

Clinical Profile and Outcome of Malaria Patients with Acute Kidney Injury

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Abstract- Malaria has protean clinical manifestations and renal complications, particularly acute kidney injury that could be life threatening. This study was a prospective study of 50 patients with malaria-associated AKI at our hospital. Smear positive and Parasite V and F positive malaria patients with AKI as defined by RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease) classification were selected to evaluate the clinical profile and outcome. Out of 50 patients in our study 38 were males and 12 were females. 42% were between 26-40 years. Fever was the most common presenting complaint (100%), followed by chills and rigors (90%), headache (74%), vomiting (70), myalgia (60%), altered sensorium (30%) and discolouration of sclera (36%). Pallor (62%) was the most common sign followed by splenomegaly (62%), icterus (40%) and hepatomegaly (34%). Artemisinin combination therapy was given for all patients and renal replacement therapy was given to 12 (24%) patients. We had a mortality of 12%, all of them had multiple complications. Acute kidney injury in malaria occurred most commonly in plasmodium falciparum 70% infected patients. Applying RIFLE criteria helps in early identification of high risk cases, so that prompt treatment is instituted early, thereby reducing the mortality rate.

Index Terms- acute kidney injury (AKI), plasmodium vivax (PV), plasmodium falciparum(PF),RIFLE criteria

I. INTRODUCTION

Malaria is a common life-threatening protozoan disease transmitted to people through the bites of infected female anopheles mosquitoes. Malaria is endemic throughout South America, the Indian subcontinent, eastern Asia and Africa.¹ According to the latest estimates, released in December 2014, there were about 198 million cases of malaria in 2013 (with an uncertainty range of 124 million to 283 million) and an estimated 584 000 deaths (with an uncertainty range of 367 000 to 755 000).²

AKI occurs commonly in Plasmodium falciparum (PF) malaria and rarely in Plasmodium vivax (PV) malaria.^{3,4,5} The overall prevalence of AKI in falciparum malaria varies between <1 and 60%, with the mortality rate up to 45%.^{6,7,8,9}

Prompt and accurate diagnosis of malaria is needed for implementation of appropriate treatment to reduce associated morbidity and mortality. The management of malaria-induced AKI includes appropriate antimalarials (parenteral artesunate or

quinine), fluid electrolyte management, supportive therapy, avoidance of nephrotoxic drugs and renal replacement therapy (RRT) at the earliest.^{6,10} Hemodialysis (HD) is effective for malaria-associated AKI.^{11,12}

This study was conducted to evaluate the clinical profile, outcome, and predictors of mortality of malaria patients with AKI.

II. MATERIALS AND METHODS

This is a Prospective study of 50 patients with malaria-associated AKI at our hospital. Smear positive and Parasite V and F positive malaria patients with AKI as defined by RIFLE Classification (based on Serum Creatinine and Urine output) were included in the study. Post renal AKI, patients with intake of nephrotoxic drug intake and contrast nephropathy were excluded.

The diagnosis of malaria was confirmed by direct visualization of the parasite in Giemsa-stained peripheral blood smear and serological tests. Clinical history and assessment were recorded and all other known etiological causes of fever and jaundice were excluded by relevant investigations. All the patients were subjected to complete hemogram, liver function tests, renal function tests (blood urea, serum creatinine, serum electrolytes). Intake output chart was maintained in all patients. Urine samples were examined for routine and microscopic examination. Serological tests for Human Immunodeficiency Virus and hepatitis B and C were performed. Estimation of blood sugar, coagulation profile for disseminated intravascular coagulation (DIC), and arterial blood gas analysis were carried out when indicated. Chest x-ray and ultrasonography (USG) of abdomen were recorded in all the patients.

AKI was defined according to RIFLE s criteria, with normal kidney size on USG. All patients received artesunate 2.4 mg/kg intravenously, followed by 2.4 mg/kg at 12 and 24 hours, followed by 2.4 mg/kg once daily for a total of 7 days and doxycycline (100 mg orally twice daily. Supportive measures were instituted as needed. Renal Replacement Therapy (RRT) was initiated for fluid overload, hyperkalemia, clinical evidence of uremia, metabolic acidosis, rapidly increasing S.Cr level, blood urea nitrogen (BUN)>100 mg/dl, and S.Cr >4 to 5 mg/dl. RRT was initiated prior to the development of overt symptoms and signs of renal failure due to malaria. Heparin-free (in most of patients) intermittent hemodialysis (HD) was provided on alternate days through temporary femoral/jugular catheter for 4

hours and peritoneal dialysis(PD) were done in hemodynamically unstable patients.

III. RESULTS

Out of 50 patients in our study 38 were males and 12 were females, maximum number of patients were young (42%) between 26-40 years. Fever was the most common presenting complaint (100%), followed by chills and rigors (90%), headache (74%), vomiting (70), myalgia (60%), altered sensorium (30%) and discoloration of sclera (36%). Pallor (62%) was the most common sign followed by splenomegaly (62%), icterus (40%) and hepatomegaly(34%). Plasmodium falciparum infection was seen in 35(70%), p.vivax in 6 (12%) and mixed infection in 9 (18%) patients.

Table 1. Showing Laboratory investigations:

Bilirubin (mg/dl)	1.2- 3	4 (8%)
	3- 6	20 (40%)
Blood urea (mg/dl)	<45	4 (8%)
	45- 100	39 (78%)
	100- 150	7 (14%)
Serum creatinine (mg/dl)	<1.7	29 (58%)
	1.7 -3.0	12 (24%)
	3 – 4.5	5 (10%)
	4.5 -6	4 (8%)
Haemoglobin (gm/dl)	<6	7 (14%)
	6-8	14 (28%)
	8-10	10 (20%)
	>10	19 (38%)
Platelet count (lacks/cumm)	>1.5 lac	30 (60%)
	1 – 1.5	10 (20%)
	0.5 - 1	2 (4%)
	0.2 -0.5	8 (16%)

Table 2. Patients were classified according to Serum Creatinine

Risk[>1.5 times the baseline]	33 (66%)
Injury[> 2 the baseline]	8 (16%)
Failure[> 3 the baseline or creatinine > 4].	9 (18%)

Table 3. Patients were classified according to urine output

Risk [<0.5ml/kg/hr for 6 hrs]	33 (66%)
Injury[<0.5 ml/kg/hr for 12 hrs]	5 (10%)
Failure[<0.3 ml/kg/hr for 24 hrs Anuria for 12 hrs]	12 (24%)

Patients are classified according to RIFLEs criteria depending on whichever is the worst of the two. 33 [66%] of the patients were classified as under Risk, 5 [10%] patients had Injury and 12 [24%] patients were classified as under Failure. Complications associated with AKI noticed were anuria in

3(6%), hyperkalemia in 8(16%), acidosis in 4(8%), volume overload in 3(6%) patients. Injection artisunate was given to all patients. Dialysis in 12 (24%) patients of whom 7(14%) had hemodialysis and 5 (10%) had peritoneal dialysis. The overall mortality was 12% in our study and all of them had multiple complications.

Table 4. Correlation between complications and outcome [death]

Decreased urine output	6	100%
Altered mental status	6	100%
Hyperkalaemia	6	100%
Hypotension	5	83.33%
Bleeding	5	83.33%
Acidosis	4	66.66%
Mechanical ventilation	4	66.66%
Anuria	3	50%
Hypoglycaemia	2	33.33%

IV. DISCUSSION

The pathogenesis of acute kidney injury in malaria is unclear but may be related to erythrocyte sequestration and agglutination interfering with renal microcirculatory flow and metabolism. Clinically and pathologically, this syndrome manifests as acute tubular necrosis. Renal cortical necrosis never develops. Acute renal failure may occur simultaneously with other vital-organ dysfunction (in which case the mortality risk is high) or may progress as other disease manifestations resolve. In survivors, urine flow resumes in a median of 4 days, and serum creatinine levels return to normal in a mean of 17 days. Early dialysis or hemofiltration considerably enhances the likelihood of a patient's survival, particularly in acute hypercatabolic renal failure.¹

Our analysis of malaria patients with AKI revealed that it was observed more commonly in adults and male patients similar to earlier studies¹³. This could be explained by more outdoor activities of males in Asian countries as compared with females. Most common presentation was anaemia [62 %] and jaundice [40%] with AKI. AKI occurs commonly with jaundice, thrombocytopenia, and rarely with cerebral malaria. AKI was usually seen in early second week and is oliguric in 72% of cases. The etiology of AKI was usually multifactorial due to hyperbilirubinemia, intravascular hemolysis,, volume depletion, hypoxia, shock, pigment nephropathy, Disseminated intravascular coagulation (DIC), and sepsis.^{3,4,5,6} The mortality rate with kidney injury in our study is 12% as compared to 11.8% in Kute VB et al¹⁴ and 21% in Kanodia KV et al.⁸ Haemodialysis was done in 14 % cases and peritoneal dialysis in 10 %. The overall requirement of RRT was therefore seen in 24% of cases which was much less compared to other studies, 96.6% and 3.3% in Kute VB et al¹⁴ and in Kanodia KV et al⁸ respectively.

The major factors associated with mortality in our study were severe oligo/anuria, central nervous system (CNS) involvement, hyperkalemia, bleeding and hypotension. Low mortality (12%) in our study of malaria with AKI despite of having jaundice in 40% is due to prompt diagnosis, timely HD, and supportive therapy.⁸

V. CONCLUSIONS

Most of the cases of complicated malaria occur in young and middle age group. More number of patients presented with multiple complications than single complication, mortality was more in these patients. Artemisinin combination therapy is effective in treating complicated malaria. Applying RIFLE criteria helps in early identification of high risk cases, so that prompt treatment is instituted early, thereby reducing the mortality rate.

We conclude that malaria is an important cause of AKI in Asia and particularly in tropical areas. AKI occurs most commonly in association with *P. falciparum* malaria. Early diagnosis and prompt management including dialysis can reduce mortality and expedite recovery of renal function.

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