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Plasma Concentrations of Kidney Function Indicators in Malaria Patients in Ekpoma, South-South Nigeria

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Abstract: Malaria has protean clinical manifestations and Acute Renal Failure (ARF) is one of its serious complications and could be life threatening. Information on kidney involvement in malaria in Africa is still scanty and Nigeria is no exception. Kidney function was assessed in 60 (28 males and 32 females) malaria positive patients (as test subjects) and 40 (16 males and 24 females) malaria negative individuals (as controls) using plasma creatinine, urea and uric acid as test indicators. Descriptive analysis of results obtained showed that plasma creatinine level was significantly ($p<0.05$) increased in both males and females malaria positive patients (tests) compared to their respective controls (malaria negative males and females, respectively). Female test subjects also had significantly higher plasma urea concentration compared to female controls. No significant change ($p>0.05$) was observed in plasma uric acid between female test subjects and female control subjects. Similarly, plasma urea and uric acid levels were not significantly altered in male test subjects compared to male control subjects. Males test subjects were observed to have higher plasma levels of the test parameters compared to female test subjects. Comparative study between male and female test subjects showed significantly higher concentrations in plasma creatinine and uric acid in male test subjects compared to female test subjects. From these results, it is concluded that renal impairment is a clinical feature of malaria in Ekpoma, South-South Nigeria.

Key words: Malaria, kidney function, acute renal failure, creatinine, urea, uric acid, Nigeria

INTRODUCTION

Malaria is a devastating human disease caused by a protozoan, *Plasmodium* species. Worldwide, estimated 300-500 million people contact malaria each year, resulting in 1.5-2.7 million deaths annually across well over 100 countries (Mishra *et al*., 2002). Out of the species of Plasmodium parasites, *Plasmodium falciparum*, *P. vivax*, *P. malariae* and *P. ovale* that cause malaria in humans, *P. falciparum* is responsible for most deaths and most of the severe complications though renal involvement is also known to be caused by *P. malariae* (Barsoum, 2000; Naqvi *et al*., 2003). Infection due to *P. falciparum* accounts for 80% of malaria cases in Nigeria. Cases of malaria associated renal impairment have been reported from different parts of malaria endemic countries (Wilairatana *et al*., 1994; Ogbadoyi and Tembeng, 1999; Ogbadoyi and Gabi, 2007; Sharma *et al*., 2004). The severity of malaria associated renal impairment in a particular area is largely a function of the disease prevalence and other etiological factors prevailing in the area (World Health Organization, 2000). Prevalence of Acute Renal Failure (ARF) in malaria all over the world has been reported as 0.57-60% (Mehta *et al*., 2001). In southern Asia there is an upsurge in the overall incidence of malarial ARF and has been reported in between 13-17.8% (Mehta *et al*., 2001). ARF occurs commonly in *P. falciparum* malaria although, its rare occurrence has been reported in *P. vivax* malaria (Parkash *et al*., 2003). The disease is more common in adults in those areas of the tropics where transmission of malaria is low or unstable and where symptomatic disease occurs at all ages (World Health Organization, 2000). Established ARF is usually oliguric but urine output may also be normal or even increased in the presence of increasing serum creatinine values (World Health Organization, 2000).

Malarial ARF is emerging as an important problem, especially when the disease is not diagnosed early, the referral to health centre having dialysis facility is late or when dialysis facility is not available. The major aim of

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this study therefore was to assess plasma levels of basic kidney function indicators such as creatinine, urea and uric acid in malaria positive patients attending treatment at Irrua Specialist Teaching Hospital, Ekpoma, South-South Nigeria in comparism to plasma levels of these parameters in malaria negative apparently healthy individual living in the same community.

MATERIALS AND METHODS

Study population: This cross-sectional study was carried out in infectious disease section of Irrua Specialist Teaching Hospital, Ekpoma, Nigeria over a 9 month period between April and December, 2009. The centre is one of the main hospitals in Ekpoma, a university town and Edo State and it serves as a tertiary referral centre for urban and rural populations. The study population comprised a total of 100 individuals made up of 60 (28 males and 32 females) malaria positive patients who served as tests and 40 (16 males and 24 females) apparently healthy malaria negative individuals who served as controls.

Sample collection: After consent was obtained from both patient and institution (hospital management) blood samples were collected by venipuncture technique from subjects (both tests and controls) into lithium heparinized containers, mixed gently and spun as quickly as possible at 3000 rpm for 5 min. Plasma was extracted into plain tubes and frozen at -4°C until required for further analysis.

Assays: Determination of plasma creatinine was carried out using Jaffe's method described by Bowers and Wong (1980). Urea was estimated using urease-Berthelot's method described by Richterich and Kuffer (1973) while plasma uric acid was estimated using uricase method as described by Aoki *et al.* (1992).

Statistical analysis: Data are means±SD. Data was analyzed using SPSS 11.0. The comparism of difference in the means was calculated by student's t-test and difference in proportions was compared by χ^2-test of proportions. P-value of 0.05 was considered significant.

RESULTS

Impairment of renal function as a result of malaria infection was assessed by measurement of plasma concentrations of creatinine, urea and uric acid in both malaria positive (tests) and malaria negative (controls) individuals. Plasma concentrations of creatinine and urea were observed to be significantly higher in female malaria positive test group compared to female malaria negative controls however, plasma uric acid levels in both female test and control groups were not significantly altered (Table 1). Only plasma creatinine concentration was significantly increased as a result of malaria parasite infection in males (test group) compared to male malaria parasite-free group (control). Plasma urea and uric acid in male test and control groups showed no significant modification (Table 2). Comparative study of the values obtained for the parameters study in both female and male malaria positive patients (tests groups) indicated that the male malaria positive patients had significantly higher levels of plasma creatinine and uric acid compared to their female test group, plasma urea level was not significantly different between male and female malaria positive test groups (Table 3).

Table 1: Plasma concentrations of kidney function parameters in females' malaria negative (controls) and females' malaria positive (tests) in Ekpoma, South-South, Nigeria

Parameters	Control (n = 16)	Test (n = 28)	t-cal	p-value
Creatinine (mg dL^{-1})	1.0±0.1	1.2±0.30*	3.5	<0.05
Urea (mg dL^{-1})	21.6±6.2	26.8±12.0*	2.1	<0.05
Uric acid (mg dL^{-1})	3.7±1.0	4.0±1.20	1.0	>0.05

Results are means±SD; *statistically different from control

Table 2: Plasma concentrations of kidney function parameters in males' malaria negative (controls) and males' malaria positive (tests) in Ekpoma, South-South, Nigeria

Parameters	Control (n = 24)	Test (n = 32)	t-cal	p-value
Creatinine (mg dL^{-1})	1.2±0.20	1.4±0.30*	2.6	<0.05
Urea (mg dL^{-1})	29.9±13.0	32.0±18.4	0.4	>0.05
Uric acid (mg dL^{-1})	4.5±1.40	5.0±1.40	1.6	>0.05

Results are means±SD; *statistically different from control

Table 3: Comparism of plasma concentrations of kidney function parameters in males and females malaria positive (test groups) in Ekpoma, South-South, Nigeria

Parameters	Male (n = 28)	Female (n = 32)	t-cal	p-value
Creatinine (mg dL^{-1})	1.4±0.30	1.2±0.30*	2.6	<0.05
Urea (mg dL^{-1})	32.0±18.4	26.8±12.0	1.3	>0.05
Uric acid (mg dL^{-1})	5.0±1.40	4.0±1.20*	2.9	<0.05

Results are means±SD; *Statistically different from control

DISCUSSION

Malaria is caused by 4 species of the genus *Plasmodium* namely, *Plasmodium vivax*, *P. falciparum*, *P. malariae* and *P. ovale*. Common clinical presentations of infection with all 4 *Plasmodia* species are periodic paroxysm, chills, rigors, sweating, body aches, headache, nausea, general weakness and prostration. Severe life-threatening complications such as Cerebral Malaria (CM), severe anemia, acidosis, respiratory distress, jaundice, Acute Renal Failure (ARF), Acute Respiratory Distress Syndrome (ARDS), etc., occur mostly with *P. falciparum* infection. Renal involvement has been reported in *P. falciparum*, *P. malariae* and recently *P. vivax* infections. *P. malariae* associated nephropathy was reported mainly from Africa that too before 1980.

Incidence of progressive glomerulonephritis was significantly higher inmalaria-endemic areas of Africa (Barsoum and Sitprija, 1996). The pathogenesis of renal involvement in malaria is possibly mediated through immune complex deposition.

Histopathologic observations include features of mesangiocapillary glomerular and subendothelial immune complex deposits containing IgG, C3 and malarial antigens. The disease progresses to renal failure even after successful eradication of the infection (Das, 2008).

In contrast to other studies (Manan *et al*., 2006; Naqvi *et al*., 2003; Parkash *et al*., 2003) there were more female malaria patients in this study. A similar study (Ogbadoyi and Tsado, 2009) carried out in Nigeria also revealed the same trend. Data presented in this study show that plasma creatinine level is significantly elevated due to malaria parasite infestation in both males and female test groups. This is consistent with the report of Ogbadoyi and Tsado, 2009) who had earlier observed that serum creatinine concentration was elevated in male and female malaria patients in Minna, North Central Nigeria compared to male and female malaria negative control groups, respectively. In accordance with the submission of Delanghe *et al*. (1989), elevated plasma creatinine concentration could be suggestive of ineffective filtering ability of the kidney which could results from renal function impairment.

Plasma urea was also observed to be higher in malaria patients (though not to a significant level in males) compared to malaria negative control as has been reported by Friedman *et al*. (1980) that Blood Urea Nitrogen (BUN) is increased in intrinsic renal disease. This observation also agrees with the report of Ogbadoyi and Tsado (2009) who also reported increased serum urea in malaria patients in Minna, North Central Nigeria. It is important to state that plasma urea level is affected by a number of non-kidney related factors. However, in catabolic-type malarial acute renal failure a rapid rise in plasma urea and creatinine may result due to increased catabolism.

CONCLUSION

Results of this study show that male malaria subjects tend to present higher plasma levels of creatinine, urea and uric acid. This observation contradicts earlier report by Ogbadoyi and Tembeng (1999) and Ogbadoyi and Gabi (2007) carried out in Minna, North Central Nigeria, it however, agrees with the report of Ogbadoyi and Tsado (2009).

A study on the effect of antimalaria drug therapy on plasma levels of kidney function parameters is warranted in order to be able to make a reasonable conclusion from the results of this study. However, early and prompt diagnosis along with with antimalarial therapy are the main measures likely to reduce malarial acute renal failure. Early referral of malarial ARF patients to dialysis facility unit may further reduce mortality and enhance recovery function.

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