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Biochemical Indices in Malaria Infection among Residents of Isu Community, Onicha L.G.A., Ebonyi State Nigeria

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Abstract: This study investigated the biochemical indices of patients with malaria in Isu community, Onicha Local Government Area of Ebonyi State. A simple random sample of 240 individuals was taken from three villages using 95% confidence level and a margin of error of 6.32% with a standard deviation of 0.5. Thick blood smears of venous blood stained with Giemsa were examined microscopically for malaria parasite (MP) and its intensity. Malaria negative individuals served as control. Biochemical parameters (urea, albumin and creatinine) of malaria positive and negative individuals were determined using standard procedures. The overall prevalence and parasite intensity in the study population were 37.5% (n = 90) and 2361+857.55 p/µL respectively. Most of the infected individuals had mild infection. There was no difference in infection rate due to sex. Biochemical indices of malaria positive individuals (urea 4.76 ±2.76 mmol/l, albumin 45.84 ±6.38 mg/dl and creatinine 92.54 ±27.09 µmol/L) were higher than those of the control (urea 4.08 ±1.69, albumin 44.72 ±5.16 and creatinine 76.26 ±19.31µmol/L). The differences were statistically significant (P<0.05) except for the albumin level (P> 0.05). This study has revealed a possible link between malaria parasitaemia and renal dysfunction which would require further investigations to establish. Laboratory diagnosis of malaria infection may be followed up with renal function tests to enhance survival rate of malaria patients.

Key words: Malaria · Effects · Biochemical · Indices · Infected · Residents

INTRODUCTION

Malaria is a term used for acute or chronic infection caused in man or other vertebrates by a protozoa parasite, the *Plasmodium*. It is a life threatening parasitic disease transmitted by infected female *Anopheles* mosquitoes. It is transmitted in the tropics and sub tropic regions containing about three billion people and causes nearly one million deaths each year [1]. It is the most important infection of great global public health concern and by far the world's most important tropical parasitic disease. Despite local and international efforts towards the prevention of the disease, the rate at which people become sick and eventually die as a result of malaria is still worrisome. According to the report of [2], about 500 million people are affected by malaria at any time and approximately 2 million of them mostly children die each year. In 2010 alone, about 216 million cases of malaria occurred all over the world, out of which 655,000 deaths were recorded [3]. This report further revealed that 81% of the occurrence and 91% of those that died were from sub-Saharan Africa. Severe falciparum malaria remains an important cause of mortality in the tropical world with an annual mortality of 1-2.7 million people and a mortality rate as high as 15-30%, despite various anti-malarial treatment available [4].

The infection may be acquired wherever there are human hosts carrying the parasites and a sufficiency of suitable *Anopheles* mosquitoes together with conditions of temperature and humidity which favour the development of the parasite in the mosquitoes as well as problems associated with its treatment and drug resistance.

Four of the known species of *Plasmodium* that commonly infect man are *Plasmodium falciparum, P. ovale, P. vivax and P. malariae.* In the tropics, *Plasmodium falciparum* and *P. vivax* are the most common but mixed infection with two or more of the

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Plasmodium species may also occur. Blood stage cycle of *Plasmodium falciparum* is responsible for most cases of malaria and for the most severe, often fatal forms of the disease. It has varied modes of presentation with occasional life threatening complications. It is said to be complicated when any one or more of the clinical features such as cerebral malaria, jaundice, renal failure, pulmonary oedema, hypoglycemia, circulatory collapse, spontaneous bleeding, repeated generalized convulsion and acidosis are manifested [2].

Malaria affects almost all organ systems (e.g lungs, liver, spleen, brain and kidney). Clinically, significant renal involvement is associated with infections by *Plasmodium falciparum* and *Plasmodium malariae.* Such impairments most of the time lead to nephrotic syndrome or nephrosis which is a group of symptoms caused by the excretion of large amount of protein in the urine (>3g of protein /day) due to kidney impairment or glomerula disorder. It occurs at any age and is characterized by such symptoms as high levels of protein and biochemical markers in the blood [5].

There is paucity in studies on association of malaria with biochemical parameters of the human body in Nigeria particularly in Ebonyi State. Knowledge from such studies would be very necessary because any imbalance in various biochemical markers in the body may affect the organ systems of the body and lead to disease condition.

MATERIALS AND METHODS

Stydy Area: This community based cross sectional survey was conducted in Isu Community in Onicha Local Government Area of Ebonyi State, South-eastern Nigeria. Isu comprises of seven (7) villages with a population of 8544 [6]. The villages include Agbabor, Isuachara, Mgbaleze, Amanator, Uminiko, Mgbala Ukwu-ukwu and Obeagu. Its vegetation is characteristic of derived savannah with high rainfall intensity, high run-off volumes, high relative humidity and an average rainfall of about 1600mm-2000mm per annum [7]. The mean daily maximum and minimum temperatures are 32°C and 25°C respectively.

A government owned General Hospital is the largest health institution located in the area. There are also some comprehensive health centres that operate under the supervision of medical doctors. There is also a strong belief in and use of herbal medicine in the area.

There are two distinct seasons, the wet and the dry seasons, the former runs from April to October, while the latter occurs from November to March.

Ethical Consideration: Clearance was obtained from the Ethical Committee of FETHA, Abakaliki, Ebonyi State. The consent of the village heads and the study participants was sought and permission granted before the commencement of the work.

Sampling Techniques: A two-stage sampling design was adopted in which selection of villages constituted the first stage/Primary Sampling Units (PSUs) and three (3) villages (Isuachara, Agbabor and Mgbala-ukwu) were selected out of the seven villages that make up the community. In the second stage, a simple random sample of 240 individuals was taken from the population of the selected villages (8544) using 95% confidence level and 6.32% error margin with a standard deviation of 0.5. The study was conducted between April 2015 and July 2016.

Thick smears of venous blood obtained from the 240 individuals were stained with Giemsa and examined microscopically for malaria parasite (MP) and its intensity using x100 objective with oil immersion. Parasitaemia was quantified in thick films by counting parasites against white blood cells [8]. Intensity of parasitaemia was measured per high power field or microscopic field. Up to 5-10 high power fields were examined before intensity was confirmed and the number of parasites per field noted per sample. Intensity of parasitaemia was assessed as parasitic index (P1) and expressed as scanty, mild and severe (+, ++ and +++) [9]. All individuals not positive for malaria parasite served as controls.

Determination of Biochemical Parameters

Determination of Serum/ Plasma Urea: Urea levels of both malaria positive and control individuals were determined using the diactetylmonozine methods of [10]. Blood samples were collected with heparin bottles and 100 ml of urease reagent was added to three test tubes. Ten (10) ml of standard solution was added to the standard test tube while 10 mls of the sample was added to the sample test tube. These were incubated for 10mins at 37^0 C. Then 2.5 ml each of the second and third reagents (phenol and hypochlorite) were added to each test tube, mixed and re-incubated for another 20 mins. The value was then read with spectrophotometer at 546 nm and calculated using the equation below.

$$\text{Serum urea} = \frac{\text{Absorbance of sample test}}{\text{Absorbance of standard}} \text{X Concentration of standard}$$

Determination of Serum /Plasma Creatinine: Creatinine levels of malaria positive and negative individuals were determined by the Jaffe-Slot modified alkaline picrate colorimetric method using a Hitachi 407 auto-analyser [11]. Two reagents (sodium hydroxide and sodium bicarbonate) and picric acid were used. Five hundred mililitres of sodium hydroxide, sodium bicarbonate and picric acid were added into a blank test tube and used for zeroing the machine. The same value of these reagents was added to reagent standard tube and mounted into the machine and read immediately.

After 30 seconds, first reading,(Absorbance A) was taken, the second Absorbance (B) was taken after one hour while the final Absorbance (C) was obtained by subtracting Absorbance B from Absorbance A i.e. A-B. This was repeated for sample test and the level of creatinine was obtained using the formula below.

$$\text{Plasma Creatinine} = \frac{\text{Absorbance of sample Test}}{\text{Absorbance of standard}} \text{X Concentration of standard}$$

Measurement of Serum Albumin: The Bromo-cresol Green (BCG) binding method described by [12] was adopted. Three mililitres of blood was centrifuged to separate the plasma from the cells. One mililitre of biuret reagent was added to each of both the sample test tube and standard test tube. Then 10 microlitres of the sample test was added to the sample test tube while standard reagent was added to the standard test tube. These were mixed thoroughly and allowed to stand on the bench for 10 mins. The value was then read with the spectrophotometer at wavelength of 680 nm and the level of serum albumin was calculated using the following equation.

$$\text{Serum albumin} = \frac{\text{Absorbance of test sample}}{\text{Absorbance of standard}} \text{X Concentration of the standard}$$

RESULTS

Overall Prevalence of Malaria Parasitaemia: Out of the 240 samples 107 (44.58%) males and 133 (55.42%) females, 90 (37.50%) were positive for malaria parasite. The mean age ± standard deviation is 30.19±14.69 years while prevalence of infection by sex showed 45 (44.56%) males and 45 (55.42%) females were positive for malaria parasite (Table 1).

Mean Parasite Intensity among Malaria Positive Individuals: The mean parasite intensity was 2361.89±857.55 p/μ with 1854±1066.59 p/μ for positive males and 2869.11±1351.19 p/μ for positive females (Table 1). The mean parasite intensity is highest in individuals in 45 – 51 years age group (7876.67±7307.73 (p/μ) but least in the age group 52 – 58 years (165.00±26.30 p/μ (Tabe 1). The mean malaria parasite intensity is highest in individuals with severe infection, followed by those with moderate infections and least in individuals with mild infections (Table 2).

Biochemical Parameters in Malaria Positive and Negative Individuals: The levels of albumin, urea and creatinine in malaria positive individuals are higher than those of the control. However, the differences in the level of albumin of positive and negative individuals are not statistically significant ($P>0.05$) while those of urea and creatinine are statistically significant ($P<0.05$) (Table 3). Correlation analysis also showed that there is positive but insignificant association between malaria parasitaemia and albumin ($r= 0.052$) (Figure 1) while significant positive association exists between malaria parasitaemia, urea and creatinine ($r= 0.348$ and $r= 0.602$) respectively (Figures 2 and 3).

Biochemical Parameters among Malaria Positive and Negative Individuals by Sex: The mean values of urea, albumin and creatinine are higher in malaria positive males than their negative counterparts but the differences are significant only in the values of creatinine ($P < 0.01$) (Table 4). In the same way, the mean values of urea, albumin and creatinine are higher in positive females than in the negative females but the difference is only significant in the creatinine value ($P < 0.05$) (Table 4).

Comparison of Biochemical Parameters among Malaria Positive and Negative Individuals by Age: The mean values of urea are higher in malaria positive individuals of all age groups except in the age group 3 – 9 years where the value is higher in malaria negative individuals but the differences are not significant ($P > 0.05$) (Table 5). The mean values of albumin of positive individuals were higher in all the age groups except in the groups 31 – 37 years and 38 – 44 years but the differences are not statistically significant ($P > 0.05$) (Table 5). The mean values of serum creatinine of all the age classes were higher in positive individuals than in the controls but the differences are significant only in the 17 – 23 years and 38 – 44 years age groups ($P < 0.05$) (Table 5).

Table 1: Prevalence and Mean Malaria Parasite intensity by Age and Sex.

Number Examined	Number positive (%)	Mean ± S.E(p/µ)
Overall 240	90 (37.5)	2361.89±857.55
Male 107	45 (42.1)	1854.671066.59
Female 133	45 (33.8)	2869.11±1351.19
P value		0.557^{ns}
Total 240	90 (37. 5)	
Age(years)		
3-9 13	2 (15.4)	5320.0 ± 5080.00^{ab}
10-16 25	14 (56.0)	6074.27 ± 4118.971^{a}
17-23 49	18 (36.7)	1567.78 ± 1116.024^{ab}
24-30 56	27(48.2)	324.07 ± 63.79^{b}
31-37 34	12 (35.3)	525.00 ± 160.89^{ab}
38-44 20	4 (20.0)	5795.00 ± 3272.92^{ab}
45-51 18	6 (33.3)	7876.67 ± 7307.73^{a}
52-58 13	4 (30.8)	165.00 ± 26.30^{ab}
59-65 7	3 (42.9)	840.00 ± 680.00^{ab}
66-72 5	0 (0)	0
Total 240	90 (37.5)	2361.89 ± 857.55

In age groups, mean parasite intensity with different alphabet show significant difference (P<0.05).
In sex, 'ns' = no significant difference.

Table 2: Mean Intensity of Parasitaemia in Infected Individuals

Intensity of malaria parasite (N= 240)	Number of individuals infected (%)	Mean ± S.E(p/µ)
Mild	70 (77.8)	$246.\ 43\pm11.56^{b}$
Moderate	13 (14.4)	2040.00 ± 704.78^{b}
Severe	7 (7.8)	$2.41E4\pm7213.73^{a}$

Mean Intensity with different alphabet shows significant difference (P<0.05).

Table 3: Comparison of Biochemical Parameters for Malaria Positive and Negative Individuals

Biochemical Parameters	Malaria +ve individuals (n = 90)	Malaria -ve individuals (n=150)	p value	r value
Albumin (mg/dl)	45.84±6.38	44.72±5.16	0.161^{ns}	0.052
Urea (mmol/L)	4.76 ± 2.76	4.08±1.69	0.018*	0.348
Creatinine (µmol/L)	92.54±27.09	76.26±19.31	0.0001**	0.602

** Significant difference (P<0.05)
* Significant difference (P<0.05)
^{ns} no significant difference (P>0.05)

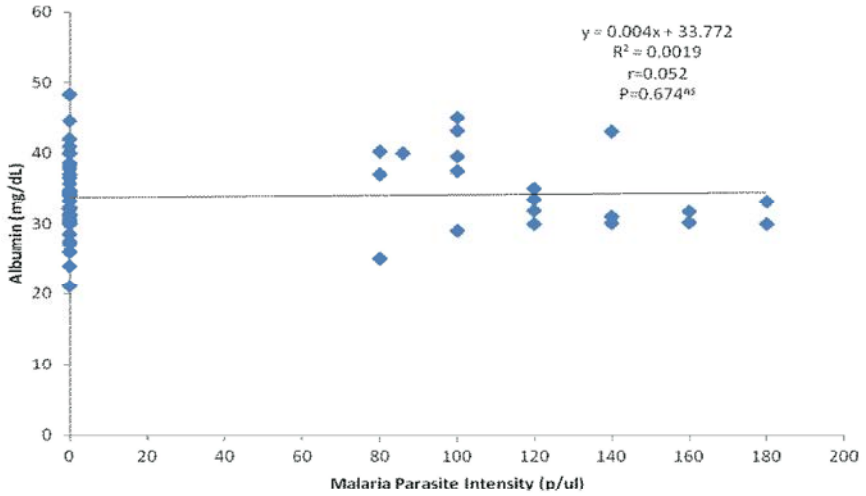

Fig. 1: Malaria Parasite Intensity in Relation to Albumin Concentration among Malaria Infected Individuals

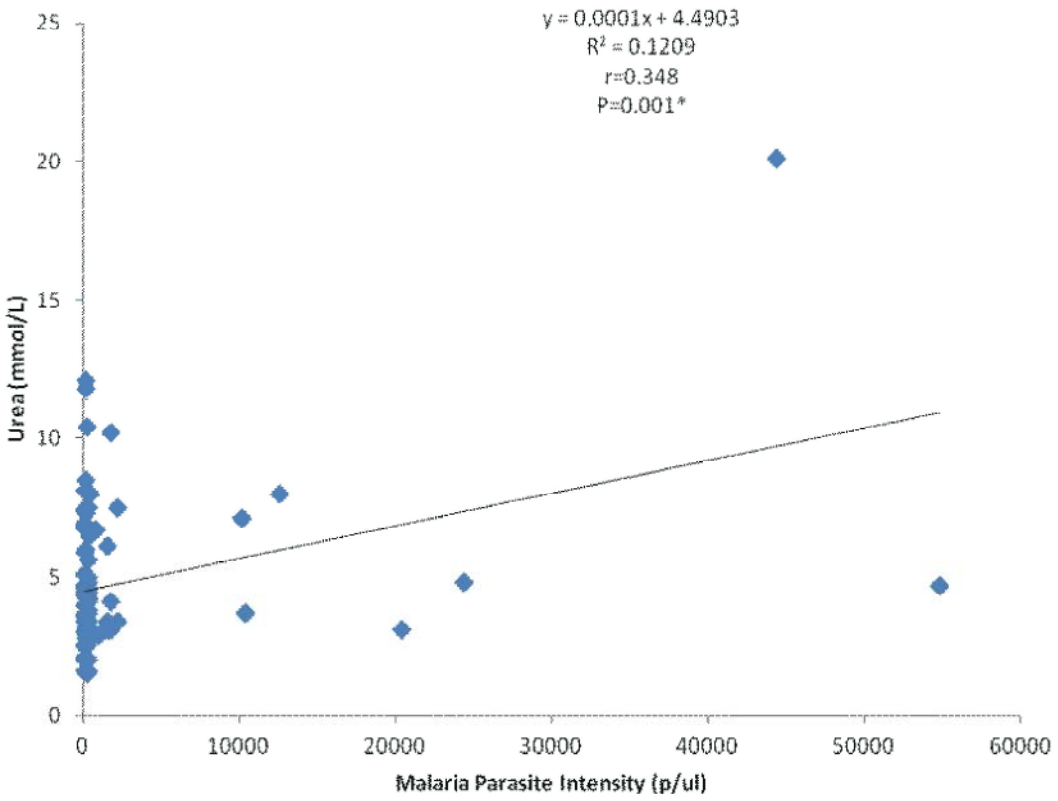

Fig. 2: Malaria parasite intensity in relation to urea concentration among malaria infected individuals

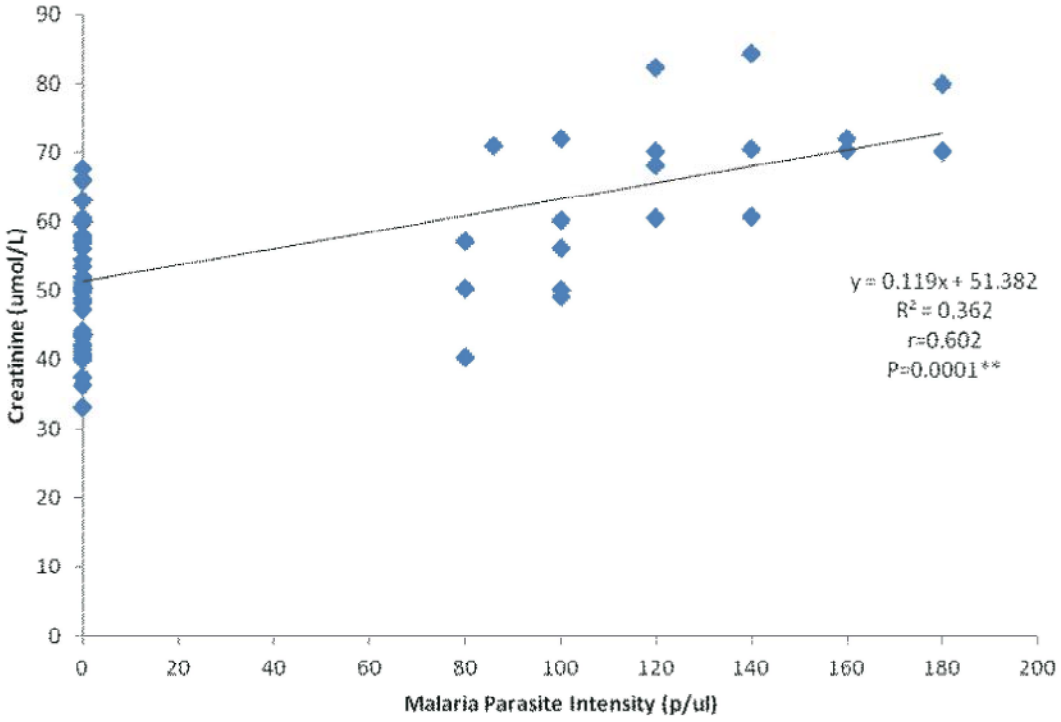

Fig. 3: Malaria Parasite Intensity in Relation to Creatinine Concentration

Table 4: Comparison of Biochemical Parameters of Malaria Positive and negative Individuals by Sex

	Males			Female		
Biochemical Parameter	Malaria +ve (n=45)	Malaria -ve (n=62)	p. values	Malaria positive	Malaria negative	p. values
Urea (mmol/L)	4.99±3.29	4.14±1.35	0.067ns	4.54±2.12	4.05±1.90	0.919ns
Albumin (mg/dl)	44.76±6.87	44.37±4.12	0.717ns	4.69±5.73	4.96±5.79	0.068ns
Creatinine (µmol/L)	102.21±30.14	79.72±25.51	0.0001**	82.87±19.63	73.82±18.14	0.012*

** = Significant difference (P<0.01)

* = Significant difference (P<0.05)

ns = no significant difference (P>0.05)

Table 5: Comparison of Biochemical Parameters of Malaria Positive and Negative Individuals by Age

	UREA (mmol/L)			AIB (mg/dl)			CREAT (µmol/L)		
Age (yrs)	Pos	Neg	P value	Pos	Neg	P value	Pos	Neg	P value
3 – 9	3.7±0.00	4.30±1.77	0.289 ns	44.10±0.14	42.57±3.84	0.218 ns	80.25±8.13	75.88±24.16	0.656 ns
10 – 16	3.81±1.17	3.23±0.80	0.157 ns	46.26±6.21	43.84±3.96	0.249 ns	90.16±33.11	74.57±20.42	0.162 ns
17 – 23	4.54±2.79	3.47±1.09	0.063 ns	45.51±7.21	44.35±5.24	0.558 ns	90.59±29.32	72.80±18.26	0.029*
24 – 30	4.56±2.39	4.12±1.56	0.421 ns	46.17±5.93	44.93±5.33	0.417 ns	89.32±22.07	79.46±17.88	0.074 ns
31 – 37	5.04±2.75	5.05±2.07	0.995 ns	45.07±6.47	46.25±4.55	0.586 ns	89.22±25.34	71.12±24.91	0.057 ns
38 – 44	5.72±2.23	4.52±2.61	0.392 ns	45.35±10.12	46.61±6.73	0.825 ns	107.30±21.84	71.22±15.57	0.038*
45 – 51	7.5±6.22	3.83±1.54	0.055 ns	45.10±4.17	44.61±4.67	0.825 ns	100.23±27.64	80.83±12.54	0.152 ns
52 – 58	5.25±1.53	3.86±0.71	0.168 ns	44.60±2.25	44.39±4.29	0.910 ns	88.73±23.57	87.74±12.50	0.941 ns
59 - 65	4.70±2.44	3.73±0.67	0.564 ns	50.8±13.27	43.15±4.09	0.424 ns	135.77±31.69	77.88±21.42	0.064 ns

* = significant difference (p<0.05)

ns = no significant difference (p>0.05)

DISCUSSION

The result of this study showed that the overall prevalence of *Plasmodium* parasite was 37.50% (n=90). The finding is consistent with several reports from both within and outside the country [13] [14]. This may be due to the fact that factors that favour malaria transmission such as human hosts carrying the parasites and sufficient *Anopheles* mosquitoes, together with conditions of temperature and humidity that favour the development of parasites in the mosquitoes abound in the tropics. However, the prevalence of malaria parasitaemia in this present study is much lower than that of [15], who reported 80% parasitaemia. The wide differences between the result of the present study and those of earlier studies may be attributed to the increased awareness about the infection and the increased use of insecticide treated nets and similar measures recentiy developed for the prevention of malaria.

Among the sexes, the study showed that there was no sex difference in infection. This is contrary to studies by [16], [17] and [18]. These studies reported higher prevalence in males than females. This may be due to the fact that the males expose themselves more than the females especially during hot weather. At such times, they tend to expose themselves more to mosquito bites than the females who cover themselves for decency. However, in most of the studies that reported sex differences, such differences were not statistically significant. The present study is, however, consistent with the findings of [19] who reported that sex do not affect the prevalence of malaria.

Majority of the infected individuals had mild infection (Table 2). Furthermore, the mean parasite intensity of the 90 positive individuals was 2361.89 + 857.55p/µl showing that majority of the infected individuals had low parasite densities. This could be attributed to inate immunity acquired by these individuals from persistent attacks of malaria wich is consistent with protozoa infections. This is in agreement with previous findings of [20] who stated that in hyper-endemic areas, the disease is mild and asymptomatic especially in the adults. Therefore age of the host may represent natural or acquired resistance and hence can play a role in the severity of the disease produced.

The study revealed higher values of urea, albumin and creatinine in malaria positive individuals than the uninfected ones. The differences were statistically significant except in albumin levels. This confirms the earlier report of [21]. High level of proteinuria is an indication of renal impairment [22]. Proteins are normally filtered completely and reabsorbed from the blood stream of healthy kidneys, allowing no protein or only untraceable amounts into the urine. When a reasonable

amount is persistently present in the urine, it is a useful indicator of kidney dysfunction. The infected individuals also had higher mean concentration of serum urea (4.76±2.76 mmol/L) than the control group (4.08±1.69 mmol/L) and the difference was statistically significant ($p < 0.05$). There was also positive significant association between malaria infection and serum urea r=0.348 which corroborates the report of WHO, (2000b). However, worthy of note is the fact that plasma urea level is also affected by a number of non-kidney related factors such as dehydration, food intake and tissue catabolism [23]. The mean serum albumin concentration of malaria patients (45.84±6.58 mg/dl) was higher than that of the control group (44.72±5.16 mg/dl) but the difference was not statistically significant at $p>0.05$. This corroborated the report of [24]. Similarly, the mean serum concentration of creatinine (92.54±27.09 µmol/L) in the infected subjects was significantly higher when compared to that of their control counterparts ($p<0.01$). Malaria parasitaemia and serum creatinine were also positively correlated with r=0.602. These findings are comparable to that of [25].

Serum urea and creatinine concentration are some of the parameters used in assessing renal performance/efficiency. Hence, when their concentrations are higher than normal (>3 gm/dl), renal dysfunction is suspected. This could be suggestive of ineffective filtering ability of the kidneys which could lead to impairment of renal function.

Between the sexes, no significant differences were observed in serum urea, albumin and protein levels. This contrasted the reports of [25]. Serum creatinine level on the other hand was significantly higher in the malaria positive males (101.75±30.32 µmol/L) than in the females (82.84±19.63 µmol/L) ($p<0.05$). High serum creatinine level is usually an indicator of inefficiency in renal function, sex difference in susceptibility to renal dysfunction in patients with falciparum malaria may be possible. There was no significant difference in the serum levels of albumin. On the other hand, the differences in the serum levels of creatinine and urea among the younger and older individuals were significant. As creatinine and urea are the main markers for renal impairment, it is suggested that age may be a factor in renal impairment due to malaria parasitaemia.

CONCLUSION/ RECOMMENDATIONS

The results of this study have revealed possible links between the intensity of malaria parasitaemia and renal impairment. It is therefore recommended that laboratory diagnosis of malaria and renal function should go hand in hand in our health institutions to enable early diagnosis and treatment of both infections. Renal impairment occasioned by malaria infection will therefore be prevented and recovery of already diagnosed patients achieved by early treatment of malaria. This will invariably lead to control and reduction in both mortality and morbidity rates of both infections.

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