

JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article:

Chowta M N, Chowta K N. STUDY OF CLINICAL PROFILE OF MALARIA AT KMC HOSPITAL, ATTAVAR. *Journal of Clinical and Diagnostic Research* [serial online] 2007 June [cited: 2007 June 4]; 3:110-115

Available from

http://www.jcdr.net/back_issues.asp?issn=0973-709x&year=2007&month=June&volume=1&issue=3&page=110-115&id=33

ORIGINAL ARTICLE

Study Of Clinical Profile Of Malaria At KMC Hospital, Attavar, India

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ABSTRACT

Introduction India being a vast country with different geographical regions, the pattern of diseases may vary from place to place. The present study was undertaken to study the clinical features, complications, and response to treatment in a tertiary care hospital.

Methodology A prospective analysis of adult patients suffering from malaria was carried out at KMC hospital, Attavar during the year 2002-2003. Diagnosis of the patients was based on clinical features and by peripheral smear. The mode of presentation, clinical course, laboratory investigations, antimalarials administered, and complications were recorded. The response to treatment was noted both clinically and by repeating peripheral blood smear examinations.

Results Out of the 54 patients, 39 were males and 15 females. The age group of the patients ranged from 17 to 65 years. Fever was present in all the patients. 51.55 % of patients complained of headache and 31.55 % had vomiting. Jaundice was observed in 11 patients. Cough was also a complaint in four patients. Symptoms of gastritis were observed in two patients and two other patients had diarrhoea. Anaemia was present in 20 patients. Out of the 54 patients, 31.48% had infection with *P.falciparum*, 33.33% with *P.vivax*, and 29.62% had mixed infection. Chloroquine resistance was observed in nine patients. Complications were seen in 10 patients.

Conclusion Injudicious use and inadequate dosage of the available drugs need to be curbed. To achieve the global aim of malaria control, we must carry out an epidemiological survey to monitor the progression of resistance while planning an effective antimalarial strategy.

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. In addition to the direct effects it exerts by increasing premature mortality and morbidity, it is responsible for considerable economic wastage owing to lost man power and treatment costs.

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These constitute a serious impediment to the economic development of countries in which this disease is endemic[1].

The plasmodium species have staged a devastating global comeback by imposing an alarming burden on the healthcare system. The worldwide prevalence of malaria is estimated to be approximately 300 to 500 million clinical cases each year and is endemic in 101 countries. It remains the world's most important tropical parasite disease and kills more people than any

other communicable disease except tuberculosis. Malaria has an estimated mortality of 1 million per year[2]. Although there has been a decline in the total number of cases in India, plasmodium falciparum registered a significant increase. The mortality in malaria is due to plasmodium falciparum[3].

The epidemiological situation of malaria has shown a gradual deterioration in India. There has also been a quantum jump in the incidence of falciparum cases of malaria. It has also become apparent that chloroquine resistance of malaria has become a global problem, 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[4].

The morbidity and mortality associated with malaria has been held in check by the widespread availability of cheap and effective antimalarial drugs. However, the development of resistance to these drugs may represent the significant important threat to the health of the people in tropical countries.

Awareness of atypical presentation is important to detect cases of malaria in endemic areas. India being a vast country with different geographical regions, the pattern of the disease may vary from one place to the other. The present study was undertaken to study the clinical features, complications, and response to treatment in a tertiary care hospital.

Methodology

A prospective analysis of adult patients suffering from malaria was carried out at KMC hospital, Attavar during the year 2002-2003. Both males and females were included in the study. The diagnosis of the patients was based on clinical features and by peripheral smear. The mode of presentation, clinical course, treatment history, laboratory investigations reports, antimalarials administered, response to therapy, and complications were recorded. Fever clearance period was defined as the number of days required for the abatement of fever after starting the antimalarials.

Response to treatment was noted both clinically and also by repeating peripheral blood smear examinations. Sensitivity to Chloroquine was

noted as per the WHO guidelines for extended field tests (1973)[5]. Chloroquine resistance has been defined as the ability of the malarial parasite to survive and/or multiply despite administration and absorption of the drug given in doses equal or higher than usually recommended but within the tolerance of the subject [6].

It has been observed that if the features of malaria and slide positivity reappear within two weeks of treatment, the condition can be called recrudescence due to resistance. If the features recur between two and four weeks it may be due to either relapse or recrudescence. If the features occur after 4 weeks, it is most probably due to relapse.

Statistical analysis was done by chi square tests.

Results

Out of the 54 patients, 39 (72.22%) were males and 15 (27.77%) were females in the age group of 17 to 65 years. Sexwise distribution of patients is statistically significant ($p=0.025$). Fever was present in all the patients (Statistically highly significant, $p<0.001$). The duration of fever was around 2 to 7 days. 51.55% of the patients complained of headache and 31.55% had vomiting. Jaundice was observed in 11(20.37%) patients. Cough was also a complaint in four patients. Symptoms of gastritis were seen in two patients and two other patients had diarrhoea. Anaemia was present in 20 patients (37.03%) in addition to fever. All other presenting symptoms are statistically not significant [Table/Fig 1].

Out of the 54 patients, 31.48% had infection with *P.falciparum*, 33.33% with *P. vivax* and 29.62% had mixed infection. Three patients received empirical treatment without the smear being positive [Table/Fig 2]. Distribution of species is not statistically significant ($p=1$). Recurrent infections were observed in seven patients and two patients had recrudescence. Chloroquine resistance was seen in nine patients.

Complications were seen in 10 patients. The complications are cerebral malaria in one patient, pancreatitis in one patient, derangement of liver function in five patients, renal impairment in one patient, and thrombocytopenia in two patients. [Table/Fig 3]. Incidence of complications were statistically not significant ($p=0.20$) There was no death reported in the present study.

All the patients responded to treatment. Patients with chloroquine resistance received other antimalarials. The average duration required for smear negativity (parasite clearance time) was 3 to 5 days, and the average fever clearance period was 2 to 5 days. Apart from chloroquine, quinine was given to 5 patients, artemether to 12 patients; pyrimethamine/sulfadoxine combination to 17 patients. Sixteen patients also received doxycycline.

Table/fig 1
Presenting signs and symptoms

Signs and symptoms	Number of patients (%)
Fever	54 (100)*
Head ache	28 (51.6)
Vomiting	17 (31.6)
Anaemia	20 (37.4)
Jaundice	11 (20.7)
Cough	4 (7.4)
Gastritis	2 (3.7)
Diarrhoea	2 (3.7)

$X^2=183.44$ * $P<0.001$

Table/fig2

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[7],[8]. 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. Awareness of atypical presentation is important to detect cases of malaria in endemic areas where a careful search for the malarial parasite in the peripheral blood film should be undertaken in all the patients demonstrating clinical problems. The clinical suspicion alone can be the basis of an effective antimalarial drug.

Peripheral smear: Species differentiation

Species	Number of patients (%)
Plasmodium falciparum	17 (31.5)
Plasmodium Vivax	18 (33.3)
Mixed	16 (29.6)
Smear negative	3 (5.6)

$X^2=0.172$

$P=1$

Table/fig 3
Complications

Complications	Number of patients (%)
Cerebral malaria	1 (1.9)
Pancreatitis	1 (1.9)
Liver impairment	5 (9.3)
Renal impairment	1 (1.9)
Thrombocytopenia	2 (3.7)

$X^2=6.23$ $P=0.20$

A study from Jamshedpur in Jharkhand state of India has described the atypical presentation of falciparum malaria comprising convulsion in 28.55 %, abdominal pain in 5.7 %, hemiplegia in 2.8 %, generalized weakness and palpitation in 5.5 % of cases[9]. In the present study, patients demonstrated atypical symptoms, such as cough, diarrhea, and gastritis.

The sequestrations of erythrocytes containing metabolically highly active parasites in the vascular beds of internal organs can explain almost all the pathological events in severe and complicated falciparum malaria. Malarial parasite also induce the release of cytokines (TNF-alfa, IL-1,IL-6), initiating many of the symptoms and signs of malaria[10].

Anaemia is an important cause for high morbidity and mortality in falciparum malaria. Pathogenesis of anaemia in malaria is multifactorial. A complex chain of pathological processes involving

parasite-mediated RBC destruction, marrow suppression, and accelerated removal of non-parasitized RBCs have all been implicated. In one study from Orissa, 86.7 % had anemia and 10 % had severe anaemia[11]. The present study demonstrated anaemia in 20 (37.07%) patients.

Two of our patients had decreased platelet count. Thrombocytopenia is a common observation in falciparum malaria with spontaneous recovery on treatment. The mechanism suggested includes DIC or excessive removal of platelets by the reticuloendothelial system[12].

The present study showed hyperbilirubinemia in 11 patients. Hyperbilirubinaemia in falciparum malaria results from intravascular haemolysis of parasitized RBCs, hepatic dysfunction, and an element of microangiopathic haemolysis due to DIC[13].

Cerebral malaria is an important complication of falciparum malaria. Cerebral malaria was seen in one of the patients in the present 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[14].

Chloroquine remains the drug of first choice in *P. vivax* malaria because of its low cost, good tolerance, suitability for pregnant women and young children and easy availability. *P. vivax* resistance to chloroquine can pose a significant treatment problem because mefloquine and halofantrine, although effective, have not been studied in large number of vivax patients. Mefloquine, though marketed, is expensive as compared to chloroquine. Sulfadoxine-pyrimethamine, which works well against chloroquine resistant *P. falciparum*, is inexpensive but less efficacious against *P. vivax*. Pregnant women and children with resistant *P. vivax* pose yet another problem. Quinine is difficult to administer, and primaquine is contraindicated in pregnancy[15].

Malaria is a threat to almost half the world's population, and the presence of MDR strains of falciparum pose a significant health problem. This problem has been further compounded by the emergence of chloroquine-resistant strains of *P. vivax* from several parts of the world including India[16]. Chloroquine resistance was observed in nine patients in the present study. The cause of

growing chloroquine resistance especially in falciparum malaria may be a result of the use of the drug in suboptimal doses or by prophylactic use of the drug in people living in the endemic zone or genetic mutation of the parasite. Therefore, suboptimal dose and prophylactic use amongst populations living in the endemic zone is not recommended except in travellers from the non-endemic to the endemic zone. Simultaneously, early detection of chloroquine resistance and prompt and effective management are the key to curing the disease and preventing transmission of chloroquine resistance in the community[4].

Several drugs are currently available to treat chloroquine-resistant malaria. The common amongst them are quinine, sulfadoxine-pyrimethamine combination, mefloquine, arimisinine and its derivatives, halfantrine and certain antibiotics[17]. Resistance to quinine and sulfadoxine-pyrimethamine combination is now widespread, though the former is often used as a first line drug in severe complicated malaria. Arimisinine and its derivatives are safe and effective drugs. Compared to quinine, they shorten the fever clearance time by 17 % (7.7 hrs) and parasite clearance time by 32 % (19.8 hrs). However, the recrudescence rate is high (up to 50%) when they are used as monotherapy[18].

A two-pronged approach has been used to tackle plasmodium resistance. This includes the use of judicious combinations of the existing drugs along the lines used in tuberculosis or leprosy and the development of new antimalarial drugs. Among the newer antimalarials that have been developed are the artemisinin derivatives. It is quite possible that artemisinin and its derivatives, such as artesunate are of great impetus today. This is because they represent besides quinine, a major therapeutic option for the treatment of multidrug-resistant severe malaria. Above all, in the era of rapidly emerging resistance, it is imperative that physicians prescribe artemisinin derivatives rationally only to patients who really require it to prevent resistance from developing secondary to indiscriminate use[2].

Indiscriminate use of drugs has given a new dimension to the situation. Combination chemotherapy is indicated to increase the efficacy and to delay the appearance of resistance. Antibiotics, such as tetracycline, doxycycline,

erythromycin, and newer macrolides and clindamycin can be combined with chloroquine, quinine, or other antimalarial drugs[19].

Malaria continues to be a major public health problem. Injudicious use and inadequate dosage of available drugs need to be curbed. There is an inescapable need to develop new antimalarial drugs. To achieve the global aim of malaria control, we must carry out an epidemiological survey spreading over different areas of the country. The tasks would be to monitor progression of resistance while planning an effective antimalarial strategy.

Conflict of Interest: None declared

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