

A Study on Acute Renal Failure in patients of Falciparum Malaria in Jharkhand

Abhay Kumar¹, Manmeet Topno², Rohit Keshav², Aman Sinha², Upendra Prasad Yadav²

ABSTRACT

Introduction: Malaria is one of the most important of the parasitic diseases of humans. It is a protozoan disease transmitted by bite of female Anopheles mosquito. Malaria continues to be a major public health threat in India, particularly due to P.falciparum which is prone to complications, acute renal failure (ARF) is one of the most common complications in adults with falciparum malaria. We aimed to study the incidence, severity, clinical presentations, prognostic factors, complications and outcome of ARF in falciparum malaria cases in our hospital, a Tertiary care center.

Material and Methods: A hospital based Prospective observational study was done on 60 admitted patients of falciparum malaria in Rajendra Institute of Medical Sciences, Ranchi, Jharkhand.

Result: Most of the malaria cases were seen in younger age group between 20-39 years (71.67%). Males outnumbered females in this study (45 versus 10). ARF was found to be more frequent in age group ≥ 60 years(83.33), females (40%), in rural population (27.27%) and in poor socio-economic groups (56.25%). ARF was seen in 16 cases (26.67%) with 3 deaths (18.75%) compared to cases without ARF with 44 cases (73.33%) in which 1 death (2.27%) occurred. Overall mortality in patients with Falciparum malaria was 6.67%.

Conclusion: Falciparum malaria is a dreadful disease and Acute Renal Failure especially when present with other complications has grave prognosis. Educating local residents with specific measures for prevention of malaria together with early diagnosis and treatment with identification and referral of malarial ARF can significantly affect mortality.

Keywords: Falciparum Malaria, Complicated Falciparum Malaria, Acute Renal Failure

of malaria cases and 97% of deaths due to malaria are reported from North-Eastern states.¹⁵ Jharkhand is amongst the malaria endemic states of India. Jharkhand as the name suggests means 'Bushland' or land of forest. Much of Jharkhand is covered with hills and forests with rich variety of flora and fauna, inhabited by tribals. The aim of this study was to find the incidence, severity, clinical presentations, prognostic factors, complications and outcome of acute renal failure in P. Falciparum malaria cases in Jharkhand. Acute renal failure (ARF) occurs due to complication of P. falciparum malaria in less than 1% of cases, but the mortality may be upto 45% in these cases. It occurs more commonly in adults than in children. Malarial acute renal failure is diagnosed when serum creatinine level rises above 3 mg/dL (265 mol/L) and/or when urinary output is less than 400 ml in 24 hours. Renal involvement varies from mild proteinuria to severe azotaemia associated with metabolic acidosis.

In severe Falciparum malaria, renal involvement is very common and can be life threatening. Three types of renal lesions are known to occur in malaria.

They are-

- 1 Acute renal failure (ARF)
2. Glomerulonephritis (GN)
3. Nephrotic syndrome (NS)

Specific effects of parasitized erythrocytes with hemorrhagic changes and non-specific inflammatory and associated factors like hypovolemia, intravascular haemolysis, intravascular coagulation, catecholamine effects, endotoxaemia, jaundice, cytokines and free oxygen radicals are two mechanisms responsible for pathogenesis of ARF (Acute renal failure) in P.falciparum malaria.¹⁶ The contribution of malaria to overall hospital admission for ARF varies from range of 2 to 39% according to the local prevalence of the disease, the relative preponderance of the other causes, patient referral policy and other factors.¹⁷ Jaundice is the most common association with malarial ARF occurring in more than 75% of the cases. Both

INTRODUCTION

Malaria is caused by protozoan parasites of the genus Plasmodium, namely, P. falciparum, P. vivax, P. malariae, P. ovale, and P. knowlesi.¹ According to the latest estimates, there were about 216 million cases of malaria in the year 2016 and an estimated 445000 deaths. The African Region accounted for 91% of all malaria deaths in 2016, followed by the SouthEast Asia Region (6%).² Almost all deaths are caused by falciparum malaria. Patients with P. falciparum infection are prone to develop severe malaria in 30% of cases, which resulted in case fatality rate of 20%.^{4,5}

In Southeast Asia, acute renal failure (ARF) is one of the most common complications in adults with falciparum malaria, incidence of ARF in patients with severe malaria varies widely ranging from 15% to 48%.⁶⁻¹⁴ In, India 92%

¹Associate Professor, ²Junior Resident, Department of General Medicine, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India

Corresponding author: Manmeet Topno, RIMS Boys Hostel no.5, Room no. 89, Bariatu, PO. R.M.C.H, Ranchi, Jharkhand, PIN – 834009, India

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conjugated and unconjugated bilirubin and bile acid as well have been shown to be involved in the pathogenesis of acute renal failure in falciparum malaria.^{18,19,20} Anemia occurs in at least 70% of the patients. ARF is a serious complication of malaria with a reported mortality of 15 to 45%. A report from India described a reduction of MARF mortality from 75 to 26% when a specialized MARF (Malarial acute renal failure) task force was established in the same institution.⁴ We aimed to study the incidence, severity, clinical presentations, prognostic factors, complications and outcome of ARF in falciparum malaria cases in our hospital, a Tertiary care center.

MATERIAL AND METHODS

This was hospital based prospective observational study done on 60 confirmed cases of falciparum malaria admitted in hospital from July 2017 to June 2018 after taking informed consent of the patient/attendant. The approval of institutional ethics committee was taken prior to the commencement of this study. A case sheet proforma was prepared and data regarding demographic profile, clinical features, investigations, treatment, and complication were recorded. Severe falciparum malaria was diagnosed as per guidelines of WHO.³

Inclusion criteria

Only those cases whose blood was found to be positive for plasmodium falciparum by peripheral blood smear examination or antigen test were considered for the study.

Exclusion criteria

- Pre-existing neurological disease
- Pre-existing hematological disease
- Pre-existing acute or chronic renal failure
- Pre-existing liver disease

Two groups were studied, one had the patients with features of uncomplicated malaria and other group had the patients with clinical features of complicated Plasmodium falciparum malaria.

Group I – Uncomplicated *P. falciparum* malaria (n=16): Common presenting complaints in this group were fever with chills, headache, fatigue, abdominal discomfort, muscular ache, nausea, vomiting, mild anemia and (in some cases) a palpable spleen.

Group II – Complicated or severe *P. falciparum* malaria (n=44): This group of patients presented to the hospital with cerebral malaria, severe normochromic, normocytic anemia, renal failure, pulmonary edema /adult respiratory distress syndrome (ARDS), hypoglycemia, hypotension/shock, bleeding/disseminated intravascular coagulation, convulsions, hemoglobinuria, acidemia/acidosis, jaundice.

The following investigations were done in cases under study:

- 1) Blood for TC and DC of WBCs, Hb% estimation.
- 2) Peripheral blood smear, both thick and thin for the presence of *P.falciparum*.
- 3) Rapid diagnostic kit test for *P.falciparum*.
- 4) Random blood sugar

- 5) Renal function test – Blood urea and serum creatinine.
- 6) USG Abdomen – Only those cases with relevant findings suggestive of deranged renal function.

STATISTICAL ANALYSIS

Microsoft office 2010 was used for the statistical analysis. Descriptive statistics like mean and percentages were used in the analysis.

RESULT

The total no. of case studied were 60 (n=60). Majority of the cases (43) were seen in age group 20 -39 years (71.67). On seeing the sex distribution, total no. of cases among male-45(75%) and female-15(25%), no. of males was more than females. Majority of the cases were from rural areas (27.27%) as compared to urban areas (25%) due to poverty, lack of proper education and living in unhygienic conditions. 31.67% of the patients (19) were tribal and 68.33% (41) were nontribal (table-1).

Although proportion of tribal community in study was very less as compared to nontribal, frequency of ARF is slightly

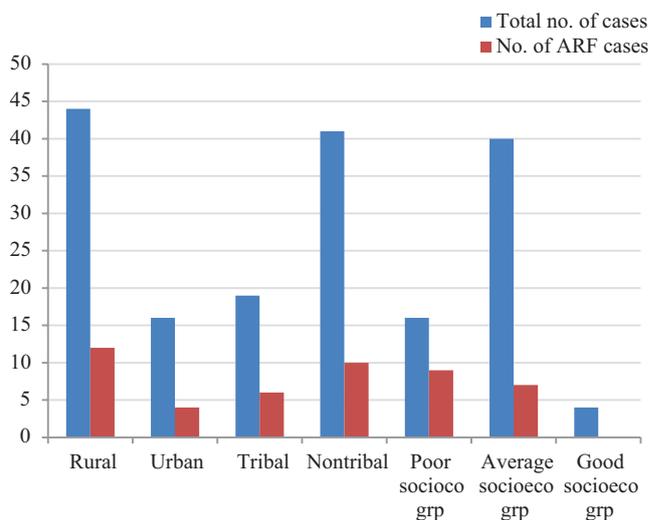


Figure-1: Distribution of ARF among the rural and urban population, Tribals and non -tribals population and in different socio-economic groups

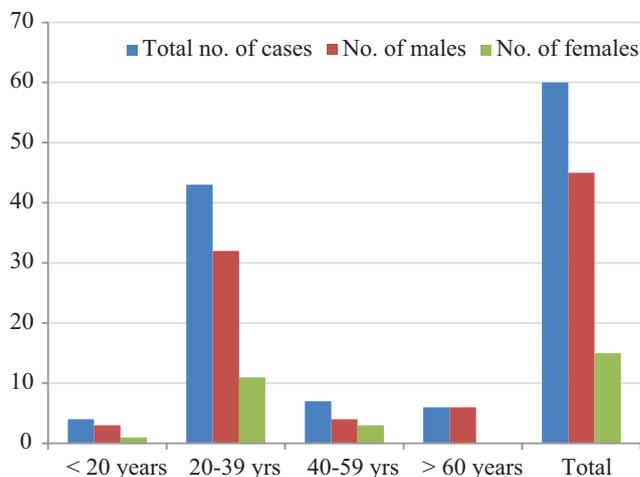


Figure-3: Age and sex distribution of acute renal failure among the cases under study

Indewellers Tribal/nontribals Socioeconomic grp	No. of cases (n=60)	No. of cases with ARF	% of ARF cases in various groups
Rural	44	12	27.27
Urban	16	04	25
Tribal	19	06	31.58
Nontribal	41	10	24.39
Poor socioeco grp	16	09	56.25
Average socioeco grp	40	07	17.50
Good socioeco grp	04	00	0

Table-1: Showing distribution of ARF among the rural and urban population, Tribals and non -tribals population and in different socio-economic groups

Clinical Presentation	No. of Cases N = 60 (%)	No. of ARF cases N = 16	Percentage
Fever with chills and rigor, headache	60(100)	16	100
Altered sensorium	16(26.67)	09	56.25
Neck rigidity	39(65)	10	62.5
Convulsion	04(6.67)	01	6.25
Coma	10(16.67)	05	31.25
Severe anaemia	06(10)	02	12.5
Jaundice	20(33.33)	09	56.25
Hypoglycaemia	04(6.67)	02	12.5
ARDS	01(1.67)	01	6.25
Shock	03(05)	02	12.5
Splenomegaly	07(11.67)	01	6.25
Hepatomegaly	03(05)	00	0
Acidosis	14(23.33)	13	81.25
Hemoglobinuria	06(10)	04	25
DIC	02(3.33)	01	6.25

Table-2: Different clinical presentation of cases with ARF under study

Age group and sex	No. of cases (n=60)	No. of cases with ARF	% of ARF cases in given age group and gender
<20	04	02	50
20-39	43	08	18.60
40-59	07	01	14.29
>60	06	05	83.33
Male	45	10	22.22
Female	15	06	40
Total	60	16	26.67

Table-3: Age and sex distribution of acute renal failure among the cases under study

Treatment	No. of cases (n= 16)	Percentage
Standard antimalarial treatment	16	100
Antimalarial+Dopamine + furosemide infusion	09	56.25
Haemodialysis	07	43.75

Table-4: Treatment received by cases with ARF

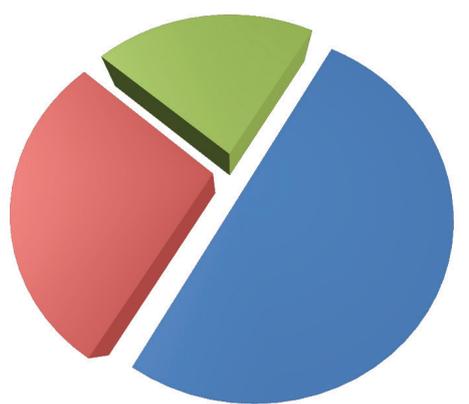
	No. of cases	Cured	Death
With ARF	16	13	03
Without ARF	44	43	01
Total	60	56	04

Table-5: Outcome of cases with ARF in comparison to total cases under study

more in tribals (31.58%) than non-tribals (24.39%). Maximum no. of cases were having fever with chills 100%, cases with splenomegaly 11.67%, anaemia 10%, hepatomegaly 05% and ARF was present in 26.67% (figure-1). Numbers of patients with ARF is maximum in age group of

20-39 years but frequency of ARF is maximum in age group >60 years (83.33%) and minimum in age middle age group (14.29%) (table-2).

The negligent act by our society towards old person is one of the main reasons for such complications, whereas



■ Standard antimalarial
 ■ Antimalarial+Dopamine+Furosemide infusion
 ■ Haemodialysis
Figure-4: Treatment received by cases with ARF

people in middle age group are themselves capable of attending hospitals which prevents further development of complications in malaria. Standard anti-malarial therapy was given to all cases of ARF (16). 9 cases out of 16 received antimalarial and (dopamine + furosemide infusion) (56.25%) to increase renal perfusion and in 7 out of 16 cases with severely impaired renal function, haemodialysis was needed (43.75%) (table-3, figure-3).

Treatment with haemodialysis was started in those patients of ARF, who were refractory to conservative treatment with antimalarial and (dopamine + furosemide infusion). There was significant difference in outcome (mortality) of patients who were with ARF than those without ARF, most of ARF cases (16 cases with recovery 81.25% and cases without ARF (44 cases with recovery 97.73%) were seen. But in spite of all, out of 60 cases 4 deaths occurred. All the cases that died despite the best possible treatment were having severely impaired renal function, jaundice, anemia, unconsciousness/ altered sensorium, shock in varying combination causing multiorgan failure. Overall mortality in patients with Falciparum malaria was in our study was 6.67%.

The additive factors like poor hygiene and improper care of the patients leading to aspiration pneumonia, secondary infections and septicemia made the situation grave. In developing nations, limited medical resources are available at primary health care centers and late referrals result in poor outcome (table-4).

DISCUSSION

In severe malaria P. Falciparum is the most common cause of Acute renal failure.^{4,6} In a study carried out by Mehta KS, Halankar AR and et al (2001)⁹ out of 402 detected smear positive malaria cases, 24 had ARF. Eighteen were of the age group 21-40 years. In another study by Krishnan A, Karnad DR (2003)¹¹ most of the patients of Acute Renal Failure in complicated malaria were of young age group with mean age of patient being 26 years. Our study also shows the same results as most of the cases (8 out of 43) were seen in age group 20-39 years. Krishnan Anand, Karnad Dilip R (2003)

also reported renal failure in 91 patients out of 301 malarial cases (30%) out of which 33 required dialysis (36%). Hepatic failure occurred in 77 patients.

Regardless of the organ system involved, only 11 of 172 patients with one or no organ failure died (6.8%), whereas mortality rate increased to 48.8% in 129 patients with multiple organ failure. In our study 16 out of 60 cases of malaria developed ARF (26.67%) (table-3) which is similar to the above study but requirement of dialysis in our study was slightly more, 7 out of 16 cases (43.75%), (dopamine + furosemide infusion) was used in 9 cases out of 16 (56.25%) which reduced the need of dialysis. The complications noticed in patients of ARF with P.Falciparum malaria were Jaundice, cerebral malaria, severe anemia, hypoglycemia and ARDS. Our study is comparable to Kochar DK et al.¹³ Several factors including various chemical mediators, catecholamine release, cytoadherence of parasitized erythrocytes, dehydration, intravascular hemolysis, intravascular coagulation, sepsis, hyperbilirubinemia and hyperparasitemia have been implicated in the pathogenesis of ARF in malaria.⁴

Men were more affected in our study as compared with women, similar to observations of other groups.^{9,22,23} This could be explained by the fact that men are more mobile and moving about, including the swampy areas as compared with women in Asian countries, since women are more confined to their homes and near cooking fire, which offers them protection from biting mosquitoes. Since, Acute Renal Failure is a serious complication of falciparum malaria dreaded for its mortality commonly found in South East Asia.⁶ Our study showed 18.75% mortality in malarial ARF, consistent with 15-45% mortality reported by others.²⁴

CONCLUSION

Thus, we conclude that Falciparum malaria is a dreaded disease in Asian subcontinent particularly in tropical areas and when associated with acute renal failure has poor prognosis. Mortality is increased with complications. In our study when ARF was associated with 3 or more organ dysfunction mortality was 100%. Cerebral malaria, jaundice and ARDS were amongst the commonest associations. We believe that since our hospital is a tertiary care center, the patients were referred for treatment, when they were already in a morbid condition.

So, prevention of malarial infection, early diagnosis and prompt management including dialysis are needed to reduce mortality and expedite recovery of renal function which is only possible in a tertiary care center. People living in villages should be made aware of environmental sanitation so as to reduce breeding places (fresh or salt water marshes, mangrove swamps, rice fields, grassy ditches, the edge of streams and rivers, and small temporary rain pools) of mosquitoes. They should be educated about use of residual insecticides (DDT, malathion, fenitrothion). They should be encouraged to use individual protection measures such as repellents, bed nets particularly those impregnated with long acting repellent insecticides. Male members of the family

should wear protective clothings. More epidemiological studies focusing on complications and prognosis of acute renal failure in Falciparum malaria are needed to quantitate the problem. Thus, survival can be improved by education and early transfer to a tertiary care center, where prompt dialysis and supportive management could be initiated.

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