Special Feature: "Short Communication"

A study of various complications and outcome of falciparum malaria in patients of a rural South Indian medical college hospital

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ABSTRACT

Background: Sparse published data are available regarding clinical presentation and complications of falciparum malaria from Andhra Pradesh state**.**

Methods: In this prospective, observational study conducted during the period November 2012 to June 2014 at our teaching hospital in Kuppam, Andhra Pradesh, adult patients (n=96) admitted with fever confirmed to be suffering from falciparum malaria based on peripheral blood smear examination and / or malaria antigen test positive by rapid diagnostic test were studied. The clinical presentation and various complications of falciparum malaria were documented.

Results: The male to female ratio was 2:1. Majority of the patients (70%) were in the age group 26-60 years. Fever was present in all cases. Splenomegaly (66%) was the most common physical sign followed by pallor (31%) and icterus (22%). Anaemia (51%), was the most common complication, followed by cerebral malaria (33.3%), acute respiratory distress syndrome (ARDS) (32.3%), acute kidney injury (AKI) (29.2%), and jaundice (25%). Majority of the patients presented with multiple complications (73%) than single complication (27%). Artemesinin-based combination therapy was administered to 72 of the 96 patients of whom 43 patients recovered. Quinine therapy was given to 14 patients of whom 10 recovered. Quinine plus ACT combination therapy was given to 10 patients and 7 recovered. seven of the 96 patients died; and 29 out of 96 patients were taken home against medical advice. Overall 36/96 (37.5%) patients had a poor outcome. All 7 patients who expired had multiple complications. Mortality was higher in patients who had co-existent AKI, hypotension and cerebral malaria.

Conclusion: Early identification of high risk cases and institution of prompt treatment can reduce the mortality rate in falciparum malaria.

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INTRODUCTION

Malaria is one of the most serious vector borne tropical disease of the world affecting 300-500 million people and causing over 1 million deaths each year. According to the World Malaria report 2013 there were in 2012 an estimated 207 million cases of malaria and 627000 deaths. By comparison, in 2008 there were an estimated 225 million malaria cases and 747000 deaths.

P. falciparum is well recognized to cause life threatening complications with multiple organ dysfunction, the cumulative effects of which cause fatality. Knowledge regarding the changing spectrum of malaria is very helpful for early diagnosis and prompt treatment, preferably in an ICU setup. Awareness of relative prevalence of different complications in a particular geographic area could greatly facilitate management.

MATERIAL AND METHODS

Hospitalized patients aged 18 years or more diagnosed to have falciparum malaria were included in this study. The study was conducted

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at the PES Hospital, Kuppam, Andhra Pradesh between November 2012 and June 2014. The study was cleared by Ethics committee of PESIMSR, Kuppam. In all of them, a detailed history was obtained and physical examination with a focus on complications was carried out. All patients were subjected to the following laboratory investigations; Thick and thin peripheral smear for malarial parasite (up to 6 smears obtained at different times as required), stained with Giemsa /Leishman stain and seen under oil immersion microscope by a competent microscopist, malaria antigen test [(Rapid diagnostic test) (Alere Trueline Rapid test kit for malaria Ag Pf/Pan)], arterial blood gas analysis, complete blood counts, coagulation profile, serological testing for human immunodeficiency virus (HIV), hepatitis B surface antigen (HBs Ag), urinalysis including testing for haemoglobinuria, ultrasonography of abdomen, chest radiograph, cerebrospinal fluid analysis, plasma glucose, blood urea, serum creatinine, serum electrolytes and liver function tests.

Cases were managed following the standard treatment protocol as per World Health Organization (WHO). All patients were treated with oral, intravenous (IV) quinine, artemisinin-based therapy or in combination as appropriate for the clinical condition of the patient. All the proven cases of severe malaria were treated with parenteral anti-malarial, either quinine or artemesinin derivatives along with either sulphadoxime and pyrimethamine (SP) or lumefantrine, changing over to oral drugs once the general condition improved. Seven days course of doxycycline, 100 mg twice daily was also administered to all patients. Any untoward drug reactions were noted. Necessary supportive measures and treatment of complications, which included assisted ventilation and blood transfusions, were instituted.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation. Categorical variables are presented as percentages.

RESULTS

Majority of the patients (70%) belonged to the age group 26-60 years (Table 1). The male to female ratio was approximately 2:1. Clinical presentation and complication of falciparum malaria are depicted in Tables 2 and 3 respectively. Almost all the patients (99%) belonged to the low socio-economic status. Fever was present in all cases. Splenomegaly (66%) was the most common sign followed by pallor (31%) and icterus (22%). Anaemia (51 %), was the most common complication, followed by cerebral malaria (33.3%), acute respiratory distress syndrome (ARDS) (32.3%), acute kidney injury (AKI) (29.2%), and jaundice (25%).

Presentation with multiple complications (73%) was more common than presentation with a single complication (27%). All

Table 1: Age distribution (n = 96)

Age (years)	No.	%
18-25	14	14.6
26-40	28	29.2
41-60	40	41.7
>60	14	14.6

Table 2: Clinical presentation (n = 96)

Symptoms	No.	%
Fever	96	100
Chills and rigors	81	84.3
Nausea and vomiting	50	52.0
Headache	40	41.7
Myalgia	40	41.7
Altered sensorium	36	37.5
Abdominal pain	30	31.2
Cough	28	23.2
Breathlessness	23	24.0
Diarrhoea	16	16.7
Convulsions	15	15.6
Bleeding	8	8.3
Jaundice	6	6.3
Decreased urine output	4	4.2
Chest pain	3	3.1

Table 3: Complications

Complications	No.	%
Anaemia	49	51.0
Thrombocytopenia	38	39.6
Cerebral Malaria	32	33.3
ARDS/Respiratory failure	31	32.3
AKI	28	29.2
Hypotension	25	26.0
Jaundice	21	21.9
MODS	20	20.8
Algid malaria	19	19.8
Convulsions	15	15.6
Bleeding / DIC	8	8.3
Haemoglobinuria	4	4.2
Hypoglycaemia	3	3.1
Acute pancreatitis	3	3.1

ARDS = acute respiratory distress syndrome; AKI = acute kidney injury;
MODS = Multiple organ dysfunction syndrome; DIC = disseminated intravascular coagulation

uncomplicated falciparum malaria cases responded well to oral quinine or artemesinin-based combination therapy. Majority of patients with complicated falciparum malaria responded to IV quinine or artemesinin-based combination therapy (Table 4). There was no statistically significant difference in the outcome between various treatment regimens (p=0.338).

The overall mortality was 7 out of 96 in our study; 29 patients who were critically ill were discharged against medical advice (Table 4). All 7 patients who expired had multiple complications and they constituted 7.3% of all complicated malaria cases. Higher mortality was noted in patients who had co-existent AKI, hypotension and cerebral malaria, even if the total number of complications were not taken into account.

DISCUSSION

This cross-sectional study shows males (67%) were affected more when compared to females (33%). Majority belonged to the age group 40-60 years. In the present study fever was the most common symptom (100%) and the majority of patients presented with complications within 7 days.

A study[9] from Jamshedpur in Jharkhand state of India documented the atypical presentation of falciparum malaria to be convulsion in 28.6%, abdominal pain in 5.7%, hemiplegia in 2.8%, generalized weakness and palpitations in 5.5% cases. In the present study, patients demonstrated atypical symptoms such as vomiting in 50%, loose motion in 16%, cough and breathlessness 23%, convulsions in 15%, bleeding in 8% and jaundice in 6%.

The sequestration of erythrocytes, containing metabolically highly active parasite in the vascular bed of internal organs is thought to be the likely explanation for all the pathological events in severe complicated falciparum malaria.[10]

There were 70 (73%) patients with multiple complication and 26 (27%) patients with single complication in the present study. In a study[11] from Orissa, 86.7% had anaemia and 10% had severe anaemia. In the present study anaemia was found in 51% of patients.

Table 4: Treatment modalities and outcome

Treatment	No. of patient	Outcome		
		Death No. (%)	DAMA No. (%)	Recovery No. (%)
Quinine	14	0	4 (28)	10 (71.4)
ACT	72	6 (8.3)	23 (32)	43 (59.7)
Quinine + ACT	10	1 (10)	2 (20)	7 (70)
Total	96	7	29	64

ACT = artemisinin-based combination therapy; DAMA = discharge against medical advise

Thrombocytopenia has been reported to be associated with malaria with incidence ranging from 40.5% - 85%.[11] Thrombocytopenia is thought to be caused by increased splenic sequestration; immune mediated destruction and shortened platelet survival.[11] The present study documented thrombocytopenia in 39% patients.

In another study,[12] 11 patients (20%) showed hyperbilirubinemia. The present study documented hyperbilirubenemia in 21.8% patients. Hyperbilirubenemia in falciparum malaria results from intravascular haemolysis of parasitized erythrocytes, hepatic dysfunction and microangiopathic haemolysis due to DIC. Deranged renal function in falciparum malaria has been attributed to various factors like dehydration, increased catabolism and impaired renal function. Deranged renal profile was observed in 27.7% patients in the study from Orissa.[13] In the present study, AKI was observed in 28% of subjects.

Of the 96 cases of complicated falciparum malaria, 14 patients received quinine, 72 patients received artemesinin-based combination therapy and 10 patients received both. Doxycycline was given to all the patients.

In our study, 7 patients out of 96 patients died. Causes of death included AKI with metabolic acidosis, aspiration pneumonia secondary to seizures, cerebral malaria and circulatory shock. The lower mortality recorded in the present study could also be due to the fact that 29 critically ill patients were discharged against medical advice.

The present study provides real-time data regarding clinical characteristics and outcome in patients with falciparum malaria from Kuppam, Chittoor district, Andhra Pradesh state.

Our observation suggest that a high index of clinical suspicion, early initiation of anti malarial treatment can be life-saving in falciparum malaria.

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