Acute Renal Failure in Plasmodium vivax Malaria

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Abstract

Objectives: To analyze incidence, clinical feature and outcome of acute renal failure due to Plasmodium vivax malaria.

Material & Method: This is retrospective analysis of smear positive Plasmodium vivax patients with acute renal failure between Jan 1995 to Dec 2000.

Result: Out of 577 cases of ARF, 93 [falciparum 74 (79.61%); vivax 19 (20.4%)] were related to complicated malaria. 3.2% (19/577) patients, 16 males and three females with age range 17-72, mean 43.3 ± 13.4 years were due to vivax malaria. Thirteen had only vivax and six had mixed falciparum and vivax infection. The presenting features were fever (100%), jaundice (36.8%), hypotension-eight (42%), encephalopathy-11 (57.9%), sepsis-five (26.3%) and DIC-four (21%). The probable contributory factors for ARF were heavy parasitemia-11 (57.9%), hypotension-six (31.5%), hyperbilirubinemia-seven (36.8%), hemolysis-eight (42%) and DIC-four (21%). Oliguria was present in 47.3%, 13 (68.4%) patients required dialysis. Mortality was noted in 15.7% (3/19) patients.

Conclusions: P. vivax malaria can cause ARF, which occurs more commonly in P. falciparum malaria. Renal ischemia is the dominant pathogenic mechanism that results in acute tubular necrosis. The prognosis of ARF in P. vivax malaria is favorable.

INTRODUCTION

Plasmodium falciparum can cause a wide spectrum of renal and renal related disorders, ranging between urinary abnormalities, proteinuria (<1 gm/24 hour) to acute renal failure. Acute renal failure occurs more frequently in falciparum malaria. Reported incidence of ARF in falciparum malaria is highly variable between 1-4%. However ARF in association with P. vivax malaria is rarely reported. Recent outbreak of malaria in our country provides us an opportunity to study ARF complicating P. vivax infection. The objective of this study was to analyze clinical feature, course and outcome of ARF in patients with P. vivax malaria.

SUBJECT AND METHODS

The case records of patients with acute renal failure of different etiology between the period from Jan. 1995 to Dec. 2000, were analyzed retrospectively. A total of 577 cases of ARF were studied and malarial ARF was identified in 93 patients. The laboratory data included thick and thin blood film for malarial parasite. The paracheck test and CBC examination were carried in patients who showed negative blood films for malarial parasite. Hemoglobin, total and differential leukocyte count, biochemical assay (urea, creatinine, sodium, potassium, glucose, s. protein, albumin, globulin, bilirubin, SGOT, SGPT and uric acid) and urine examination were carried in all patients. Coagulation profile, platelet count and LDH were studied as and when required. All patients received quinine hydrochloride in the dose of 10 mg/kg (oral/IV) three times daily and the dose was modified in patients with ARF based on s. creatinine levels. Artesunate compound were given in patients with hypotension or multiple organ failure. Hematological and biochemical assay was repeated during hospital stay as and when required. All patients were followed till death or 4-6 weeks after discharge from hospital. The complications of malaria were recorded in individual patients during the course of hospitalization.

RESULT

A total of 577 cases of ARF of diverse etiology were studied between Jan 1995 to Dec 2000 and 93 (F malaria 74; V malaria
Malaria is a parasitic disease of great epidemiological importance in the tropics and malarial ARF is emerging as a big nephrological issue. Clinically significant renal disease could complicate the infection of *P. falciparum* and *P. vivax*. Renal manifestations of falciparum malaria have a wide spectrum, which can cause electrolyte imbalance, glomerulonephritis and acute renal failure (ARF). Acute renal failure occurs commonly in *P. falciparum* malaria although its rare occurrence has been reported in *P. vivax* malaria. The contribution of malaria to the overall hospital admission for ARF varies from 2-39% according to the local prevalence of the disease.1,3,4 We have reported ARF in association with *P. falciparum* malaria in 4.8% of total ARF cases over a period of 10 years.6 Thus *P. falciparum* is the causative species of ARF in the overwhelming majority of cases.7 *P. vivax* occasionally is incriminated.3,4 Most cases are oliguric, hypercatabolic and associated with other malarial complications, probably depending on the relative impact of different pathogenetic mechanisms. Jaundice, hemolysis, thrombocytopenia and hypotension are common associations with malarial ARF.7 Jaundice occurred in 36.8% of patients. Hypotension and intravascular hemolysis were seen in equal number of cases (42% each) in the present study.

*P. falciparum*, *P. vivax* and mixed infection were reported to cause ARF in 16, three and five patients respectively in an Indian study from Mumbai.8 Malaria has been and continues to be one of the leading causes of ARF in South East Asia, Vietnam, India and Africa.6,7 In the present study *P. vivax* contributed 3.2% of all cases of ARF. Ahmad et al reported acute renal impairment in children due to *P. vivax* malaria. He noted *P. falciparum* was responsible for 66% and *P. vivax* accounted for 33% case of acute renal impairment in children.9 Parasitized red cells are sticky. They tend to adhere to adjacent healthy erythrocyte, blood platelets and the capillary endothelium. This results in the formation of intravascular rosettes and clumps that can impede the microcirculation of internal organs. Although this features is observed with all plasmodium infection its major impact is in falciparum malaria, where it has been associated with serious sequelae.3,7 The endothelial cytoadherence, sequestration, increases whole blood viscosity and capillary lumen obstruction by sticky cell aggregates together contributes to renal ischemia and acute renal failure.1,3,7 The hemodynamic changes are confirmed to be more pronounced in falciparum malaria than in other types of malaria. The various non-specific effect of infection like hemolysis were observed on 100%, 57.9%, 42%, 36.8% and 42% of cases respectively, reflecting majority of patients had severe malarial infection. The renal failure was of ischemic origin and several factors contributing to ARF were presented in Table 3. The various renal complications in patients with *P. vivax* associated ARF is shown in Table 4. Beside ARF, urinary sediment abnormalities and proteinuria of less than 1.0 gm were noted in five and three cases respectively. All urinary abnormalities including proteinuria resolved completely with antimalarial drugs within 3-4 weeks. Dialysis was required in 13 (68.4%) cases and only three (15.7%) patients died.

### DISCUSSION

Malaria is a parasitic disease of great epidemiological importance in the tropics and malarial ARF is emerging as a big nephrological issue. Clinically significant renal disease could complicate the infection of *P. falciparum* and *P. vivax*. Renal manifestations of falciparum malaria have a wide spectrum, which can cause electrolyte imbalance, glomerulonephritis and acute renal failure (ARF). Acute renal failure occurs commonly in *P. falciparum* malaria although its rare occurrence has been reported in *P. vivax* malaria. The contribution of malaria to the overall hospital admission for ARF varies from 2-39% according to the local prevalence of the disease.1,3,4 We have reported ARF in association with *P. falciparum* malaria in 4.8% of total ARF cases over a period of 10 years.6 Thus *P. falciparum* is the causative species of ARF in the overwhelming majority of cases.7 *P. vivax* occasionally is incriminated.3,4 Most cases are oliguric, hypercatabolic and associated with other malarial complications, probably depending on the relative impact of different pathogenetic mechanisms. Jaundice, hemolysis, thrombocytopenia and hypotension are common associations with malarial ARF.7 Jaundice occurred in 36.8% of patients. Hypotension and intravascular hemolysis were seen in equal number of cases (42% each) in the present study.

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hemolysis, disseminated intravascular coagulation, jaundice, hypovolemia, also contribute to ARF. The associated endothelial activation leads to the release of several vasoactive cytokines and mediators which leads to decreased systemic vascular resistance and eventually reduction in renal blood flow and renal ischemia. Volume depletion, hypotension, intravascular hemolysis and hyperbilirubinemia were noted in 42%, 31.5%, 42%, and 36.8% of our patients. Pernicious syndrome consisting of anemia, hypotension, hematopoietic and cerebral involvement can occur in *P. vivax* malaria but less frequent in comparison to *P. falciparum* malaria. We observed pernicious complications (cerebral and hemopoietic) in mixed malaria (27.4%), *P. falciparum* (14.2%) and *P. vivax* infection in 2.3% of cases in the present study. These changes may account for the development of ARF in *P. vivax* infection. However, possibility of mixed infection is difficult to rule out in these patients. Rhabdomyolysis causing ARF had been reported in association with *P. vivax* malaria in patients with myoadenylate deaminase deficiency.

Thus, acute renal failure occurs commonly in *P. falciparum* but *P. vivax* infection can cause ARF. The prognosis of *P. vivax* associated ARF is favorable and antimalarial drugs remain the cornerstone in treatment of malarial acute renal failure.

**REFERENCES**


11. Poels PJ, Dolmans WH, Gabriels FJ. Rhabdomyolysis

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**Announcement**

The office bearers of the Association of Physicians of India, Roorkee - Hardwar Branch, for the year 2003-2004.

**Chairman** : JM Bhatnagar

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