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LIVER PROFILE CHANGES AMONG MALARIA PARASITE INFECTED PATIENTS

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ABSTRACT
Hepatic dysfunctions are part of the pathological effect of malaria infection among patients. This dysfunction is characterized by increase in liver enzyme activities. In this study, the effect of malaria parasites on liver enzymes among patients attending University Clinic, Federal University Dutsin-Ma, North-Western Nigeria is reported. Blood samples were collected from 118 patients and were examined for parasites using standard methods. Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP) activities were determined using Randox enzymes kits. Out of the 118 examined, 107 (90.68%) were positive for malaria parasites. Prevalence of parasite showed significant association with age groups of patients (P = 0.000), with 6 – 15, 36 – 45, and 46 - 55 years having the highest prevalence of 100% each, while 26 – 35 years had the lowest prevalence of 79.31%. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were significantly higher in the severe group than in the mild and negative groups, with ALT (P = 0.002) and AST (P = 0.02) having significant difference. Only ALT (P = 0.004) had significant difference with age groups of patients. This study revealed very high prevalence of malaria among patients visiting the University Clinic and that malaria infection has effect on hepatic functions, and the level of dysfunction is determined by parasite loads/intensity.

Keywords: *Plamodium, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP),*

INTRODUCTION

Malaria remains a complex and deadly disease that puts approximately 3.3 billion people at risk in 109 countries and territories around the world (Roll Back Malaria, 2008). It constitutes a major health problem in developing countries, accounting for about 0.584 million mortality, 90% of which occur in sub-Saharan Africa, predominantly in children less than 5 years of age (WHO, 2015). It is endemic to over 100 nations and territories in Africa, Asia, Latin Africa, the Middle East, and South Pacific. Malaria is essentially a tropical disease occurring in regions between latitude 62^0N and 40^0S, with an altitude of 1,500m. This region is formed mainly within the tropics and sub-tropics, an environment favourable for mosquitoe breeding; this makes malaria endemic in this region (Walter and Davis, 1976). Malaria can be transmitted via three known ways; vector transmission, blood transfusion and congenital transmission (Ezechukwu *et al*., 2004). In vector transmission, the disease is transmitted by the bite of an infected female anopheles mosquito (Klonis *et al.*, 2013). Four species of the *Plasmodium* parasite can infect humans. Most serious forms of the disease are caused by *P. falciparum* (Giboney, 2000). Malaria caused by *P. vivax*, *P. ovale* and *P. malariae* is milder in humans and it is not generally fatal (Wilaratna *et al.*, 1994).

A mosquito infects a person with sporozoites in the process of taking a blood meal. The sporozoites then enter the bloodstream and migrates to the liver. In the liver, they multiply into merozoites which infect and rupture the liver cells, killing the liver cells they occupy and make them detach from neighbouring cells in an attempt to escape back into the bloodstream and thereafter infection continues (Uzuegbu and Emeka, 2011). The invasion of liver cells by the sporozoite form of the malarial parasites can cause organ congestion, sinusoidal blockage and cellular inflammation (Jarikre *et al*., 2002). These changes in hepatocytes can lead to the leakage of parenchyma (transaminases) and membranous (alkaline phosphatase) enzymes of the liver into the circulatory system (Burtis *et al*., 2001); hence the increase in liver enzymes Aspartate aminotransferase(AST), Alanine aminotransferase(ALT) and Alkaline phosphatase(ALP), which has been observed among malarial infected patients (Maegraith, 1981). Onyesom and Onyemakonor (2011) also demonstrated that the various liver enzymes (AST, ALT and ALP) activities in serum increased with increase in malaria parasite density and confirmed that the hepatic (liver) stage of the parasite's life cycle in its human host is accompanied by significant perturbation in the hepatocyte's parenchyma and membrane, leading to leakage of the liver enzymes into the general circulation (Edington, 1967). Hepatic dysfunctions result from cytoadherence, rosetting and sequestration of erythrocytes containing mature forms of malaria parasites in deep vascular bed. These cases are more likely to have acute renal failure and their prognosis is bad (Sharma *et al*., 2012).

Though Auta *et al.* (2016) reported haemoprevalence of malaria and haematological parameters of febrile patients in a hospital in Dutsin-Ma town and other reports abound on effects of malaria parasites on liver enzymes (Onyesom, 2012), evaluation of liver functions in falciparum malaria (Sharma *et al.*, 2012); there is dearth of these information among patients attending University Clinic, Federal University Dutsinma (FUDMA), Katsina State. This work reported the effect of malaria parasites on liver enzymes among patients attending University Clinic, Federal University Dutsinma, Katsina State, Nigeria.

MATERIAL AND METHODS

Study Area

The study was carried out in Dutsin-Ma Local Government Area of Katsina State. Dutsin-Ma LGA lies on latitude 12°26'N and longitude 07°29'E. It is bounded by Kurfi and Charanchi LGAs to the north, Kankia LGA to the east, Safana and Dan-Musa LGAs to the west, and Matazu LGA to the southeast. Dutsin-Ma

LGA has a land size of about 552.323 km^2 with a population of 169,829 as at 2006 national census. The people are predominantly agro pastoralists (Runka *et al.,* 2015), though the location of the University in this area has resulted to an influx of Civil and Public Servants of recent.

Sampled Population
A total of 118 patients attending Federal University Dutsin-Ma (FUDMA) clinic were used for this research.

Sampling and Collection
Two types of specimen bottles were used for blood samples collection; anticoagulant bottle containing Lithium heparin for malaria parasite count and plain, sterile bottle for serum liver enzymes assays.
Blood samples were collected into already labelled clean bottles with undue pressure on either the arm or the plunger of the syringe. Samples in the Lithium heparin anticoagulant bottles were tested immediately for malaria parasite after staining the thin film with leishman stain, while those samples in the plain tubes were allowed to clot and then centrifuged at 1200 x g for 7 minutes at room temperature (29- 31^{0}C) to obtain the sera. The sera samples were collected by aspiration, using a pasture pipette, into sterile bottles and stored frozen until required for analysis.

Test for Plasmodium Parasites
Thin blood films were prepared; air dried, fixed with methanol and stained with 4% Giemsa stain. Slides were examined under microscope at x100 objective overlaid with immersion oil, as described by Auta *et al.* (2016). A slide was considered positive only if any stage of the parasite was seen or negative where no parasite is seen after viewing at least 200 fields (Akambi *et al*., 2004).
No parasite is recorded when no stage of the parasite is observed, and scanty when the parasite load is equal or less than 5 per 100 field, + when it is between 1 and 10 per 100 field, ++ when it is between 11 and 100 per 100 field and +++ when is above 100 per 100 field.

Serum Liver Enzymes Assay
To evaluate the hepatic functions, the activities of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) were determined using RANDOX enzyme kits, with 1cm light path and incubation temperature at 37^{o}C.

Statistical Analysis
The data obtained were analysed using the student's t-test and level of significance was set at $p<0.05$. Results were expressed as mean±standard deviation (±SD).

RESULTS AND DISCUSSION
Among the 118 patients used for the study, 107 patients tested positive for malaria parasites, accounting for 90.68% prevalence. Female patients had higher prevalence (91.67%) than males (89.66%), though no significant association between sexes (P = 0.935) was recorded (Table 1). Among the different age groups of patients (Table 2), 6 – 15, 36 – 45, and 46 - 55 years had the highest prevalence of 100% each, while 26 – 35 years age group had the lowest prevalence of 79.31%. Prevalence of malaria parasite showed significant association with age groupings (P = 0.000).
Considering liver enzymes activities according to parasite load (intensity), ALT and AST showed significantly higher activities among patients with higher malaria parasite (*Plasmodium*) load in the blood (P = 0.002 and 0.020 respectively), with highest activities of the three enzymes among patients with the highest parasite load (+++), presented on Table 3.
In relation to the age groups of sampled patients, only ALT had significant difference in activities (P = 0.004); with age group of 5 – 15 having higher activities of ALT (47.23 U/L), AST (51.42 U/L) and ALP (195.61 U/L) than other age groups, except 46 – 55 age group, which had the highest of ALT, AST and ALP (Table 4).

Table 1: Malaria parasite intensity and prevalence according to the sex of patients examined

Sex	**No Parasite**	**Scanty**	**+**	**++**	**+++**	**Prevalence (%)**	**X^2**	***P-Value***
Male	6	9	19	18	6	89.66	0.827	0.935
Female	5	12	18	17	8	91.67		
Total	**11**	**21**	**37**	**35**	**14**	**90.68**		

Table 2: Malaria parasite intensity and prevalence according to the different age groups of patients examined

Age	No Parasite	Scanty	+	++	+++	Prevalence (%)	X^2	P Value
5 – 15	0	0	2	6	8	100	45.158	0.000
16 –25	5	12	22	22	4	92.31		
26 –35	6	8	7	6	2	79.31		
36 –45	0	0	3	0	0	100		
46 –55	0	1	3	1	0	100		

Table 3: Activities of liver enzymes in relation to malaria parasite load among patients visiting University Clinic, Federal University Dutsin-Ma

Parasite Load	ALT	AST	ALP
No Parasite	21.92±2.62	25.46±4.86	133.49±25.29
Scanty	21.44±3.67	32.23±4.56	168.97±23.90
+	29.96±4.30	40.22±4.07	165.30±20.92
++	32.35±4.47	38.80±4.70	195.16±21.56
+++	55.30±9.06	57.32±8.07	233.83±43.02
P Value	**0.002**	**0.020**	**0.269**

Table 4: Activities of liver enzymes among the different age groups of patients visiting University Clinic, Federal University Dutsin-Ma

Age	ALT (U/L)	AST (U/L)	ALP (U/L)
5 – 15	47.23	51.42	195.61
16 – 25	24.85	35.80	181.56
26 – 35	36.02	39.71	187.68
36 – 45	12.87	27.24	117.39
46 – 55	50.46	44.58	102.23
P value	0.004	0.241	0.565

DISCUSSION

World Health Organization in 2006 reported malaria as a major cause of mortality and morbidity in the tropical and subtropical regions of the world. It was estimated that 300 to 500 million persons suffer from and more than 1 million die of malaria each year, with sub-Saharan Africa accounting for majority of malaria deaths, particularly those in children under five. In 2016, Auta *et al.* reported high prevalence of 61.6% among febrile patients in a hospital in Dutsin-Ma town. The very high prevalence of 90.68% observed in this study is typical of the tropics, where climatic conditions, poor environmental sanitation and high exposure to mosquito bites aid breeding of mosquitoes and transmission of plasmodium parasites among humans. Though this prevalence is higher than the earlier report by Auta *et al.* (2016) and 36.5% prevalence among pregnant women reported by Bawa *et al.* (2014), it is 'not unexpected of a typical tropical area. The nonsignificant association of malaria infection with sex indicates that transmission have no gender preference, as individuals of both sexes have equal risk of infection. This finding is inconsistent with the reports of Deshwal (2012), Wasnik *et al*. (2012), Aundhakar *et al*. (2017) who reported males to have higher prevalence than females and Melhotra *et al.* (1997) who reported malaria prevalence to be higher in females than males.

Prevalence of malaria with age group, marital status and occupation

Intrusion and development of liver cells by the plasmodium sporozoites have been linked with organ congestion, sinusoidal blockage and cellular inflammation (Jarikre *et al*., 2002; Anyasor and Olorunsogo, 2011). These changes in hepatocytes can lead to the leakage of parenchyma (transaminases) and

membranous (alkaline phosphatase) enzymes of the liver into the circulatory system (Burtis *et al*.,2001), which often results to increase in liver enzymes Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP), which have been observed among plasmodium infected patients (Maegraith, 1981). *Plasmodium falciparum* is the major cause of malaria that causes complications, resulting to deaths in most cases (Akanbi, 2015). Renal and hepatic dysfunctions are common complications associated with falciparum malaria, among others in patients living in malaria endemic regions (Ogbadoyi *et al*., 2009; Uzugbue *et al*., 2011). The roles of these organs in the body are very vital, hence the need for early detection and management of their impairment (Akanbi, 2015).

The increase in liver enzymes activities with intensity of parasites reported in this study is similar to the findings of Onyesom and Onyemakonor (2011), who also demonstrated that the various liver enzymes (AST and ALT) activities in serum increased with increase in malaria parasite density. The increase in the serum liver enzymes with intensity of parasites when compared with the parasite negative group in this study shows that malaria parasite infection may be responsible for the increase in the liver enzymes. The increase in liver enzymes could cause hepatic dysfunctions, which is a result of cytoadherence, rosetting and sequestration of erythrocytes containing mature forms of malaria parasites in deep vascular bed. Patients with such conditions are more likely to have acute renal failure and their prognosis is bad (Sharma *et al*., 2012).

The nonsignificant higher level of ALP in the malaria patients when compared to patients with no malaria infection is similar to the finding of Akanbi (2015), who reported ALP level not to be significantly different between malaria infected patients and the control group. There could be unknown factors that may be responsible for this contrary result when compared with other studies and this calls for further study to confirm this.

CONCLUSION

There is very high prevalence of malaria among patients visiting the University Clinic in Dutsin-Ma and malaria infection has immense impact on hepatic functions, and the level of dysfunction caused is determined by parasite load/intensity.

In order to avoid the impairment of the liver caused by malaria parasites, it is highly recommended that patients in the tropical region, where malaria is endemic be tested regularly for malaria parasites, so that suitable medication could be administered before the infection becomes intense. Intermittent preventive malaria treatment as recommended by the WHO could also be useful. The use of insecticide treated mosquito nets is encouraged.

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REFERENCES

Akanbi OM (2015). The influence of malaria infection on kidney and liver function in children in Akoko area of Ondo state, Nigeria. *Journal of Parasitology and Vector Biology* 7(8): 163-168.

Anyasor GN, Olorunsogo OO (2011). Evaluation of selected biochemical parameters in renal and hepatic functions following oral administration of artesunate to albino rats. *Researcher* 3(7).

Aundhakar S., Prajapati P, Prajapati S, Aundhakar A, Kothia D, John D, Shrisath A, Khatri M (2017). Study of Clinical and Hematological Profile of Plasmodium vivax Malaria in a Tertiary Care Hospital in Western Maharashtra, *International Journal of Scientific Study*, 5(3): 257-260.

Auta T, Runka JY, Bawa JA, Sa'adatu SK (2016). Haemoprevalence of malaria and haematological parameters of febrile patients in a hospital in Dutsin-Ma Town, North Western Nigeria. *Biosciences Research in Today's World,* 2:8 – 14.

Bawa JA, Auta T, Liadi S (2014). Prevalence of Malaria: Knowledge, Attitude and Cultural Practices of Pregnant Women in Katsina Metropolis, Nigeria. *European Scientific Journal* 10(21): 148 – 167.

Burtis C, Ashwood E, Border B (2001). Liver Functions: In: Tietz Fundamental of clinical Chemistry: 5th Edn. Saunders Company, pp: 748-770.

Deshwal R (2012). Clinical and Laboratory Profile of Hospitalized Malarial Patients: An Agra-Based Study. *Journal of the Association of Physicians of India* 64(8): 44-47.

Edington GM (1967). Pathology of malaria in West Africa, *British Med. J*., 1: 715-718.

Ezechukwu C, Ekejindu I, Ugochuklwu E, Oguatu M (2004). Congenitally acquired malaria in hyper-endemic area. A Cohot study, *Trop. J. Med. Res*. 8 (2): 44.

Giboney, L., 2000. Mildly elevated liver transaminase levels in the asymptomatic patients. Am. Fam. Phys., 43: 28-35.

Jlarike AE, Emuveyon EE, Idogun SF (2002). Pitfalls in the interpretation of liver parenchymal and membranous enzymes results. In: Preclinical P. falciparum and malaria in the Nigeria Environment. Nig. Clin. Med., 10 (2): 21-27.

Klonis N, Creek DJ, Tilley L (2013). Iron and heme metabolism in Plasmodium falciparum and the mechanism of action of artemisinins. *Current Opinion in Microbiology* 16(6): 722-727.

Melhotra B (1997). Haematological manifestation of Malaria. *Indian Journal of Haematology and Blood Transfusion* 1997; 15- 40.2.

Ogbadoyi EO, Tsado RD (2009). Renal and Hepatic Dysfunction in Malaria Patients in Minna, North Central Nigeria. *Online J Health Allied Scs.* 8(3):1-6.

Roll Back Malaria (2008). Global Malaria Action Plan. 2008, (http://www.rbm.who.int/gmap/index.html)

Runka YJ, Jibia AB, Janaidu S, Nana AB (2015). A field survey on the assessment of awareness about contagious bovine pleuropneumonia (CBPP) in rural pastoral communities of Dutsinma Region, Katsina State, Nigeria. *Sci. J. Vet. Adv.* 4(1):1-12.

Sharma M, Nand N, Kumar H., Suman L (2012). Evaluation of Liver Functions in Falciparum Malaria, *Journal of International Medical Sciences Academy,* 25(4): 229-230.

Uzuegbu UE and Emeka CB (2011). Changes in Liver Function Biomarkers among Malaria Infected Patients in Ikeja Lagos State, Nigeria, *Current Research Journal of Biological Sciences* 3(3): 172-174.

Walter BJ, and Davis JE (1976). Malaria parasite, Historical background. 3rd Edn. W.B. Saunders. *Medical Parasitology* pp: 275.

Wasnik PN, Manohar TP, Humaney NR, Salkar HR (2012). Study of Clinical Profile of Falciparum Malaria in a Tertiary Referral Centre in Central India. *Journal of the Association of Physicians of India,* 60:33-36.

Wilaratna P, Looareesuwan S, Charoenlarp P (1994). Liver profile changes and complications in jaundiced patients with falciparum malaria. *Trop. Med. Parasitol*., 45: 298-302.

World Health Organization (2015). "Achieving the malaria MDG target: reversing the incidence of malaria 2000-2015." (PDF). UNICEF.

Amorim VL, Gomes CM, Lira HL, Franca KB, Ferreira HC, (2007). Bentonites from Boa Vista, Brazil: Physical, Mineralogical and Rheological Properties. *Material Research,* 7(4): 583-593.

Apugo-Nwosu TU, Mohammed-Dabo IA, Ahmed AS, Abubakar G, Alkali AS, Ayilara SI, Nwobi BE (2011). Modeling Rheological Behaviour of UbakalaBentonite as Bingham Plastic and Power Law Fluids. Annual International Conference, Workshop & Exhibition of the Chemical Society of Nigeria, held at University of Ilorin, 19th - 23rd, September.