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Clinical Profile of Malaria in Adults

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ABSTRACT

Background : Malaria remains the most important human parasitic infection globally and continues to pose a major public health threat in India , particularly due to plasmodium falciparum which is prone to complications. Hence the study was undertaken to analyse various types of clinical presentation of Malaria in Adults , its complications and response to treatment guidelines followed by The National Vector Borne Disease Control Programme(NVBDCP).

Materials and Methods: A cross sectional study of 50 patients with positive lab results , aged more than 15 years were included in study. Patients with history of allergy to antimalarials and who cannot be followed for initial 5 days were excluded. Average number of parasites was calculated for initial 5 days .Based on treatment ,patients were divided into early(ETF) and late treatment failure(LTF) group and adequate clinical response group(ACR). NVBDCP Treatment guidelines are based on WHO advised drug regimen for South East Asia region .Artesunate combination therapy (ACT) was used in patients with treatment failure groups.

Results : 25 patients(pts) had P.vivax and 25 had P.falciparum. No siginificant difference in age distribution was observed. Most common symptom was fever 98% and commonest sign was splenomegaly 80% with serum bilirubin, elevated in 48% patients .6 pts had multiple organ dysfunction.There was significant reduction in daily parasite count and body temperature in initial 5 days after treatment .32 pts responded to chloroquine and primaquine therapy(CQ+PQ) (64%) and 18 pts to second line drugs.Among P.vivax , all pts showed ACR but 14 out of 25 in P.falciparum group showed ACR and 11 had ETF. out of 14 pts in ACR in Falciparum group 7 reponded to CQ+PQ therapy & 7 responded to second line drugs .

Conclusions : Use of ACT in complicated malaria as advised by NVBDCP especially in high falciparum failure areas prevents deaths. Hence use of combination drugs in treating complicated &resistant cases helps in reducing complications.

Introduction :

Malaria, a most serious vector-borne disease, is one of the major causes of illness and death in

tropical and subtropical regions of the world. It is one of the most common parasitic infections in our country(1)and over 1.65 and 1.77 million cases were reported in 2003 and 2004 respectively(2).Malaria has been a serious problem in some parts of our country due to the slow progress in its control. Lack of proper health infrastructure, inability to control the disease in endemic areas, and movement of the population are some of the factors responsible for failure to curb malaria . The epidemiological situation of malaria has shown a gradual deterioration in India. There has been a quantum jump in the incidence of falciparum cases of malaria. It has become apparent that chloroquine resistance of malaria has become a global problem and is perhaps one of the important causes of malarial resurgence, and needs update studies in all the states of India. This will help to form the effective therapeutic strategies to control its associated mortality and morbidity[1].The NVBDCP reports 2.5 – 3.2 million parasite positive cases and about 1000 malarious deaths each year in India(3) . The National Vector Borne Disease Control Programme (NVBDCP) aims to control the disease through early diagnosis and treatment, preventive measures. This programme is under supervision of District Malaria and District Health Officer . Hence study was conducted to analyze various types of presentation of Malaria in Adults , its complication and response to treatment and treatment guidelines followed as per NVBDCP guidelines.(2004)(4)

Materials and methods

Patients with clinical symptoms and signs of malaria were tested for confirmation . 50 patients 25 Plasmodium vivax (P.Vivax) and Plasmodium falciparum (P.Falciparum) with positive lab results were thoroughly investigated with history and clinical examination, treated as per NVBDCP guidelines. NVBDCP guidelines is based on WHO advised drug regimen for South East Asian region (SEA region) 2004. Study was conducted between 2004-2006.

Patients aged more than 15 years of age with Smear positive for Malaria were included in study. patients who cannot be followed up for initial 5 days of treatment and those known to have allergy to antimalarial drugs were excluded.

The average number of parasite is calculated, by counting the parasites and WBCs in 200 oil field immersion fields in thick smears. Parasite density per microlitre calculated by multiplying it by WBC count.

Following initiating the treatment daily clinical examination, axillary temperature recording, parasitemia and hemoglobin was checked and depending on response to treatment patients were classified into

Early treatment failure :

Patients who develop danger signs or severe malaria on D1 , D2 , D3 with parasitemia

Axillary temperature of >37,5 'C on day 2 with parasitemia more than compared to day 1 or on Day 3 in presence of

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parasitemia

Parasitemia on day 3 >25 % of parasite count of day 0

Late treatment failure
Presence of danger signs or severe Malaria with parasitemia on any day from day 4 to 14 or Axillary temperature > 37.5 ' C in presence of parasitemia on any day 4 to 14 days without meeting any criteria of ETF

3. Adequate clinical response:
a. Absence of danger signs with absence of parasitemia on day 14 irrespective of axillary temperature or axillary temperature <37'5 C irrespective of presence of parasitemia without meeting any criteria of ETF /LTF. NVBDCP guidelines for treatment for malaria based on WHO guidelines for SEA region 2004(3).(Table no 1)

table no 1

Sly no	Area	Unconfirmed	Plasmodium Falciparum			Plasmodium vivax	
1	India	CQ 10 mg/kg	Lab confirmed	Treatment failure	Severe Malaria	Treatment failure	Lab confirmed
			CQ 25 mg/kg + PQ 45 mg stat	SP + PQ	Inj quinine 10 mg / kg for 7 days or inj ATM derivatives	CQ 25 mg /kg + PQ 15 mg/ day for 15 days	CQ 10 mg/kg +PQ 15 mg/ day for 15 days

Reference no 4

Danger signs of Malaria:
Following are monitored

Signs
Cerebral malaria(unarousable coma)
Severe anemia (Hb < 5 g/dl)
Renal failure(creat>1.5 mg/dl)
Hypoglycemia (RBS<40 mg/dl)
Systolic BP < 70mm hg
Convulsions
Acidosis

Artesunate combination therapy is the first line treatment in chloroquine resistant areas. The dose of it is 4 mg / kg daily for 3 days +25 mg / kg of sulfadoxine and 1.25 mg / kg pyrimethamine on the first day. ACT should be given in lab confirmed cases. Primaquine was given in the dosage of 45 mg stat or 0.75 mg /kg body weight.

Results:
There were 50 patients in this study, 25 patients had P.Vivax and 25 had P.Falciparum. With 31 Male patients (62%) and 19 female patients (38%). Most of the patients were in age group of 30 – 40 years. There was no significant difference in age distribution (p>0.367). Most common symptom was fever 98% , chills 79% , headache 70% , and diaphoresis 64% and common sign seen was splenomegaly in 80% cases with elevated Bilirubin being the commonest lab abnormality seen in 48% cases and other abnormalities like low hemoglobin 30% and thrombocytopenia in 28 % patients. 6 patients had multiple organ dysfunctions with increased bilirubin, creatinine, and low hemoglobin.

Figure 1: Sex wise distribution of Malaria

Figure 2: Clinical features and associated lab abnormality.

There was significant reduction in temperature which was measured every day with following readings, Day 0-38.49, Day 1-37.7, Day 2-37.45, Day 4-37.2 and day 5-37' c. Paired difference test shows very high significant `p' value of treatment from Day 0 to Day 5. There was significant decrease in Parasite count from Day 1 to Day 5.(Paired samples test).

Parasite count	Mean	Standard deviation	Z	'P' Value	
D0 – D1	29629.71	40334.88	3.029	0.008	HS
D0 – D2	45665.12	46784.73	4.024	0.001	vHS
D0 – D3	20673.16	38644.59	3.783	0.001	vHS
D0 – D4	62952.00	60119.05	3.627	0.004	HS
D0 – D5	22878.18	40590.57	3.985	0.001	HS

32 patients responded to Chloroquine and Primaquine constituting 64 % and 18 patients to second line drugs. Among P.Vivax, all patients showed adequate clinical response but 14 out of 25 P.Falciparum showed ACR and 11 had ETF. Out of 14 patients of ACR in Falciparum group 7 responded to CQ + PQ therapy and 7 to second line drugs

Figure 3: Clinical response of Malarial Parasites.

	Adequate clinincal response	Early treatment failure	
P.VIVAX	P.FALCIPARUM	P.VIVAX	P.FALCIPARUM
25	14	0	11

Results of Falciparum treatment:
Patients with danger signs:

Severe Anemia	1
Cerebral malaria	1
Renal failure	3
Hypoglycemia	0
Systolic BP < 70mm hg	3
Spontaneous bleeding /DIC	4
Convulsions	1
Acidosis	0

Discussion:
The considerable morbidity and mortality in falciparum malaria is mainly due to its protean manifestations, multiorgan involvement and delay in diagnosis and failure of administration of treatment promptly and adequately. The emergence of gradually spreading drug resistance adds to the seriousness of the problem[1]. It is important for the clinician in tropical countries to be alert to the symptoms and signs that may progress to the life-threatening disease of falciparum malaria . In the last decade the clinical pattern of severe malaria has been changed in different parts of the world including India.

This cross sectional study shows males (62%) were commonly affected compared to females(38%). Most of the patients were between the age group of 30-40 years(75%). Majority of patients are outdoor workers like coolie workers, fish vendor, hotel workers, watchman, which increases the chance of mosquito bite and transmission and indicat-

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ing lack of personal protection. Chandrashekar UK et al observed infection more common in males than in females. (5)

In our study, fever was most common symptom(94%) with hyperpyrexia observed in 3 patients. These results were similar to study conducted by Chandrashekar UK et al in which fever was seen in 92 % of patients.(5) Other symptoms include headache , vomiting . Awareness of atypical presentation is important for early detection of malaria in endemic areas , in present study, patients demonstrated atypical symptoms , such as cough, diarrhea and myalgia. Gastrointestinal manifestations occur mainly due to intense congestion of gastrointestinal mucosa and abdominal organs severe enough to cause mucosal sloughing and haemorrhage.(5)

Commonest clinical sign was splenomegaly seen in 80% patients with hepatomegaly in 20% patients.

Elevated bilirubin is the commonest lab abnormality observed in 24(48%)patients with clinical evidence of jaundice in 5 patients ,especially in Falciparum malaria . Hyperbilirubinemia results from intravascular hemolysis of parasitzed RBC's , hepatic dysfunction and an element of microangiopathic hemolysis due to DIC. In one study from KMC hospital, Attavar , 11(20%) showed hyperbilirubinemia.The results were similar to study of G. Lalitha Murthy et al(6). Mohapatra et al (7), they observed jaundice as the important lab abnormality. Kocher et al studied 2 epidemics and had similar results(8).

Cerebral malaria is an important complication of falciparum malaria. It was seen in one of patients In our study. The onset of coma may be sudden ,often following a generalized seizure or gradual initial drowsiness , confusion, disorientation, delirium, or agitation followed by unconsciousness(1).

Anemia of varying degree is a common accompaniment in severe malaria. The pathophysiology of anemia in malaria is multifactorial . It results from accelerated red cell destruction and removal by spleen in conjunction with ineffective erythropoiesis. In a study from Orissa, 86.7% had anemia and 10% had severe anemia(1)and Chowta et al from KMC Attavar observed 37% patients with anemia. The present study demonstrated 15(30%)patients with anemia out of which one patient had severe anemia.

14(28%) of our patients had decreased platelet count, seen more commonly in Falciparum group. In a study by Preetham S Wasnik et al observed 57.5% patients especially in falciparum group(10) .Thrombocytopenia is a common observation in Falciparum patients with spontaneous recovery on treatment .The mechanism suggested includes increased splenic sequestration, immune mediated destruction and shortened platelet survival.(9)

The pathophysiology of renal failure is still unclear. It is thought that cytoadherence, multifactorial changes in cortical perfusion ,cytokine release and hypovolumia lead to tubular necrosis.(5) The deranged renal function was observed in 10 patients in our study with serum creatinine more than 3 mg/dl in 3 patients.In a study by Preetham S wasnik et al observed 26 (32%) of subjects had deranged renal function(.)

Hypoglycemia is one of the complications in malaria, we observed a Random Blood Sugar of <80 mg/dl in about 8 (16%) patients.

As per WHO definition of severe falciparum malaria, in present study 6 members had multiple organ dysfunction and these patients responded to second line of therapy.

Parasite density is associated with disease severity and must be monitored during and after treatment to ensure adequate resolution of infection. High parasitemias have been correlated with mortality in falciparum malaria(11). M K Mohapatra et al observed patients with single complication from Malaria had higher parasite count compared to patients with multiple complications due to sequestration in internal organs(7). But In our study patients with high parasite count especially in Falciparum group had early treatment failure and complications than compared to patients with low parasite count who had adequate clinical response. The mean temperature and parasite count decreased from day 1 to day 5 which was statistically significant.

32 (64%)out of 50 responded to CQ + PQ therapy, other 18(36%) patients to second line drugs . In P.Vivax all 25 cases showed adequate clinical response . In P.Falciparum out of 25 cases , 14 showed ACR and 11 early treatment failure. Out of 14 patients 7 showed ACR and 7 responded to second line drugs. Patients with ETF were treated Artesunate combination treatment according to NVBDCP guidelines .The result of treatment of Malaria in our study is ACR 39 pts (76%), ETF 11(24%). In falciparum group 56% had ACR , 44% had ETF. In a study by Preetham S Wasnik et al , maximum no of patients received ACT and had 93.54 % improvement(10).

Conclusions

Use of ACT combination in treatment of complicated malaria as advised by NVBDCP , especially in high Falciparum failure areas prevents death from malarias. Use of combination drugs in treating complicated and resistant cases helps in reducing complications.

Limitations :

Study analysis requires larger prospective study.

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