

## ACUTE RENAL FAILURE AND HEPATIC DYSFUNCTION IN MALARIA

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### ABSTRACT

The clinical presentations of severe and complicated malaria vary. The prognosis is poor when associated with cerebral malaria and acute renal failure. Clinical profile, biochemical parameters and outcome were studied in 46 adult patients of malaria admitted in a tertiary care hospital between April 2002 to April 2003. The age of the patients ranged from 15 to 60 years. Majority (n=30) of the patients were in age group of 15 to 34 years. 67% of the patients were from terai belt. Mean duration of febrile illness was 10 days at the time of presentation. 39% (n=18) patients had hepatic dysfunction and 22% (n=10) had acute renal failure (ARF) according to WHO criteria. All patients with ARF were oligo-anuric and required dialysis support. Four patients died of which three were patients with ARF and hepatic dysfunction. Although malaria still remains a major health problem, malarial renal disease has not been formally reported previously from Nepal. Early initiation of antimalarial therapy, close observation for organ failure and early initiation of dialysis in ARF is instrumental in the recovery of the patient.

*Key Words: Malaria, Organ Failure.*

### INTRODUCTION

Malaria, a protean disease is widely prevalent throughout South East Asia, Africa and Latin America. Malaria is endemic in Nepal and at present >70% of the total population of Nepal are at risk of disease<sup>1</sup> and it is prevalent up to 4000 ft.

The clinical presentations may vary and prognosis is worse when it is associated with anemia, hepatosplenomegaly, and cerebral and renal involvement. Although renal involvement in malaria is usually observed with *Plasmodium falciparum* and *Plasmodium malariae* infection.<sup>2,3,4,5,6</sup> *Plasmodium vivax* has also been incriminated in recent studies.<sup>7</sup> In general, *falciparum* is associated with acute renal failure (ARF) and *P.malariae* with Chronic Progressive Glomerulopathy.<sup>8</sup>

The hepatic involvement is usually due to intravascular hemolysis, disseminated intravascular coagulation and rarely due to malaria hepatitis.<sup>9</sup>

### OBJECTIVE

To study the clinical profile, biochemical parameters and outcomes in malarial patients.

### MATERIALS AND METHODS

A total of 46 patients admitted with diagnosis of malaria in the department of medicine in B P Koirala Institute of Health Sciences, Dharan between April 2002 to April 2003 were analyzed. The case sheets of the patients were retrieved from the medical record section using ICD 10 code. Detail clinical features, biochemical parameters and outcomes of the patients were recorded. Analysis was done by using Microsoft XL 2000.

Patients having malarial parasite either on peripheral blood smear or buffycoat was considered as malarial patients. Acute renal failure was considered according to recently revised WHO criteria of serum creatinine >3mg/dl (265 $\mu$ mol/L) with/without urine output less than 400 ml per 24 hrs despite rehydration.<sup>10</sup>

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## RESULTS

Out of forty-six adult malarial patients (M=28, F=18) most were in age group 15-34 years (n=30) as shown in Fig. 1. The presenting features are as depicted in table I. The mean duration of febrile illness was 10 days at the time of presentation (Fig. 2). 68% of the patients were anemic, of whom 5% had severe anemia (hemoglobin below 5gm/dl). Out of 24 patients having their bilirubin measured, 10 (41.6%) had total bilirubin greater than 3mg/dl indicating hepatic dysfunction (Fig. 3) while 9 patients had elevated transaminase and alkaline phosphatase. Out of 39 patients of whom serum creatinine was estimated 10 (25.6%) had acute renal failure (Fig. 4). All the patients with ARF had oligo/anuria. 76% improved with dialysis, antimalarial and other supportive

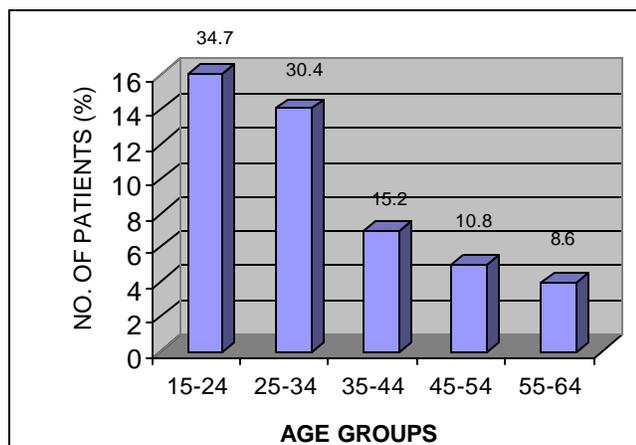


Fig. 1 : Age distribution of patients (n=46)

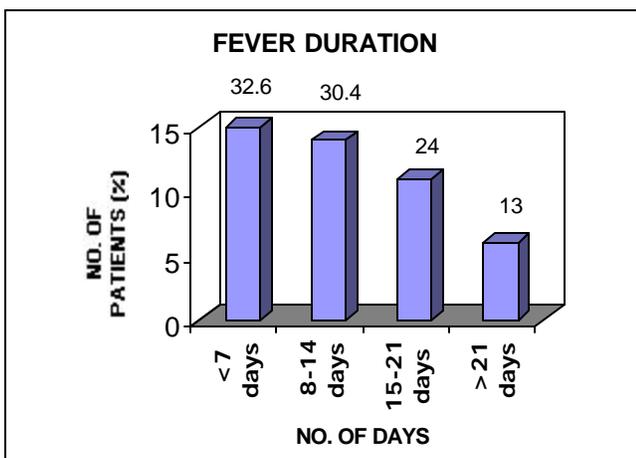


Fig.2 : Bar diagram depicting the duration of Fever in days.

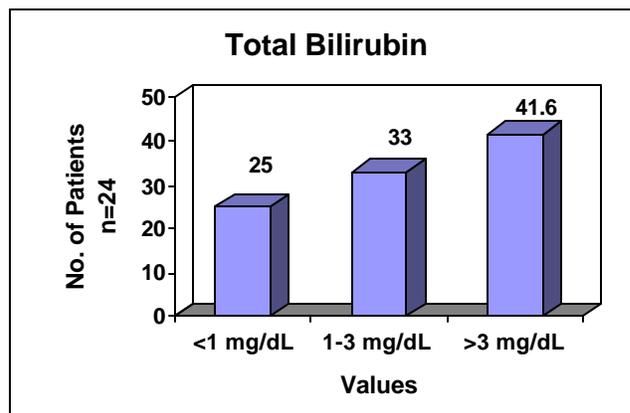


Fig. 3 : Level of bilirubin in mg

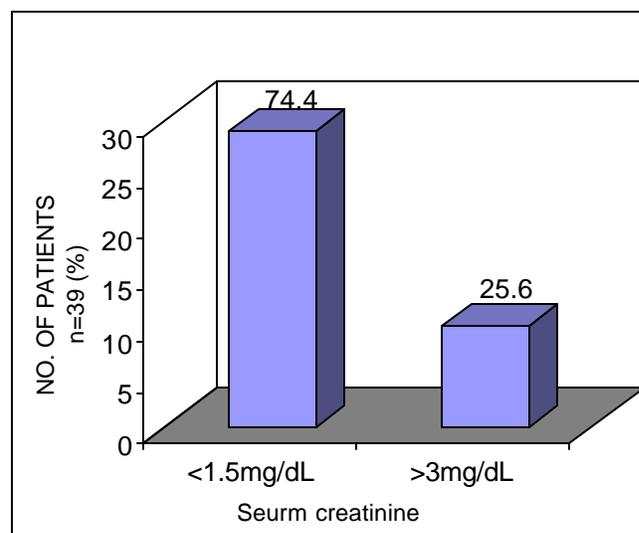


Fig. 4 : Serum creatinine in mg%

managements. Thirty six patients were treated with quinine while remaining patients received artemisinin derivatives. Out of 7 (15%) death during therapy 3 had ARF.

## DISCUSSION

Malaria is a major public health problem in Nepal including other countries of Southeast Asia<sup>2</sup>, Vietnam<sup>11</sup> and Africa,<sup>12</sup> which is endemic for the disease. The situation is more alarming with increasing incidence of falciparum malaria in the region<sup>1</sup>. Early identification of malaria and related condition and their management is extremely important to prevent morbidity and mortality related to it. ARF is a common complication in falciparum malaria infection and occurs almost

Table I : Distribution of Presenting Complains (n=46)

S. No.	Presenting complaints	No of patients	Percentage
1	Fever	46	100
2	Altered Consciousness	21	45.65
3	Cough	11	23.91
4	Oligo- anuria	10	21.73
5	Dyspnoea	4	8.69
6	Bleeding manifestation	3	6.52
7	Algid malaria	1	2.17

exclusively in adults and older children with an incidence of 1 to 4%.<sup>2,3,4,7,10</sup> However, the incidence may reach up to 60% and condition is more common in males.<sup>4</sup> In our study, almost all the cases were adult and older children; mostly males and 25.6% had acute renal failure. However, 25.6% of patients having acute renal failure should be interpreted cautiously as the study place (BPKIHS) is the only tertiary care hospital in the region and the facility to diagnose and treat complicated malaria is limited to few other hospitals.

Patients with ARF are usually oliguric (<400ml/dl) or anuric (<50ml/dl).<sup>2,5,6</sup> However, it may be normal or increased and duration of oliguric phase usually lasts for a few days to several weeks.<sup>10</sup> In our study all patients with ARF were oligo/anuric.

Earlier studies in Thailand have shown that 30% of adult patients with cerebral malaria had serum creatinine levels higher than 2mg/dl.<sup>7,13</sup> Such patients had higher incidence of hypoglycemia, jaundice, more prolonged coma and pulmonary edema.<sup>7,13</sup> Similar studies recently done in Vietnam showed that about 50% of patients had serum creatinine levels greater than 2mg/dl.<sup>7,14</sup> What is more interesting is, 63% of the patients with ARF were jaundiced, compared with 20% of the ones without ARF.<sup>11,14</sup> In our study, all the patients with ARF had hepatic dysfunction i.e. raised total bilirubin level > 3 mg/dl.

Hyperbilirubinemia usually results from the complication of hemolysis and intrahepatic cholestasis rather than hepatocellular necrosis.<sup>9</sup> The true malarial hepatitis is usually distinguished by more than three fold elevation of ALT and is rare.<sup>15</sup> In our study, 41.6% had hyperbilirubinemia according to WHO criteria of severe and complicated malaria.<sup>9</sup>

ARF is a serious complication with a reported mortality of 15 to 33%.<sup>16,17,18</sup> In our case mortality was 15% (n=7) of which 3 (i.e. 43%) were having ARF.

Prognosis of the disease depends upon the severity of condition, associated extra renal complications, response to antimalarial drugs and earlier indication of dialysis. 50% to 75% of patients without dialysis die rapidly.<sup>10</sup> The selected mode of treatment is hemodialysis and should be initiated early in the course of illness, as peritoneal dialysis would be less effective because of impaired peritoneal microcirculation.<sup>2,3,6,7,11,13</sup> However in our study all the patients had undergone peritoneal dialysis. The cause of all the patients undergoing peritoneal dialysis is due to lack of adequate number of hemodialysis machines and also its affordability.

Quinine is the drug of choice and is most widely used antimalarial drug in case of severe and complicated malaria.<sup>10</sup> In our study also most of the patients recovered from the quinine therapy and rest were treated with artemisinin derivatives.

From the above discussion, it shows that malarial acute renal failure and hepatic dysfunction is fairly common in Nepal. However, till date no such studies have been done and this is the first of its kind. So the true incidence and prevalence of the disease in this region needs to be reevaluated.

Thus in conclusion, malaria is an important clinical entity in these regions and the physicians should be vigilant about the deteriorating kidney function as early initiation of antimalarial drugs and dialysis can be life saving.

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