,* 15(2): 469.

Mieebi, M. W., Alabrah Peter, W., Eni-Yimini S. A. (2020). The Effects of *Plasmodium Falciparum* Parasitaemia on Liver Synthetic Fidelity and Oxidative Stress Markers. *EJMED, European Journal of Medical and Health Sciences*, 2: 4. DOI: http://dx.doi.org/10.24018/ejmed.2020.2.4.421.

Mosab, N. M. H., Huda, B. A., Rofida, A. A., Khadija, E. M., Mozdalifa, B. O., Fatima, A. S. (2008). Effect of *Plasmodium Falciparum* and *Plasmodium Vivax* on Liver Function: Mainly Alanine Aminotransferase and Bilirubin among Known Malaria Patient's in River Nile State. *Advancements Bioequiv Available*, 2(1): 2-5.

Mulu, A., Legesse, M., Erko, B., Belyhun, Y., Nugussie, D., Shimelis, T, Kassu. A, Elias D, Moges B. (2013). Epidemiological and clinical correlates of malaria-helminth co-infections in southern Ethiopia. *Malaria Journal;* 12: 227. DOI: https://doi.org/10.1186/1475-2875-12-227, PMID: 23822192.

Nhamoyebonde, S, Leslie, A. (2014). Biological differences between the sexes and susceptibility to tuberculosis. *Journal of Infectious Diseases*, *209 Suppl* 3:S100–S106. DOI: https://doi.org/10.1093/infdis/jiu147, PMID: 24 966189.

Philip, A. E. (2011). A malaria transmission-directed model of mosquito life cycle and ecology. *Eckhoff Malaria*

Journal, 10: (303) 1-17. DOI: 10. 1186/1475-2875-10-303.

Roberts, C.W., Walker, W., Alexander, J. (2001). Sex-associated hormones and immunity to protozoan parasites. *Clinical Microbiology Reviews*; 14:476–488. DOI: https://doi.org/ 10.1128/CMR.14.3.476-488.2001, PMID: 11432 809.

Sherman, I.W. (1998). Malaria: Parasite Biology, Pathogenesis and Protection. Washington, DC: ASM Press.

Snow, R.W., Amratia P, Kabaria CW. (2017). The prevalence of *Plasmodium falciparum* in sub-Saharan Africa since 1900. *Nature*, 550(7677): 515–518. https://doi.org/10.1038/nature24059

Walker, N., Nadjm, B., Whitty, C. (2017). Malaria Medicine. *Microorganism*. 7(6): 179.

WHO. (2021). World malaria report 2021. Geneva: *World Health Organization;* 2021.

World Health Organization. (2023). *World Malaria Report 2023*. Geneva: WHO. https://www.who.int/teams/ global- malaria- programme/reports/ world-malaria-report-2023

Wiedermann, C. J., Wiedermann, W. Joannidis, M. (2017). Causal relationship between hypo-albuminemia and acute kidney injury. *World Journal of Nephrology* 6(4): 176–187.

Zuk, M., McKean, K.A. (1996). Sex differences in parasite infections: patterns and processes. *International Journal for Parasitology*, 26:1009–1024. DOI: https://doi.org/10. 1016/S0020-7519 (96)80001-4, PMID: 8982783.