

A study on incidence and severity of acute renal failure and its association with parasite density in hospitalised patients with falciparum malaria

Mukhopadhyay P¹, Das BK², Biswas N.M.³

¹Dr. Pinaki Mukhopadhyay, Associate Professor, Department of Nephrology, ²Dr. Biman Kumar Das, Post Graduate trainee, Department of Medicine, ³Dr.NM. Biswas, Professor, Department of Medicine, NRS Medical College, Kolkata, West Bengal, India.

Address for Correspondence: Dr. Pinaki Mukhopadhyay, Associate Professor, Department of Nephrology, N.R.S. Medical College & Hospital, Kolkata, India. Email: drpinaki71@yahoo.com

Abstract

Aims of the study: To find out the incidence of acute renal failure in falciparum malaria and to correlate between the degree of parasitism at presentation with acute renal failure and its outcome in falciparum malaria. **Methodology:** Each patient with a history of fever, suggestive of severe malaria was subjected to peripheral blood smear examinations, up to 3 samples were examined or till positive and/or Pf antigen positive cases. The selected patients were then grouped according to the clinical features, laboratory parameters and were followed up for the outcome. **Results:** Out of the 50 cases of acute renal failure due to falciparum malaria, 21 had Parasite density <5% (42%), 13 had 5-10% (26%) and 16 had >10% (32%). Out of 21 cases of mild ARF 12 patients had parasite density<5% and 9 had >5%. Out of 29 cases of severe ARF 9 patients had parasite density<5% and 20 had >5%.Dialysis was done in a total of 31 cases (62%). In the severe form of acute renal failure. hemodialysis was required in 29 cases (58%), in the milder form of renal failure; only 2 cases (4%) required hemodialysis. Rests of the cases were managed by conservative treatment. **Conclusion:** Parasite Density has significant impact to predict the severity of renal failure,duration of hospital stays as well as the number of dialysis required. As the study was conducted with small number of cases, further study is necessary with large number of cases to arrive at a conclusion regarding the malady of acute renal failure in falciparum malaria.

Introduction

Malaria is one of the most widespread diseases in the world, reaching latitudinal extreme of 64° north and 32° south. Approximately 5% of the world's population is infected (3 billion people) and approximately one to three million deaths each year [1]. Malaria is characterized by intermittent fever with chill and rigor; and Hepatosplenomegaly being its main clinical features. Within the scope of the definition is included "malignant tertian malaria", a potentially fatal form of malaria where blood flow to vital organs like kidney, brain; and lung may be compromised leading to complications like acute renal failure, cerebral malaria; and pulmonary oedema.

Parasite Density is an important marker of degree of infection. It is calculated by different methods. Of them the reliable methods are of two types; one is based on the parasite/leucocyte ratio in the thick smear, the second on the mean number of parasites per oil immersion field [2]. The latter requires standardization of the thickness of the smears, which is usually difficult to achieve. Various studies show the strong correlation between the parasite density and severity of both falciparum and vivax malaria. In West Bengal, incidence of malaria, particularly that of the virulent plasmodium falciparum form is high and specially Kolkata with its suburban area and foothills of North Bengal become endemic zone for malaria. A significant number of patients with falciparum malaria get hospitalized due to acute renal failure

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which often has an adverse outcome despite therapy. There have been reports from other countries showing high incidence of acute renal failure which has significantly influenced the prognosis of falciparum malaria [3].

In view of the potential reversibility of the acute renal failure, if adequate treatment is given early in the course of the disease the survivors usually show complete recovery.

Materials and Methods

Type of study: This is an observational prospective nonrandom consecutive selection study

Place of study: The present study was conducted in Nil Ratan Sircar Medical College and Hospital, Kolkata. Patients admitted in the in-patient department of Medicine at Nil Ratan Sircar Medical College and Hospital from 1st January 2011 to 30th June 2012 were considered for the study.

Inclusion Criteria- The inclusion criteria were all cases of *P. falciparum* malaria, confirmed by detection of *P. falciparum* antigen and/or in peripheral blood smear (thick and thin films) and acute renal failure will be determined by the following criteria: 1. Malarial ARF (MARF) is diagnosed when serum creatinine level > 3 mg/dl, and/or urine output < 400 ml/24hrs despite adequate rehydration. No past history of renal failure or insufficiency.

Exclusion Criteria- The exclusion criteria were patients' ≤ 12 years, patients already on anti-malarial therapy, known cases of chronic renal failure or other renal disease and *P. Vivax* malaria infection.

Results and Observations

Table-1: Showing incidence of ARF in *P. falciparum* malaria.

Category	No. of patients	Percentage
No renal involvement	124	71.3%
Acute renal failure	50	28.7%

Table 1 depicts out of the 174 patients with severe falciparum malaria, 50 patients (28.7%) had acute renal failure in falciparum malaria.

The above shows that 36 (72%) cases were males and 14 (28%) were females, indicating a much higher incidence in males. In the present study, the maximum numbers of cases 32% were seen in the third decades followed by 4th decades 26%. Approximately 78% of the cases in the present study were below the age of 40

Sampling Procedure- A total of 50 cases of acute renal failure were selected from 174 patients diagnosed to be suffering from falciparum malaria.

The parameters studied were falciparum antigen, parasite Density, urea, serum creatinine during admission, at 1st, 3rd and 6th months, ultrasonography of KUB and urine output.

Each patient with a history of fever, suggestive of severe malaria was subjected to peripheral blood smear examinations, up to 3 samples were examined or till positive and/or Pf antigen positive cases. 2. Patients with falciparum malaria only were considered for the study. The selected patients were then grouped according to the clinical features, laboratory parameters and were followed up for the outcome. All complicated malaria cases were treated with Quinine as 10mg/kg body weight intravenously in 5% dextrose infused over 4 hours at 8 hours interval for three days or till the patient becomes conscious and takes Quinine by mouth, whichever is longer. Quinine was given for a total duration of 7 days OR with Artesunate as 2.4 mg/kg body weight IM/IV followed by 2.4 mg/kg body weight after 12 hours and then 2.4 mg/kg body weight once daily for total duration of 5 days.

All patients were followed with thorough clinical examination and biochemical evaluation as indicated by the patients' condition for the assessment of improvement.

Aims of the Study: We intend to find out the incidence of acute renal failure in falciparum malaria and also find correlation between the degree of parasitism at presentation with acute renal failure and its outcome in falciparum malaria.

years. The youngest was 15 years old and the oldest was 61 years old (Mean age – 32 ± 11.6 years). Majority of our subjects had oliguria or anuria (72%). Out of the 50 patients 45 had marked reduction in GFR with a mean value of 10.65, whereas other 5 patients had less marked fall of GFR with a mean value of 25.58. Study of the renal function tests reveals that majority of the patients had significant rise in blood urea level with a mean value of 177 mg%. S. creatinine levels ranged between 3.2 - 13.6 mg% with a mean value of 7.2 mg%. The mean creatinine clearance rate was 12.13 ml/min. Out of the 50 cases of ARF, 29 cases were found to have severe ARF and 21 cases had milder form of ARF based on the serum creatinine levels, GFR.

Table-2: Showing Parasite Density in 50 cases of acute renal failure due to falciparum malaria.

Parasite density	No of cases	Percentage
<5%	21	42
5-10%	13	26
>10%	16	32

Table 2 shows that out of the 50 cases of acute renal failure due to falciparum malaria 21 had Parasite density <5% (42%), 13 had 5-10% (26%) and 16 had >10% (32%).

Table-3: Showing severity of ARF in relation to parasite density.

Severity of ARF	Parasite density<5%	Parasite density 5-10%	Parasite density>10%
Mild	12	5	4
Severe	9	8	12

Table 3 shows that out of 21 cases of mild ARF 12 patients had parasite density <5% and 9 had >5%. Out of 29 cases of severe ARF 9 patients had parasite density<5% and 20 had >5%.

A total of 24 patients (48%) out of 50 patients got injection Quinine and 26 patients (52%) got injection Artesunate.

Dialysis was done in a total of 31 cases (62%). In the severe form of acute renal failure hemodialysis was required in 29 cases (58%), in the milder form of renal failure; only 2 cases (4%) required hemodialysis. Rests of the cases were managed by conservative treatment.

Table-4: Showing recovery in 50 cases of acute renal failure due to falciparum malaria.

Time of recovery	No of Patients	Percentage
1st month	35	70
3 rd month	1	2
6 th month	0	0
Not Recovered	13	26

Out of 50 cases 35 patients' serum creatinine became normal within 1 month, 1 patients' serum creatinine became normal within 3 months and 13 patients died.

Table-5: Showing comparison between development of renal failure and mortality.

Groups	Cases with oliguric ARF	Cases with non-oliguric ARF	Total No. of cases & Percentage
No. of cases	36	14	50
Survival	23(63.88%)	14(100%)	37 (74%)
Mortality	13 (36.12%)	0	13 (26%)

As shown in the table 5, out of the 36 cases with oliguric ARF, 23(63.88%) survived, while 13 cases expired. All cases of non-oliguric ARF survived. So overall mortality rate was 26%.

Discussion

The present study was done with 50 patients of confirmed falciparum malaria with clinical and biochemical features of acute renal failure admitted in various units of the Medicine department of NRS Medical College & Hospital, Kolkata through a period from 1st January 2011 to 30th June 2012. Renal function status was assessed regularly in all the cases. Cases developing renal failure were further investigated to determine the type of renal failure. After recording all the results an attempt was made to analyze the observations in detail.

Analysis of the 174 cases of falciparum malaria revealed no renal involvement in 124 (71.3%) of the cases. 50 patients (28.7%) presented with clinical and biochemical features of acute renal failure. In a similar study by Sitprija et al, acute renal failure was noted in 21% of the cases[4].

The present study includes patients ranging from 15 years to 61 years and the mean age of the patients was found to be 32 years. It was observed that the maximum number of patients with falciparum malaria, were in the age group (21-30) years (32%), followed by 26% cases in the age group of 31-40 years. While, 78% of the cases were below the age of 40 years. Tasnim A et al in his study observed age ranging from 23-63 years and mean age was 38 years[5]. Joshi YK et al carried out a study with age group ranging from 19-63 years[6].

In our study 36(72%) patients out of 50 cases of falciparum malaria with ARF had oliguria at the time of admission with urine output less than 400 ml per 24 hours and 14 (28%) presented with non-oliguric renal failure with normal urine output. Junejo Abdul Manan et al was seen in 76.09% cases of falciparum malaria on admission [7]. A fewer incidence of complications and a better prognosis associated with non-oliguric renal failure has been observed in various studies by other workers. A fatal outcome was associated significantly with anuria[8].

Study of the glomerular filtration rate revealed that majority of the patients (90%) had very low creatinine clearance rate of less than 25 ml/ minute. Severe reduction in glomerular filtration rate is due to multiple factors involved such as effects of

catecholamines, hyperviscosity and hypovolemia in falciparum malaria [9]. Decreased cortical & renal blood flow was noted in renalhaemodynamic study using ^{133}Xe [10]. In the rest, 10% cases showed a moderate decline in the glomerular filtration rate, upto 50 ml/min. These patients manifested a milder form of renal failure with lesser evidence of renal injury. Similar observations have been made in Lumlertgulet al.1989 study[11].

Routine estimation of serum creatinine, blood urea and electrolytes were done in all the cases. The mean blood urea level was 177 mg% which was markedly elevated compared to normal levels. Similarly, serum creatinine levels were found to be raised in all the patients, ranging from 3.2 – 13.6. Severe azotemia with evidence of hyper catabolism, with rapid rise of blood urea nitrogen (BUN) and creatinine levels has been observed frequently in patients with malaria induced renal failure [12]. Severity of renal failure can be judged by the marked reduction in the glomerular filtration rate which ranged between 5.16 – 26.2 ml/min.

Based on the severity of renal dysfunction, reduction in glomerular filtration rate, duration of oliguria and duration of renal failure, the patients presenting with acute renal failure were divided into two groups. 29 patients manifested clinical and biochemical features of severe renal failure. There was marked rise in serum creatinine levels with a mean of 9.57 mg/dl in these patients with severe reduction in glomerular filtration rate of mean value 7.76 ml/min. The course of renal failure was prolonged and it took approximately 20 - 24 days before the blood urea and serum creatinine levels returned to normal. Dialysis was required in all these patients.

A relatively milder form of renal failure was noted in 21 patients. Renal dysfunction in these patients was less severe compared to the previous group. Serum creatinine levels ranged between 3.2 – 5 mg/dL with a mean value of 3.89 mg/dl.

Glomerular filtration rate was reduced with a mean of 18.17 ml/ min, showing less severe reduction compared to the previous group. Dialysis was required in only two patients. The serum creatinine returned to normal levels within 10 to 15 days.

Similar observations have been made by other workers. Trang TT, MJ White et al., 1992 in their study of sixty four patients with malaria induced renal failure, observed that recovery of renal function was unrelated to parasitaemia or haemoglobinuria and the mean duration for serum creatinine levels to return to normal was 17 days [13].

21 cases(42%) out of 50 showed parasite density <5% and 29(58%) showed parasite density >5% (hyperparasitism) of which 13(26%) had 5-10% and 16(32%) had >10% parasite density. In a comparative study by Ali H et al 2008 it was shown that 40.79% patients had parasite density <5%, 28.95% had parasite density in between 5% and 10% and 30.26% had parasite density >10%[14]. In 21 cases of mild ARF, 12(57.14%) cases had parasite density <5% and 9(42.86%) had parasite density >5% (hyperparasitism). Among 29 cases of severe ARF 9(31.03%) had parasite density <5% and 20 (68.97%) had parasite density >5% (hyperparasitism). Fisher's exact test was performed to determine statistical significance of the association between renal failure and parasite density. The two-tailed P value was calculated as <0.05 i.e statistically significant. So, from above findings it appears that most of the patients with ARF even mild variety had hyperparasitemia. It is also seen that hyperparasitemia made the patient more susceptible to develop severe ARF. Comparative analysis of the groups showed by Ali H et al 2008 showed that pallor, impaired consciousness, jaundice, thrombocytopenia, acute renal failure, DIC and mortality were all strongly associated with the density of Plasmodium falciparum malaria [14].

Dialysis was required in total of 31 patients (62%) due to rapid renal shutdown with development of complications. All cases Haemodialysis was performed for restoration of normal renal function. The remaining 19 patients (38%) were treated conservatively. Among 31 patients requiring the Haemodialysis 26 were oliguric and 05 non-oliguric. Compared with non-oliguric subjects, the oliguric patients had higher need of dialysis.

Most of the cases (5 out of 7 cases) of mild form of acute renal failure were treated with conservative treatment, except in 2 cases where Haemodialysis were performed. All severe cases (29 patients) were

treated with Haemodialysis and along with conservative treatment. On average, four Haemodialysis sessions were performed, with a per patient minimum of two to a maximum of 14 sessions. Similar observation has been made Weber MW et al in their study of malaria induced renal failure [15]. Dialysis was required in 69.2% and 70% of their cases respectively.

Haemodialysis is preferred in severe acute renal failure caused by falciparum malaria. Peritoneal dialysis is less effective under most circumstances because of impaired peritoneal microcirculation due to parasitized erythrocytes and vasoconstriction which results in reduced solute transport [16]. Junejo Abdul Manan et al. (2006) in their study of malaria induced renal failure shows that 88.89% were oliguric and 11.11% non-oliguric renal failure required haemodialysis and also, they measure the average number of dialysis sessions required per patient was 06, with a minimum of 03 to a maximum of 15. The oliguric patients also needed more haemodialysis sessions than the non-oliguric patient[17].

Besides dialysis management of renal failure, consisted of restriction of protein, sodium and potassium and adequate fluid intake.

During follow up of those who survived, serum creatinine level became normal in 35 patients within one month and the rest one within three months. After 6 months they maintained normal renal function.

In the current study, out of the 50 cases with acute renal failure, 13 cases succumbed showing an overall mortality rate of 26% and survival rate of 74%. Excellent prognosis has been observed in the patients of non-oliguric renal failure. Among 36 oliguric renal failure patients 23 (63.88%) survived. Out of the 36 cases with clinical and biochemical features of acute tubular necrosis, 26 survived (72.2%) while 10 patients died showing a mortality rate of 27.8%. All the patients were oliguric renal failure. Habte B. et al observed a mortality rate of 29% from their study of twenty four patients with malaria induced renal failure[18].

Conclusion

A sizeable number of cases of falciparum malaria develop acute renal failure. Cases of non-oliguric

ARF respond well to Antimalarial therapy and conservative treatment with excellent prognosis. Early diagnosis and prompt management including dialysis can reduce mortality and expedite recovery of renal function in most of the cases of malaria induced acute renal failure. Severity of oliguria and presence of one or more associated complications like pulmonary oedema, acidosis, and altered sensorium have considerable influence on the outcome of the patients.

Hence, it is essential to look for these ominous parameters which have adverse outcome in renal failure associated with falciparum malaria. Of them Parasite Density has significant impact to predict the severity of renal failure, duration of hospital stays as well as the number of dialysis required.

As the study was conducted with small number of cases, further study is necessary with large number of cases to arrive at a conclusion regarding the malady of acute renal failure in falciparum malaria.

What study adds to existing knowledge- Very few studies reported from India the incidence and severity of acute renal failure and its association with parasite density in hospitalised patients with falciparum malaria. Our study gave a clear insight in to the school of thought of Parasite Density having significant impact to predict the severity of renal failure, duration of hospital stays as well as the number of dialysis required, which has been a challenging task for specialist in field.

Author contribution- This study conducted under guidance of Dr Pinaki Mukhopadhyaya (Associate Professor) with valuable contribution from Dr. Biman Kumar Das (Associate Professor) in timely evaluation of study. Patient interviewing and data collection done by Dr N. M. Biswas (Associate Professor) in collaboration with Dr Pinaki Mukhopadhyaya (Associate Professor) doing data analysis and manuscript preparation.

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