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Original Research Article

Acute Kidney Injury in Patients of Falciparum and Vivax Malaria: A Observational Study

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Abstract:

Background: Acute kidney damage (AKI), a major consequence of Plasmodium falciparum malaria, is well-known; nevertheless, Plasmodium vivax malaria is now frequently responsible for this consequence. AKI is also caused by P. vivax malaria, according to numerous recent publications. The purpose of this study is to examine the demographic profile, clinical characteristics, mortality indicators, dialysis requirement, and overall outcome in P. falciparum and P. vivax malaria patients.

Methods: From April 2023 to March 2024, a prospective observational study involving patients diagnosed with malaria with signs of AKI was carried out in the Department of Medicine at Darbhanga Medical College and Hospital in Laheriasarai, Bihar. Rapid malarial antigen testing and thick and thin peripheral smears stained with Leishman's stain were used to confirm the diagnosis of malaria. A suitable statistical analysis was conducted to examine different parameters.

Result: Out of 200 cases of P. falciparum and 220 cases of P. vivax malaria, 43 (21.5%) and 58 (25.1%) cases of AKI caused by P. vivax malaria, respectively. In both groups, the majority of patients were under 30 years old. The majority of those affected in both groups were female. In P. falciparum malaria, pallor, hypotension, oliguria, sepsis, and altered sensorium were frequently observed.P. vivax malaria was more likely to cause jaundice, vomiting, thrombocytopenia, hepatomegaly, and splenomegaly. In both P. falciparum and P. vivax malaria, oligouria, anemia, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulopathy (DIC), cerebral malaria, hypotension, hyponatraemia, and hyperbilirubinemia were often linked independent risk factors for mortality. Patients with P. falciparum and P. vivax malaria were treated with a combination of artesunate and antimalarial drugs. Haemodialysis was used in 13 (30.23%) P. falciparum cases and 17 (29.31%) P. vivax cases. Nineteen (15.52%) patients with P. vivax malaria AKI and five (11.62%) patients with P. falciparum malaria AKI perished.

Conclusion: AKI was prevalent in malaria caused by P. falciparum and P. vivax. In the majority of India, malaria significantly increases morbidity and mortality. Early detection and treatment can lead to better results.

Keywords: Plasmodium falciparum, Plasmodium vivax, acute kidney injury, haemodialysis.

Introduction

In India, malaria is a prevalent public health issue that significantly raises death and morbidity rates. In 2023, there were a predicted 249 million new cases of malaria worldwide, and 55.11 lakh deaths from the disease [1]. The National Malaria Eradication Programme (NMEP) in India reports between 2.5 and 3 million cases and roughly 1,000 malaria-related deaths every year. The majority of cases (88%) happened in Africa, with South East Asia (10%) and the Eastern Mediterranean region (2%), following. India has the greatest malaria load in South East Asia [2]. In India, West Bengal, Jharkhand, Madhya Pradesh, Orissa, and Chhattisgarh accounted for half of all malaria cases [3]. Not only have clinical symptoms of malaria been evolving recently, but so has the pattern of sequelae. More than ten years ago, cerebral malaria was the primary symptom; however, these days,

liver dysfunction and renal failure together are more frequent. Acute kidney damage (AKI) is a highly anticipated consequence of malaria. Although it is not unusual in P. vivax malaria, renal impairment is more common with P. falciparam malaria [4,5,6].

Worldwide reports on the prevalence of AKI in malaria range from 0.57% to 60% [8–11]. Variations in the diagnostic criteria used to identify AKI and the features of the research population could be the cause of such a large range. When malaria is present, established AKI is typically oliguric and hypercatabolic, and it can linger for a few days to weeks. Despite this, urine output can remain normal even when blood creatinine levels are trending upward [12].

Material and Methods

This study was carried out in the medicine department of Darbhanga Medical College and Hospital in Laheriasarai, Bihar. It was a prospective observational study within a hospital setting. Study participants were patients admitted to the medical ward between April 2023 and March 2024. Leishman's stain was used to analyze thick and thin peripheral smears for malarial parasite and quick malarial antigen test results for all fever subjects suspected of having malaria.

Participants in the study included 220 patients with P. vivax malaria and 200 patients with P. falciparum malaria. We eliminated patients who were unwilling to participate in the trial, those with mixed malaria infections, pregnant women, those under the age of 14, and those who showed any signs of chronic renal disease in imaging, laboratory, or clinical studies. Patients underwent a thorough history before a clinical assessment. Renal function tests: complete blood count, liver function test, blood urea and creatinine, urine analysis, plasma blood sugar, coagulation profile for disseminated intravascular coagulation, chest X-ray, renal ultrasonography, serum electrolytes, and serum lactate dehydrogenase (LDH). As necessary, tests for HIV, HbsAg, anti-HCV, and serum leptospira antibodies were performed. In accordance with WHO guidelines [13,14], parenteral artesunate combination therapy was administered to all confirmed cases, and then oral artesunate combination therapy. Intermittent hemodialysate was administered as renal replacement treatment as necessary. Until their release or demise, patients were monitored.

AKI was defined as a drop in urine production of less than 400 milliliters per day, or both, or a rapid increase in serum creatinine > 2 mg/dl in a previously healthy individual[15].

The statistical software SPSS Version 22.0 for Windows was used to do the statistical analysis. The Chi-square test was used to compare the variations in proportions. For comparison, the crucial value of "p," which denotes the likelihood of a significant difference, was set at less than 0.05.

Result

After 200 patients with P. falciparum and 220 patients with P. vivax malaria were examined, 43 (21.5%) of the P. falciparum patients (14 males and 29 females) and 58 (25.9%) of the P. vivax patients (20 males and 38 females) experienced acute renal injury. According to the findings, AKI was more frequently formed in females. Table 1 indicates that AKI was also more prevalent in the younger age group.

Table 1: Demographic profile of P. falciparum and P. vivax associated AKI

	P. falciparum	P. vivax	p-value
No. of malarial patients	200	220	
No. of AKI patients	43 (21.5%)	58 (25.9%)	
Age (Years) < 30	25 (58.1%)	31 (53.44%)	p = 0.843
31 - 45	9 (20.94%)	13 (22.41%)	NS
36 - 60	5 (11.62%)	10 (17.24%)	
> 60	4 (9.3%)	4 (6.89%)	
Sex Male	14 (32.55%)	20 (34.48%)	> 0.999
Female	29 (67.44%)	38 (65.51%)	NS

NS = Not significant

Clinical profile of P. falciparum and P. vivax malaria associated AKI is shown in Table 2.

Table 2: Clinical features of P. falciparum and P. vivax malaria associated AKI

Clinical features	P. falciparumAKI (n = 43)	P. vivaxAKI (n = 58)
Fever	43 (100%)	58 (100%)
Jaundice	21 (48.83%)	35 (60.34%)
Anaemia	21 (48.33%)	35 (60.34%)
Hypotension	21 (48.33%)	15 (25.86%)
Intravascular haemolysis	23 (53.48%)	29 (50%)
Nausea and vomiting	42 (97.67%)	56 (96.55%)

Thrombocytopenia	21 (48.03%)	45 (77.58%)
Hepatomegaly	16 (37.20%)	29 (50%)
Splenomegaly	19 (44.18%)	34 (58.62%)
Oliguria	23 (53.48%)	26 (44.82%)
Sepsis	10 (23.25%)	7 (12.06%)
Altered sensorium	5 (11.62%)	4 (6.89%)
ARDS	3 (6.97%)	5 (8.62%)

Clinical characteristics that were more frequently found in 100%, 48.83%, 53.48%, 23.25%, and 11.62% of P. falciparum malaria cases linked with AKI were fever, hypotension, oliguria, sepsis, and altered sensorium. In P. vivax malaria associated with AKI, the most frequently detected clinical characteristics were fever, jaundice, thrombocytopenia, hepatomegaly, and splenomegaly, which were observed in 100%, 60.34%, 77.58%, 50%, and 58.62% of patients, respectively. Table 3 shows the factors that contribute to AKI.

Table 3: Possible aetiological factors causing AKI in P. falciparum and P. vivax

Clinical features	P. falciparumAKI (n = 43)	P. vivaxAKI (n = 58)	p-value
Heavy Parasitaemia	25 (58.13%)	28 (48.27%)	NS
Hypotension	21 (48.83%)	15 (25.86%)	
Sepsis	10 (23.25%)	7 (12.06%)	
Intravascular haemolysis	23 (53.48%)	29 (50%)	
Hyperbilirubinaemia	21 (48.83%)	35 (60.34%)	
DIC	17 (39.53%)	17 (29.31%)	

NS = Not significant

Renal manifestations in patients of P. falciparum and P. vivax malaria associated with AKI are shown in Table 4.

Table 4: Renal manifestations of P. falciparum and P. vivax malaria associated AKI

Clinical features	P. falciparumAKI (n = 43)	P. vivaxAKI (n = 58)	p-value
Oliguria	23 (53.48%)	26 (44.28%)	NS
Hyperkalaemia	5 (11.62%)	6 (10.34%)	
Volume overload	‘5 (11.62%)	6 (10.34%)	
Uraemic encephalopathy	3 (6.97%)	2 (3.44%)	
Uraemic pericarditis	3 (6.97%)	4 (6.84%)	
Metabolic acidosis	7 (16.27%)	6 (10.34%)	
Proteinuria (< 1g/dy)	5 (11.62%)	5 (8.62%)	

NS = Not significant

Among AKI linked to P. falciparum, oligouria (53.48%), uraemic encephalopathy (6.97%), and metabolic acidosis (16.27%) were the most frequently reported renal symptoms. Table 5 displays the mortality indices for patients with AKI who have P. falciparum and P. vivax malaria.

Table 5: Mortality Indicators of P. falciparum and P. vivax associated AKI

Parameters	P. falciparumAKI (n = 43)		P. vivaxAKI (n = 58)	
	Survived (n = 38)	Expired (n = 5)	Survived (n = 49)	Expired (n =9)
Oliguria/anuria on admission	19 (50%)	4 (80%)	19 (38.7%)	7 (77.7%)
Hypotension	19 (50%)	2 (40%)	10 (20.4%)	5 (55.5%)
Metabolic acidosis	6 (15.8%)	1 (20%)	4 (8.1%)	2 (22.2%)
Hyponatraemia	13 (34.2%)	2 (40%)	14 (28.6%)	3 (33.3%)
Hyperbilirubinaemia	19 (50%)	2 (40%)	30 (61.2%)	5 (55.5%)
Anaemia	18 (47.4%)	3 (60%)	29 (59.1%)	6 (66.7%)
ARDS	Nil	3 (60%)	1 (2.04%)	4 (44.4%)
DIC	14 (36.8%)	3 (60%)	15 (30.6%)	2 (22.2%)
Cerebral malaria	2 (5.26%)	3 (60%)	2 (4.08%)	2 (22.2%)
Hyperkalaemia	4 (10.5%)	1 (20%)	4 (8.16%)	2 (22.2%)

Among P. falciparum malaria patients, oligouria, anemia, ARDS, DIC, cerebral malaria, hypotension, hyponatraemia, and hyperbilirubinemia were independent risk factors for high mortality. Among P. vivax malaria patients, oligouria, anemia, hypotension, hyperbilirubinaemia, acute respiratory distress syndrome, and hyponatraemia were independent risk factors for high mortality.

Table 6: Outcome of P. falciparum and P. vivax malaria associated AKI

Outcome	P. falciparum AKI (n = 43)	P. vivax AKI (n = 58)	p-value
Dialysis requirement	13 (30.23%)	17 (29.3%)	NS
Sessions of dialysis (days)	3.85 ± 1.52	4.24 ± 1.68	
Length of stay (days)	7.69 ± 3.04	8.18 ± 3.81	
In hospital mortality	5 (11.62%)	9 (15.52%)	

NS = Not significant

Discussion

The study comprised 220 patients with P. vivax malaria and 200 patients with P. falciparum malaria. Singh et al. [16] observed AKI in 5.6% of P. vivax and 6.1% of P. falciparum malaria cases, and 43 (21.5%) and 58 (25.9%) instances of P. vivax malaria, respectively. Consistent with past research, the majority of our patients were under 30 years old for unclear reasons. The male to female ratio in a study by Naqvi et al. [8] was 4:1, while in our investigation; it was 1:2 in P. falciparum and 1:1.9 in P. vivax malaria.

The most widely accepted etiology of AKI in malaria is mechanical blockage brought on by cytoadherance and sequestration of infected red blood cells to the vascular endothelial cells of various host organs combined with rosette formation [17,18,19]. There are several hypothesized pathways of AKI in P. falciparum malaria, including immune-mediated glomerular pathology, changes in renal and systemic hemodynamics, and the release of cytokines, reactive oxygen intermediates, and nitric oxides by activated mononuclear cells. The cause of kidney injury in P. vivax malaria is yet unknown, though.

In certain circumstances, P. vivax malaria induces microvascular thrombosis, endothelial damage, and thrombocytopenia that is nearly identical to thrombotic thrombocytopenia purpura. Thrombotic microangiopathy and hemolytic ureamic syndrome linked to P. vivax also suggest AKI [20,21]. Cause of AKI in malaria whether prerenal, renal (acute tubular necrosis, acute glomerulonephritis, acute interstitial nephritis, acute cortical necrosis) could not be specified because renal biopsy could not be done as consent was not given by the patients. Other contributory causes of AKI include MODS/sepsis, hypotension, hyperbilirubinaemia, etc.

Renal ischaemia and dehydration can also be brought on by reduced blood supply to the kidneys as a result of inadequate fluid intake, vomiting, and pyrexial sweating. [12] Almost all instances of malaria linked to AKI included symptoms of nausea and vomiting. In our study, the prevalence of thrombocytopenia was higher in P. vivax malaria (77.58% vs. 48.83%) than in P. falciparum malaria. In P. vivax malaria [5], thrombocytopenia was found by Prakash et al. to be 10.5%. In 48.83% of P. falciparum and 60.34% of P. vivax malaria cases, anemia was observed. Due to splenic hyperactivity, bone marrow inhibition, or hemolysis of parasitized red blood cells, anemia can arise in malaria. According to Shukla et al., 69% of AKI [22] cases with malaria were anemic. Aside from acute renal injury, hepatic dysfunction was a frequent consequence in our investigation, which is nearly equivalent to the published data in P. falciparum and P. vivax malaria [23,24].

Increased bilirubin levels associated with malaria may serve as a risk factor for AKI. All malarial AKI patients with jaundice exhibited conjugated hyperbilirubinaemia with cholestasis, according to Naqvi et al. report [8]. This well-established link could be a factor in the development of acute tubular necrosis or a decrease in glomerular filtration rate [4,11]. Compared to individuals without jaundice, those with malaria who also had AKI had a higher death rate. According to Kaushik et al., hyperbilirubinemia was present in 41% of malarial AKI cases [25]. In our investigation, hyperbilirubinemia was found in 60.34% of P. vivax cases and 48.83% of P. falciparum cases, respectively. Up to 69% of cases of severe malaria have been found to have classical laboratory findings in malarial AKI of hyponatraemia [26]. In our investigation, hyponatraemia was found in 29.35% of P. vivax cases and 34.88% of P. falciparum cases. The syndrome of inadequate antidiuretic hormone secretion in response to hypovolemia and cerebral salt depletion can cause hyponatraemia.

According to Khan et al., dialysis was necessary in 78% of malarial AKI [27] cases. Dialysis was necessary in 30.23% of P. falciparum cases and 29.3% of P. vivax cases in our study. There have been reports of malarial AKI mortality ranging from 21 to 37.9% worldwide [8,28,29]. In our investigation, the death rate from malarial AKI was 15.52% in P. vivax cases and 11.62% in P. falciparum cases. Comparable to our work, Shukla et al. [22] reported a 9.9% death rate in malarial AKI.It has been observed that ARDS, DIC, cerebral malaria, hypotension, metabolic acidosis, hyponatraemia, hyperbilirubinaemia, anemia, and oligouria are independent risk factors for death.A rise in complications was associated with an increase in mortality. The most significant consequence in our patients that was linked to death was ARDS.

Renal replacement therapy was indicated by a rising trend in serum creatinine, anuria, refractory metabolic acidosis, refractory hyperkalaemia, uraemic pericarditis, and uraemic encephalopathy. The level of serum creatinine dropped considerably following three haemodialysis sessions. The majority of our patients needed three to five haemodialysis treatments. The severity of non-renal consequences determines the prognosis for malarial AKI.

It has been demonstrated that early hemodialysis initiation combined with antimalarial medication improves outcome. Effective dialysis or ultrafiltration, however, may lower the death rate even more [30]. Although peritoneal dialysis has been used to treat malarial AKI, inadequate clearance from microcirculation and peritoneal dysfunction restrict its effectiveness in severe cases [31].

Haemodialysis was continued in our investigation until kidney function improved as indicated by a rise in urine output or a gradual drop in serum creatinine levels.

Conclusion

AKI is a common side effect of P. vivax and P. falciparum malaria. As a result, our research emphasizes the significance of AKI linked to P. vivax malaria. The prognosis of malarial AKI may be improved by prompt detection, renal replacement treatment initiation, and antimalarial medication.

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