

Clinical profile and outcome of cerebral malaria in pediatric cases at a tertiary Care Hospital

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Abstract

Background: Cerebral malaria (CM) is a potentially fatal condition encountered in all age groups and if not treated timely can cause mortality. **Objective:** to evaluate the clinical features of cerebral malaria in children at a tertiary care Hospital of Telangana. **Methods:** This was a prospective study carried out from January 2013 to December 2014 at a tertiary care hospital of Telangana. Clinical profile, treatment and outcome of all the children diagnosed with CM aged between 5 months to 12 years were assessed. **Results:** There were a total of 65 patients with CM of which 40 (74.7%) of them were girls and 20 were boys (25%). *P. falciparum* was the main infecting species in both uncomplicated malaria and severe malaria cases. The clinical features noted were seizure (39.62%), anemia (84.9%), icterus (16.98%), hypotension (13.2%), bleeding (3.7%), hepatomegaly (5.66%), splenomegaly (5.66%), pulmonary edema (16.98%) and renal dysfunction (37.36%). Treatment received included artesunin compounds or quinine. Complete recovery was achieved in 53 (81%) of them. Three (6.1%) of them died. **Conclusion:** CM considered being a fatal disease has shown remarkable improvement in the outcome with the wide availability of artesunin and quinine components. The key to management is early diagnosis and initiation of treatment based on a high index of suspicion.

Keywords: Cerebral malaria, Clinical profile, Tertiary care hospital

Introduction

Malaria in its severe form is one of the leading causes of mortality in all ages in tropical countries. Across the world, South East Asian Region bears the second largest burden of malaria (13.0%), being next only to African region (81.0%). Among South-East Asia region, India shares two-third of the burden (61.0%) followed by Indonesia (22.0%) and Myanmar (12.0%) [1, 2]. Unlike in Africa, where most of the deaths are reported in infants and children, it is seen that in India, the deaths in infants and children below 14 years of age is only 20.6%. *Plasmodium falciparum* (Pf) is the main culprit responsible for severe and complicated malaria [3]. Recent studies suggest that *Plasmodium vivax* (Pv) is also equally responsible for severe form of malaria [4]. Cerebral malaria (CM) is one of the most common causes for non-traumatic encephalopathy in the world. It affects both the urban and rural population. It is a challenge to treat these patients in a resource limited

setting; where majority of these cases present. However, they are increasing reports of complicated malaria by other species as well [5,6]. Clinical presentation of malaria varies from uncomplicated acute febrile illness to a severe form of malaria when infections are complicated by serious organ failures or abnormalities in the patient's blood or metabolism.

The manifestations of severe malaria include CM, severe anemia, hemoglobinuria due to hemolysis, acute respiratory distress syndrome, abnormalities in blood coagulation, hypotension, acute kidney injury, hyperparasitemia (more than 5% of the red blood cells (RBCs) infected by malarial parasites), metabolic acidosis and hypoglycemia. Severe malaria is a medical emergency and should be treated urgently and aggressively [7].

So this study was planned in order to evaluate the clinical features and outcome of cerebral malaria in children at our tertiary care hospital.

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Methods

The present study was conducted in MGM Hospital, Warangal, a tertiary care teaching hospital of Telangana. This was a hospital based clinico-epidemiological study. Cases of confirmed malaria patients admitted between January 2013 to December 2014 were collected in a preformed proforma.

Out of 129 children of malaria admitted in the Department of Paediatric, 65 children satisfied the World Health Organization (WHO) criteria of severe malaria guidelines 2010 [7] with cerebral malaria and

admitted in Pediatric Intensive Care Unit. Cerebral malaria (CM) was defined as a clinical syndrome of coma (inability to localize a painful stimulus) at least 1 hour after termination of a seizure or correction of hypoglycemia, detection of asexual forms of *falciparum* malarial parasite on peripheral blood smear and exclusion of other causes of encephalopathy. We further studied the clinical profile, treatment and outcome of these patients. Data was collected in a preformed proforma and analyzed by SPSS 20.0 software. Values are expressed in number and percentage (%).

Results

In the present study, *P. falciparum* was the main infecting species in both uncomplicated malaria and severe malaria cases. Maximum number of children got admitted after rainy season and peak admission were from September to November. Maximum numbers of patients were of Pf (57.8%); *P vivax* was documented in 13.7% and mixed infection in 27.4% cases. The age of patients ranged from 5 months to twelve years with a mean age of 6 years.

There were a total of 65 patients with cerebral malaria of which 40 (71.7%) of them were girls. Among them 35 (66%) patients were less than 10 years of age all of them had presented with fever and altered sensorium with documented malarial parasite on the peripheral blood film. Twenty one (39.62%) of them had a history of seizures. Other clinical features [Table 1] noted were pallor (35%), icterus (16.98%), hypotension (13.2%), bleeding (3.7%), hepatomegaly (5.66%) and splenomegaly (5.66%). Non cardiogenic pulmonary edema was present in 9 (16.98%) of them.

Table-1: Clinical manifestations of patients with malaria.

Clinical Manifestations of malaria	Percentage (%)
Anemia	35.3%
Seizures	39.4%
Icterus	38.10%
Non -cardiogenic pulmonary edema	16.76%
Bleeding	5.76%
Hepatomegaly	5.67%
Splenomegaly	3.80%
Hypotension	13.10%
Renal dysfunction	16.20%

Majority (84.9%) of the patients had anemia. Hypoglycemia was documented in only one patient. Deranged renal function was noted in 20 (37.36%) of them.

These patients were managed conservatively. All the patients had documentation of *P. falciparum* on the peripheral blood film. Co-infection with *Plasmodium vivax* was present in 13 (24.53%) of them. Treatment received included artesunate compounds (artesunate in 37 and artether in 3), quinine (9) and quinine – doxycycline combination therapy (2). In view of clinical failure 3 of them were switched over from artesunate to quinine. Median time of defervescence was 3 (interquartile range 1-4).

Complete recovery was achieved in 43 (81%) of them. Three (6.1%) of them died. Others included children who were referred to higher center and those who left the hospital against medical advice.

Discussion

CM is a diffuse encephalopathy in which focal neurological signs are relatively unusual. It is often accompanied by multisystem dysfunction. CM is defined as severe *P. falciparum* malaria with cerebral manifestations, usually coma (Glasgow coma scale <11, Blantyre coma scale < 3).

Malaria with coma persisting for > 30 min after a seizure is also considered to be CM 4. The 2010 revised criteria for severe malaria are the presence of one or more of the following: Prostration, impaired consciousness, failure to feed, respiratory distress (“air hunger”), multiple seizures (more than two episodes in 24 h), circulatory collapse, pulmonary edema (on radiological imaging), abnormal spontaneous bleeding, jaundice, hemoglobinuria, severe anemia, hypoglycemia, acidosis, renal impairment, hyper-lactatemia, and hyperparasitemia [4].

According to the latest World Health Organization (WHO) estimates, there were about 219 million cases of malaria in 2010 and an estimated 660,000 deaths. Africa is the most affected continent: Unlike in Africa, where most of the deaths are reported in infants and children. Whereas in India, the deaths in infants and children below 14 years of age was only 20.6% which is about 90% of all malaria deaths occur there [5].

Unlike in Africa, where most of the deaths are reported in infants and children, it is seen that in India, the deaths in infants and children below 14 years of age is only 20.6%. Among the 65 patients with CM, 71.7% were girls and 66% were less than 10 years of age. Seizure was the presenting symptom in 39.62% patients. Seizures are a prominent feature in CM and repeated seizures have been associated with poor outcome. Children have a higher incidence of seizures. Camara *et al.* noted seizures in 52.5% of the children with *P. falciparum* [7].

Patel noted that 46.8% of the patients with *falciparum* malaria had anemia whereas Wasnik *et al.* noted that 65% of the cases had anemia [6,8]. In our cohort 84.9% had anemia. The higher incidence could have been due to underlying anemia prior to the infection. Studies from Ghana noted an incidence of 66.2% among the children [9].

The causes for anemia in CM patients are obligatory destruction of RBCs containing parasites at merogony, accelerated destruction of non-parasitized RBCs and

bone marrow dysfunction. Hypoglycemia in CM patients are due to increased peripheral requirement of glucose consequent upon anaerobic glycolysis, increased metabolic demands of febrile illness, obligatory demand of parasites, failure of hepatic gluconeogenesis and glycogenolysis (parasites consume up to 70 times as much glucose as uninfected cells). It is compounded by the stimulation of insulin secretion from pancreatic beta cells by quinine. Hypoglycemia was present only in one of our cases. Blood sugars of all the patients in the present study were closely monitored and glucose supplementation was given. In a previous study the incidence of hypoglycemia was 6.38% [8].

Renal dysfunction causes morbidity in these patients. Biochemical evidence of renal dysfunction was noted in 37.6% patients. None of them required hemodialysis and were managed conservatively with diuretics and fluids. It is comparable to the previous studies where the incidence was 32.5%. Out of 526 cases of CM reported from Rourkela, in Sundargarh district of Orissa state, 28.9% had acute renal failure (ARF) [10].

Mortality in this series was particularly high (59%) specifically in those with multiorgan failure. The effect of associated ARF on mortality in CM patients indicated, mortality was as high as 39.5% when associated with ARF, while it was only 13.9% when unassociated with ARF.

Metabolic acidosis is a known complication of malaria. Hyperventilation (Kussmaul breathing) with a clear chest on auscultation suggests metabolic acidosis. At our center since there was no facility for estimation of blood gases, we made a clinical diagnosis based on this and was initiated on sodium bicarbonate infusion and fluids. Clinical improvement as indicated by normal respiratory rate guided us in our management.

In our study, 16.9% patients had non cardiogenic pulmonary edema. Unavailability of mechanical ventilation in three of the patients attributed to mortality. Rest of the patients had responded to diuretics. Case fatality rate is very high in these patients and they should be referred to a facility where mechanical ventilation and intensive care is available.

Antimalarial drugs are the only interventions that unequivocally reduce mortality in patients with malaria. The cinchoids (quinine and quinidine) and artemisinin

compounds are most commonly used. The World Health Organization now recommends using intravenous artesunate in preference to quinine for the treatment of severe *P. falciparum* malaria [11]. Combination therapy with doxycycline has been recommended in the severe malaria cases.

The artemisinin components available for treatment of malaria are artemether, arteether and artesunate. In a large open label, randomized trial of Asians with severe malaria, artesunate significantly reduced mortality by 34.7% [12]. Majority (75.47%) of our patients were treated with artesunin components. Out of these except for 3 patients rest of them had responded to artesunate. Artesunate was replaced by quinine in these patients to which they had responded. Combination therapy of quinine with doxycycline was used in only 3 patients. Quinine was given under cardiac monitoring. However, no cardiac complications were noted in any of these patients.

Mortality rate was 3.7% in this study. Lon *et al.* noted a mortality rate of 35% among CM cases [13]. Wasnik *et al.* noted that the cause of death were ARF, metabolic acidosis, aspiration pneumonia and circulatory failure. Case fatality rates in the other studies from Africa have shown a high mortality rate of 13-21% [14,15]. Artesunin components as combination therapy are the drug of choice as per WHO recommendations and can be easily administered with hardly any side effects [11]. Since this was a study with small sample size, we could not demonstrate any cyclical changes in clinical profile of severe malaria over a period of two years. There is a need of prospective study with bigger sample size to find out any changing trend over years.

Conclusion

CM once considered a fatal disease has shown remarkable improvement in the outcome with the wide availability of artesunin components. Most of the complications of severe *falciparum* malaria including CM can be managed by a pediatrician.

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