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The changing spectrum of severe falciparum malaria: a clinical study from Bikaner (northwest India)

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Abstract

Background & objectives: Recently there were reports from all over India about changing spectrum of clinical presentation of severe malaria. The present study was planned to study the same in the northwest India.

Methods: This prospective study was conducted on patients of severe malaria admitted in a classified malaria ward of a tertiary care hospital in Bikaner, Rajasthan (northwest India) during 1994 and 2001. It included adult patients of both sexes belonging to all age groups. The diagnosis of *Plasmodium falciparum* was confirmed by demonstrating asexual form of parasites in peripheral blood smear. All patients were treated with i.v./oral quinine. The specific complications were treated by standard WHO protocol. The data for individual complications for both the years were analysed by applying chi-square test.

Results: In a prospective study in 1994 the spectrum of complication was dominated by cerebral malaria (25.75%) followed by jaundice (11.47%), bleeding tendencies (9.59%), severe anaemia (5.83%), shock (5.26%), Acute respiratory distress syndrome—ARDS (3.01%), renal failure (2.07%) and hypoglycemia (2.07%) whereas in 2001 it was dominated by jaundice (58.85%) followed by severe anaemia (26.04%), bleeding tendencies (25.52%), shock (10.94%), cerebral malaria (10.94%), renal failure (6.25%), ARDS (2.08%) and hypoglycemia (1.56%). The sharp difference for presence of jaundice and severe anaemia in 2001 and cerebral malaria in 1994 was statistically significant. Similarly, the important cause of mortality in 2001 was multiple organ dysfunction syndrome (71.10%) with predominant presentation of jaundice and renal failure, whereas in 1994, it was cerebral malaria (77.96%).

Interpretation & conclusion: The observation of changing spectrum of severe malaria in this study and a significant increase in presentation with jaundice as an important manifestation is highly essential for primary, secondary and tertiary level health care providers for proper diagnosis and management.

Key words Cerebral malaria – jaundice – *Plasmodium falciparum* – severe malaria

Introduction

The spectrum of severe malaria has changed worldwide as well as in India. There is an increasing trend for multiple organ dysfunctions and the jaundice is emerging as the most common complication of severe *Plasmodium falciparum* malaria in many places of southeast Asia[1,2]. Another recent change, which

needs urgent attention, is the increasing incidences of acute renal failure. The knowledge regarding the changing spectrum of malaria is very helpful for early diagnosis, because it may become untreatable if vital time is lost. Awareness of the relative prevalence of different complications in a particular geographic area could greatly facilitate the approach towards early diagnosis and prompt treatment[3].

Bikaner district is a part of the Thar desert, India having extremes of temperature. This region has always been regarded as a hypoendemic area for malaria. This is basically an arid zone, which had recently experienced changes in ecosystem due to increased rainfall and canal irrigation in the last two decades. The scenario of both disease morbidity and mortality have altered to a great extent during the past decade. In view of the large number of cases of cerebral malaria in 1994 epidemic[4] and apparent increase in the incidence of jaundice in subsequent years, a systematic study was undertaken to know the spectrum of various complications related to severe malaria in adult patients admitted in the classified malaria wards of Prince Bijay Singh Memorial (PBM) Hospital, Sardar Patel Medical College, Bikaner during 2001. The data obtained from an exactly similar study done by same workers during 1994 epidemic were used for comparison[4]. The observation of local parameters are very essential for formulating management strategies, increasing the public awareness and providing updated information to health care providers for early diagnosis[3,5].

Material & Methods

This study was conducted on severe falciparum malaria patients (*P. falciparum* only or *Pf* + *Pv* mixed) admitted in the classified malaria ward of PBM Hospital, Bikaner during the years 1994 and 2001. The diagnosis of *P. falciparum* malaria was confirmed by peripheral blood smear examination and only those patients who had evidence of asexual forms of *P. falciparum* were included in this study. All patients underwent detailed laboratory investigation, which included blood for total leukocyte count (TLC), differential leukocyte count (DLC), haemoglobin (Hb), bleeding time (BT), clotting time (CT), platelet count, widal test, blood sugar, blood urea, serum creatinine and serum bilirubin. The patients having jaundice were subjected to blood test for aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, HbsAg and hepatitis C marker. Abdominal sonography was done in all the patients having jaundice and/or increased blood urea nitrogen (BUN) level. Skiagram chest and pretreatment electrocardiogram (ECG) were done for all patients. Lumbar puncture and CT scan of head was done for all comatose patients.

The serum of patients with jaundice and renal failure were also tested for antibodies against leptospirosis. The patients having clinical features of hepatic encephalopathy were screened for different markers of hepatitis A and E to ensure that there is no evidence of concomitant viral hepatitis. The grading of hepatic encephalopathy was done by semi quantitative tests of the mental status, asterexis, psychometric test, electroencephalogram (EEG) and blood ammonia levels. All patients were categorised under various complications strictly as per WHO criteria and specific investigation for each complication was carried out as and when required for proper management.

All patients received uniform drug regimen in the form of loading dose of iv quinine sulphate 20 mg/kg in four hours followed by 10 mg/kg intravenously every eight hourly till the patient was able to take orally. Adequate dose correction was done in patients of renal failure and those requiring prolonged iv therapy. The specific complications were managed according to WHO protocol. The patients of hepatic encephalopathy received 25% glucose, lactulose along with the judicious control of serum electrolyte. Patients were kept in the hospital until the parameters related to haematological, renal or hepatic ab-

normality became normal and were discharged only after good clinical recovery. To study the changes in spectrum of complications related to severe falciparum malaria, these data were compared with the data generated from similar study on patients admitted in 1994 epidemic, which was conducted at the same place by the same team of workers using similar protocols for diagnosis and management[4]. Statistical analysis was done using standard methods.

Results

The present study was conducted on 192 adult patients of both sexes of strictly defined severe malaria admitted during the year 2001 and the same was compared with similarly generated data on 532 patients in 1994. The details of the clinical spectrum of various complications during 2001 and 1994 are presented in Fig. 1. The comparison of the spectrum of these two years was statistically analysed using chi-square test to test the significance of variables.

There was a significant increase in the incidence of the jaundice ($p<0.0001$), severe anaemia ($p<0.001$), renal failure ($p<0.05$), spontaneous bleeding ($p<0.001$), shock ($p<0.05$) and thrombocytopenia ($p<0.001$) along with significant decrease in cerebral malaria ($p<0.001$) in the year 2001 in comparison to 1994 (Fig. 1). The incidence of other complications were almost same in both the years, but there had been a statistically significant ($p<0.001$) change from the occurrence of solitary complications—cerebral malaria in 1994 towards the multiple organ dysfunction in 2001, mostly because of concomitant presentation with hepatic and renal involvement in many patients and association of severe anaemia. Death rate was also high in the patients having multiple organ dysfunction syndrome (MODS). Regarding solitary complications leading to death, shock and acute respiratory distress syndrome (ARDS) were the important terminal events in 2001 in comparison to cerebral malaria in 1994. The overall mortality in 2001 and 1994 was 10.93 and 11.09% respectively (Fig. 2).

Discussion

Severe malaria is defined by WHO[5] as the presence of one or more complications in a patient of malaria having asexual forms of *P. falciparum* infection in peripheral blood film. Depending on the severity and rapidity of infection and immune system of the host,

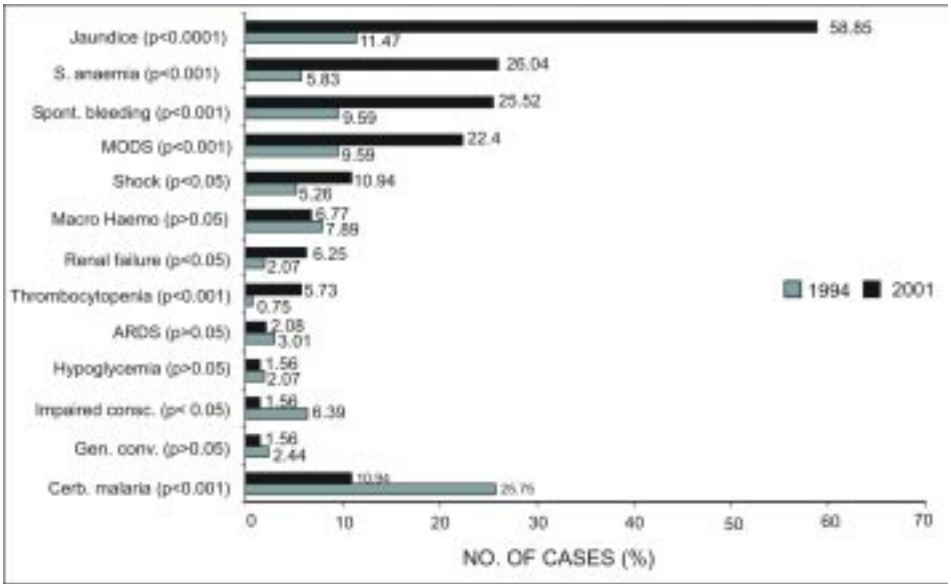

Fig. 1: The spectrum of severe malaria 2001 *vs* 1994

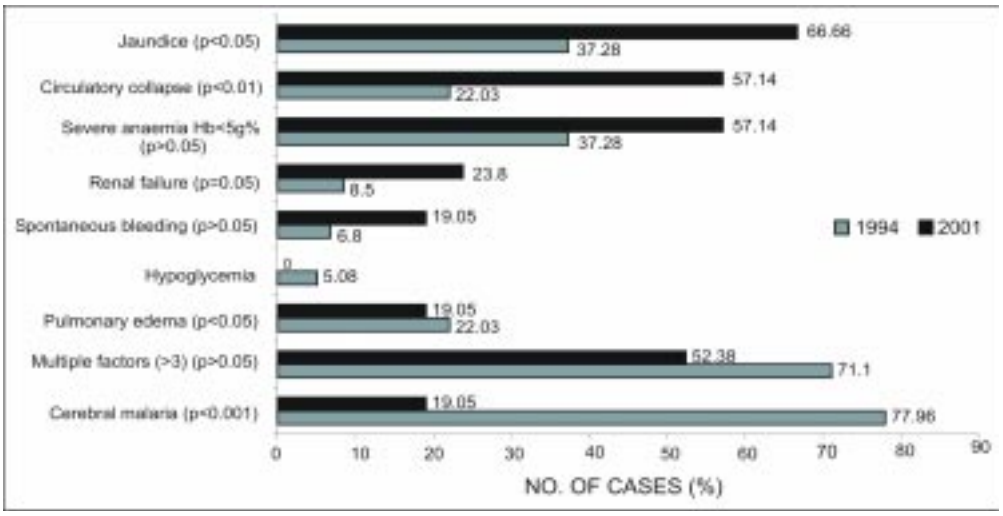

Fig. 2: Complications related to mortality in severe falciparum malaria patients 2001 *vs* 1994

the patient may have different types of clinical presentation. The spectrum of severe malaria differs from area to area and at different times in the same area. The knowledge of the changing spectrum in the region is very essential to the health care providers working in the community. The recent data percolating from different areas of India reflects a drastic change in favour of renal and hepatic involvement, whereas the predominant presentation earlier was with cerebral malaria[6].

The important changes observed were the significant increase in cases with jaundice and anaemia in 2001. Jaundice may present in all forms of human malaria but tends to be more severe in *P. falciparum* infection[7]. The knowledge of this changing spectrum is very vital because many other infective diseases presently prevalent in the community have similar clinical presentation. An ignorance on the part of treating physician may cause delay in the correct diagnosis and thus increasing mortality and morbidity.

The clinical presentation with renal failure and shock has also emerged as an important manifestation of falciparum malaria in 2001 and the observation was also statistically significant ($p<0.05$). Similar observation has also been reported from Vietnam as well as from different parts of India[6,8]. Cerebral malaria was the commonest way of presentation in 1994, but in 2001 it was seen in only 10.94% of cases. The presentation with multiple organ dysfunction was also very high and was the important cause of death in these patients. Malaria associated renal failure can be managed effectively by prompt and careful peritoneal dialysis, but more effective dialysis or diafiltration might reduce the mortality. It is a peculiar complication seen in patients with delayed referral or delayed treatment. Early intervention with haemodialysis or haemofiltration considerably enhances survival[8]. Heterogenecity in parasite virulence may be an important contributing factor for the change in disease severity in *P. falciparum* malaria[9].

While studying the natural course of illness it was observed that jaundice and anaemia alone were not associated with increased mortality, but the mortality was high when they were associated with other manifestations of severe malaria (MODS). Renal failure can be successfully treated by haemodialysis despite the presence of other complications. Shock and ARDS hold a very grave prognosis and were the terminal events in many of the patients. Thrombocytopenia is also a feature of severe malaria and most of the times decreased platelet counts are also associated with abnormal platelet function. A correlation with severity of malaria with thrombocytopenia has also been described[10].

The spectrum of severe falciparum malaria has changed worldwide. In India too, the scenario has changed dramatically. This was recently reviewed in a WHO sponsored workshop at Rourkela[6] which revealed an increasing trend in favour of renal and hepatic failure and multiple organ dysfunction. Currently a large proportion of cerebral malaria patients present with multiple complications including acute respiratory failure (ARF) and jaundice. The death rate is also very high in this group.

The exact cause of increased incidence of hepatic or renal injury is not known but may be due to selective involvement of these organ by a different strain of *P. falciparum*[9]. The presentation of jaundice with malaria including hepatic encephalopathy had also been reported recently[11]. The use of paracetamol as an antipyretic is being replaced by newer nonsteroidal anti-inflammatory drugs and may have some doubtful role in relation to hepatic or renal injury. Non-steroidal anti-inflammatory drugs can convert a latent renal failure to overt ARF by removing the compensatory mechanism of increasing the renal blood flow mediated through prostaglandin. The injury may not be severe enough to cause ARF or hepatic involvement in healthy persons but in persons whose hepatic and renal conditions are already compromised (as in the case of severe malaria), it can be detrimental. The presence of different strains of *P. falciparum* is well-known but it is extremely difficult to prove the presence of such strains.

The awareness about the changing spectrum of severe malaria is of great importance to every level health care provider. Today, in India with any level of transmission the possibility of falciparum malaria should always be suspected in a patient presenting with fever along with jaundice or renal failure.

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