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Effect of Malaria Parasitaemia on Liver Enzyme Tests

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Abstract: The activities of the liver enzymes-aspartate and alanine transaminases and alkaline phosphatase were investigated in 90 individuals comprising both sexes. Their malaria parasite status and malaria parasite densities were also determined. Sixty individuals served as test subjects, whereas 30 apparently healthy individuals were used as control subjects. The results showed a significant difference ($p<0.05$) in the mean activities of these enzymes in malaria parasite positive subjects when compared with the controls. There was a positive correlation between the enzyme activities and the degree of parasitaemia ($p<0.0001$), whereas comparison drawn between the male and female controls showed no significant difference ($p>0.05$). When the male test subjects were compared with the female test subjects, there was a significant difference ($p<0.05$). The results suggest that liver enzymes increase in malaria parasitaemia to a level dependent on the degree of parasitaemia and also suggest that the liver is involved in the pathophysiology of malaria.

Key words: Malaria, parasitaemia, liver enzymes, parasite, effect

INTRODUCTION

Malaria is essentially a tropical disease occurring in regions between latitude 62° N and 40° S with an altitude of 1,500 m. This region is formed mainly within the tropics and sub-tropics and this makes malaria endemic in this zone (Walter and Davis, 1976). There are 2 epidemiological extremes of malaria known as the stable and unstable malaria (Bulter, 1996). Epidemiological factors that make malaria endemic in the tropics include climatic factors (relative humidity, altitude, rainfall level, mean temperature between 18-29°C) and socioeconomic factors, as all these have effects on the availability of vectors which maintain that transmission of malaria (Bulter, 1996). Malaria can be transmitted by three known ways; vector transmission (Anderson *et al*., 1981), blood transfusion (Strickland, 1991) and congenital transmission (Ezechukwu *et al*., 2004).

The vector for malaria parasite is the female anopheles mosquito (Cheesbrough, 1998). Malaria is a protozoan infection caused by the parasite plasmodium. There are 4 species of the parasite that infect man, namely, *P. falciparum*, *P. malariae*, *P. ovale* and *P. vivax*, with *P. falciparum* and *P. vivax* being the most common (Mc Gee *et al*., 1992). Malaria is endemic in the tropics and sub-tropics. Each year, there are 300-500 million clinical cases of malaria (90% of them in Africa), resulting in 1.5-2.7 million deaths, mostly children under 5 years of age (Ogurin, 2001). Malaria causes such catastrophies as maternal and infant death and abortion. Susceptible groups are children ad adults who have lost or never acquired immunity (Eze and Mazeli, 2001). It precipitates such terribly mutilating afflictions (in children) as Cancrum oris and has numerous complications such as anaemia, pulmonary oedema, renal failure and coma, which may be fatal (Eze and Mazeli, 2001).

Malaria parasite interferes with 3 organs in the body, namely, the brain, kidney and liver (Edington, 1967). The invasion of the liver cells by malaria parasite can cause organ congestion, sinusoidal blockage and cellular inflammation (Jarike *et al*., 2002). When these happen, the parenchymal (transaminases) and membranous (alkaline phosphatase and gamma glutamyl transpeptidase) enzymes of the liver leak out and find their way into the

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circulation, leading to increased enzyme activity (Burtis *et al*., 2001). It has also been shown that some other pathological conditions like hepatitis, cirrhosis, myocardial infarction and muscular dystrophy also lead to increased activity of these liver enzymes (Elles *et al*., 1978). However, the level of increase in activity of these enzymes vary with the causative factors (Nsirim, 1999).

MATERIALS AND METHODS

Subjects: A total of 90 subjects, classified as symptomatic and asymptomatic for malaria were recorded for the study. Sixty symptomatic subjects (66.7%), that presented with fever (temperature> and 37.5°C), headache, joints pains, loss of appetite and vomiting and also tested positive for malaria parasite in their thick blood film, were used as the test subjects, while the asymptomatic subjects, 30 in number (33.3%), were apparently healthy students and staff volunteers of UNTH Enugu and they tested negative for malaria parasite. These served as control subjects. Informed, verbal consent was sought and given by each of the participants, with their ages ranging from 18-65 years.

The test subjects consisted of 30 males and 30 females, while the controls subjects consisted of 15 males and 15 females. Subjects with hepatitis, renal disease and myocardial disease were excluded from the study.

Sample collection and processing: Two specimen bottles were used for each subject. Anticoagulant bottles, containing K_2EDTA for malaria parasite test and plain bottles for serum enzyme assay.

Blood samples were collected by clean venepuncture from the antecubital fossa into already labeled bottles, with undue pressure on either the arm or the plunger of the syringe (Brown, 1980).

The samples in the K_2EDTA anticoagulant bottles were tested immediately for malaria parasite, after staining the thick film with giemsa stain, while those samples in the plain tubes were allowed to clot and the clotted samples centrifuged to obtain the sera.

The sera were separated into sterile bottles and were used for the enzyme assay and when not used immediately, they were stored at -20°C and later used within one week.

Analytical method

Malaria parasite density determiation: The malaria parasite density was determined by examining a thick blood film stained with giemsa stain (Cheesbrough, 1998).

Classification of the degree of parasitaemia: The malaria parasite density was graded as follows:

- 1 parasite/field: Low density (+)
- 2-9 parasites/field: Medium density (++)
- >20 parasites/field: High density (Cheesbrough, 1998)

Assay of liver enzymes: Aspartate and alanine transaminases were assayed by the Reitman and Fankel method using Beckman Spectrophotometer, whereas the method of King and Armstrong (1934) was employed for the estimation of alkaline phosphatase (ALP) activity.

Statistical analysis: Data was analyzed separately using paired t-test. Analysis of variance was done using graph pad prism software. Results were expressed as mean±standard deviation (±SD).

RESULTS

The results showed a general increase in the liver enzymes-aspartate and alanine transaminases and alkaline phosphatase, in subjects with malaria parasite infection. Table 1 shows the different enzyme activities of the test and control subjects. There was a significant increase ($p<0.05$), in the mean levels of AST, ALT and ALP for the malaria parasite positive subjects (50.0±8.7, 60.4± 12.8, 125.5± 11.7 iu L^{-1}), respectively when compared to the controls (13.7±0.8, 11.8±3.2, 62.6±18.6 iuL^{-1}), respectively.

Table 1: The liver enzyme activities of the test and Control subjects

	Test subjects	Control subjects	
No. of subjects	60 Mean±SD	30 Mean±SD	p-value
AST iu L^{-1}	50.0±8.7	13.7±4.1	p<0.05
ALT iu L^{-1}	60.4±12.8	11.8±3.2	p<0.05
ALP iu L^{-1}	125.5±11.7	62.6±18.6	p<0.05

Table 2: The liver enzyme activities of the male and Female test subjects

	Male test subjects	Female test subjects	
No. of subjects	30 Mean±SD	30 Mean±SD	p-value
AST iu L^{-1}	48.3±18.3	39.2±16.4	p<0.05
ALT iu L^{-1}	62.0±23.1	48.3±21.6	p<0.05
ALP iu L^{-1}	130.2±18.6	116.4±18.0	p<0.05

Table 3: The liver enzyme activities of the male and female Control subjects

	Male Control Subjects	Female Control Subjects	
No of subjects	15 Mean±SD	15 Mean±SD	p-value
AST iu L^{-1}	11.0±4.0	10.2±3.7	p>0.05
ALT iu L^{-1}	11.3±2.9	10.4±3.1	p>0.05
ALP iu L^{-1}	67.5±14.2	62.4±21.0	p>0.05

Table 4: The activities of the various liver enzymes at different levels of parasite density

Parasite density/Hpf	0	1-10	11-20	>20	ANOVA		
No. of subjects	30 Mean±SD	19 Mean±SD	32 Mean±SD	9 Mean±SD	F-test	p-value	R^2
AST iu L^{-1}	13.7±.4.1	27.8±6.9	45.4±0.10.3	76.8±8.3	209.4	p<0.0001	0.8796
ALT iu L^{-1}	11.8±3.2	32.3±9.0	56.3±13.6	92.7±14.5	189.4	p<0.0001	0.8686
ALP iu L^{-1}	62.6±18.6	102.9±8.9	132.8±12.5	150.0±12.5	150.7	p<0.0001	0.8402

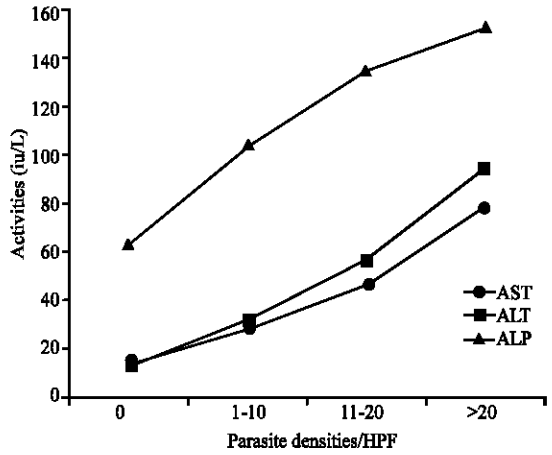

Fig. 1: Relationship Enzyme activities (iu/L) and various malaria parasite densities/HPF

When the male test subjects were compared to the female test subjects, there was a statistically significant increase ($p<0.05$) in the mean levels of the various liver enzymes (Table 2). AST, ALT and ALP for the male subjects were 48.3±18.3, 62.0±23.1 and 130.2±18.6 iu L^{-1}, respectively, while that for their female counterparts were 39.2±16.4, 48.3±21.6 and 116.2±18.0 iu L^{-1} in the same order.

Table 3 shows the enzymes levels of the male and female control subjects, without any statistically significant difference ($p>0.05$) in the mean values. The mean values of AST, ALT and ALP for the male control subjects were 11.0±4.0, 11.3±2.9 and 67.5±14.2 iu L^{-1}, respectively whereas that of the female control subjects were 10.2±3.7, 10.4±3.1 and 62.4±21.0 iu L^{-1}, respectively.

Table 4 shows the relationship between enzyme activity and malaria parasite density and there was a highly significant correlation ($p<0.0001$) between the various enzyme activities and malaria parasite density.

There was also a linear relationship between the various mean enzyme activities and malaria parasite density as shown in Fig. 3.

DISCUSSION

The results of that study show that there was a significant difference ($p<0.05$) in the activity of the liver enzymes AST, ALT and ALP in malaria parasite positive patients when compared to the controls. The International Federation of Clinical Chemistry (IFCC) estimated the reference ranges for AST, ALT and ALP as 8-20, 10-40 and 38-94 iu L^{-1}, respectively. From table 4.1, AST increased to about 3 times the upper limit of normal with a Mean± SD of 50.0±8.7 iu L^{-1}. ALT and ALP increased to about 2 times the upper limit of normal with a Mean±SD of 60.0±12.8 and 125.5±11.7 iu L^{-1}, respective. This agrees with the findings of Jarike *et al.* (2002) who reported an increase in the liver transaminases of up to 3 times the normal and a minimal increase in ALP.

This increase in enzyme activities could be attributed to the destruction of the liver parenchyma by the malaria parasite leading to the leakage of the liver enzymes into the general circulation.

There was also significant higher enzyme activities in the male test subjects when compared with their female counterparts ($p<0.05$). A previous study by Uzoegwu and Onuorah (2003) reported a percentage malaria parasite infection rate of 51.1% in males and 41.4% in females and this higher susceptibility of males to Mp infection than females could be responsible for the higher enzyme activities observed in the male test subjects.

A comparison of the various enzymes at different levels of malaria parasitaemia showed that the various liver enzymes activities increased ($p<0.0001$) with increase in malaria parasite density (Table 4) and a significant positive correlation ($p<0.0001$) was observed between the malaria parasite density and the various liver enzyme activities. This increase in enzymes may indicate the severity of the malaria attack.

RECOMMENDATIONS

Wrong treatment is sequel to misdiagnosis. Since, the activities of the liver enzymes are also increased in some other conditions like hepatitis, a person may be misdiagnosed as having hepatitis when there is an increase in the activity of these enzymes.

All cases of elevated liver enzyme should therefore be referred for malaria parasite screening, as the increased enzyme activity may be as a result of malaria parasite attack rather than primary liver cell damage or hepatitis.

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