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Original Research Article

Study of Clinical Profile of Patients with Malarial Fever admitted in a Tertiary Care Centre

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ABSTRACT

Background: Malaria remains a leading cause of human morbidity and mortality due to inability of the insecticide and chemotherapeutic agents to eliminate the vector and the agent of the disease. The present study is aimed to study the clinical profile, laboratory profile, species identification and line of treatment of the patients as per the species.

Material & Methods: Present study was conducted on 100 confirmed cases of Malaria admitted in Medicine department of Sanjeevan super-specialty hospital, Satara, Maharashtra. All patients were interviewed followed by clinical examination and relevant investigations. Data was entered in MS Excel and statistical analysis was done using EPI-5.

Results: There was male preponderance in my study and incidence was more (84%) in middle age 16-50 years. 100% cases showed fever as the major symptom followed by nausea (36%), vomiting (36%), headache (22%). Anaemia is common (56%) followed by thrombocytopaenia (30%). Spleen was palpable in 50% patients. Hyperbilirubinemia was 28% in my study predominantly of conjugated variety. 72% cases were P. falciparum, 22 % were p. vivax and 6 % were mixed. In the diagnosis, QBC was found to be more sensitive 98% than PBS 78%. for uncomplicated vivax malaria Tab chloroquine showed 60% sensitivity, tab artemether + lumefantrine showed 75% sensitivity, those who were not responding were added with quinine, doxycycline. In falciparum inj. artesunate76 % was more sensitive than quinine 69%. Artemether showed 57% response in falciparum in my study.

Conclusion: Incidence of malaria was more in males than females due to their outdoor stay, travelling and more expose part of the body. Splenomegaly is the most common elicitable sign. Anaemia, thrombocytopaenia are found in falciparum malaria. Multidrug therapy like artemisinin combination therapy has more response in complicated and non-responding cases.

Keywords: Clinical Profile, Laboratory Profile, Malarial Fever, Species Identification

INTRODUCTION

The story of malaria is a lot more exciting than one would initially expect it to be. There are tales of adventure, fraud, intrigue, corruption, and environmental destruction and of course death[1]. While the modern medicine attempt to meet the challenge of unsolved conditions like AIDS and cancer, there is one disease which had plagued mankind since antiquity, but now is largely ignored unless you contract it. Malaria parasites have been with us since the dawn of time. They probably originated in Africa (along with mankind) and fossils of mosquitoes up to 30-million-year-old show that the vector for malaria was present well before the earliest history[2]. The plasmodium parasites are highly specific, with man as their only vertebrate host and Anopheles mosquitoes as their vectors. This specificity of the parasite also points towards a long and adaptive relationship with our species.

The worldwide prevalence of malaria is estimated to be approximately 300-500 million clinical cases each year, and is endemic in 101 countries[3]. It remains the world's most important tropical parasitic disease, and kills more people than any other communicable disease with the exception of tuberculosis, which has an estimated mortality of over 1 million per year. In India alone, in 1977, 2,660,057 cases were reported and the annual economic loss due to malaria was estimated to be between US$ 0.5 to 1.00 billion[4].

Malaria remains a leading cause of human morbidity and mortality due to inability of the insecticide and chemotherapeutic agents to eliminate the vector and the agent of the disease[5]. In an effort to introduce new methods of control, vaccines targeted to the various stages of the complex life cycle of plasmodium have been developed[6]. Although an effective malaria vaccine is not yet available, considerable information has been gathered regarding complex multiple immune mechanisms induced by the different developmental stages of this parasite their complex antigenic make up and their variability.

Objectives:

1. To study the clinical and laboratory profile of patients with malarial fever.
2. To identify species and line of treatment of the patients with respect to species

MATERIAL AND METHODS

The present prospective observational study was done during the prescribed study period (Jan 2021 to June 2023), 100 confirmed cases of malaria patients who were admitted to Sanjeevan super speciality hospital, Satara, Maharashtra in department of medicine. Malaria was confirmed by QBC (Quantitative buffy coat) and PBS (Peripheral Blood Smear).

Patients with other types of fever, below 12 years, alcoholics, with renal disorders, with history of intake of primaquine, acetylsalicylic acid or nitrofurantoin drugs within two weeks of presentation.

After taking consent, all the patients were interviewed and detailed history with clinical examination done as per the proforma supported by relevant investigations, also they were followed up during their course of hospitalization till they were afebrile for 48 hours and free of other symptoms or until any other untoward end point.

Investigations includes Complete hemogram, Liver function tests, Renal function tests, detection of malarial parasite, Peripheral blood smear – thick and thin, QBC (Quantitative Buffy coat) technique, Urine Routine and Microscopy, Stool for occult blood, Ova and cyst. Coagulation profile, reticulocyte count, bleeding time, fibrin/fibrinogen degradation products (FDP) and Bone Marrow Study were done only when necessary. The data was entered in MS-Excel. Univariate frequency tables were generated using the statistical package EPI-5.

RESULTS

The present study involved 100 patients who were admitted to the medical wards of and ICU Sanjeevan Super-speciality, a tertiary referral centre, between the study periods Jan 2021 – June 2023.

The majority of the patients were males (80%) and peak incidence was seen in age group 31 to 49 years. The incidence was much less above 50 years. Age range between 16 to 72 years.

Table 1: Age and Gender distribution of the Patients

Demographic variables		**Frequency**	**Percent**
Age	<30	27	27%
	31 to 49	54	54%
	50 to 69	15	15%
	>69	4	4%
Gender	Male	80	80%
	Female	20	20%
Total		100	100%

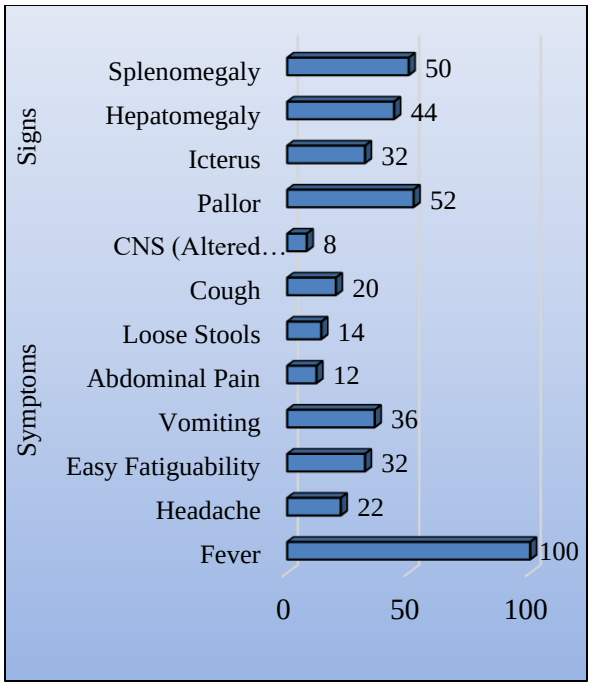

Figure 1: Presenting Symptoms and Signs of the Patients

Fever was present in all the patients. It was the initial clinical symptoms, which preceded the various pernicious syndromes. Fever was intermittent in 60% as has been classically described in malarial fever, while it was continuous in 30% and remittent in the remaining 10%. Vomiting was seen in 36% of patients prior to admission and 32% of patients had malaise.

Hepatic manifestation presenting as jaundice, one among the common pernicious syndrome was present in 18% of the patients. Eight patients of the total were in altered sensorium or delirium on admission, with three of them in a postictal state. 22% of the patients had associated headache, commonly dull aching type, which was associated with fever. A diffuse pain in the abdomen was the presenting feature in 12% of the patients. Diarrhoea of moderate quantity, 3-4 times/day were seen in 14% of the patients. 20% of patients presented with history of fever and cough with expectoration.

Pallor with moderate to severe degree anemia was seen in 52% of the patients in this study. 32% had clinical evidence of icterus on admission. Among the four patients with altered sensorium, three had bilateral brisk reflexes with extensor plantar, none of them had focal neurological deficits or meningeal signs, which includes Kerning's and Brudzinski sign. 44% patients had hepatomegaly while 50% had splenomegaly, thus making it an important elicitable sign along with history of fever.

Table 2: Laboratory investigations and Haematological Parameters of the Patients

Laboratory Parameters		**Frequency**	**%**
Hb (<10gm%)		56	56%
Leucocytosis (>10000/mm^3)		10	10%
Leucocytosis (<4000/mm^3)		13	13%
ESR (mm/hr)	<50	60	60%
	50 to 100	36	36%
	>100	4	4%
Reticulocyte Count >3%		10	10%
Thrombocytopenia (<1x10^5/mm^3)		30	30%
Prothrombin Time C/T >3 sec		8	8%
Peripheral Blood Smear	Normocytic Normochromic Anemia	55	55%
	Microcytic Hypochromic Anemia	22	22%
	Dimorphic Anemia	23	23%
Hyper Cellular Bone Marrow		14	14%
Hyperbilirubinemia		28	28%
Elevated Liver Enzymes		56	56%
Elevated Blood Urea / Creatinine		39	39%
Hypoglycemia		2	2%

Anemia (<10 gm%) was seen in 56% of the patients, out of which 6% had severe anemia. 10% had Leucocytosis indicating associated bacterial infection, while in 82% the total count was normal. Leukopenia was seen in 13%. ESR was elevated in 36% (36) of patients, while of these, two patients had an ESR above 100 mm/hr. Thrombocytopenia was seen in 30% of the patients. Reticulocytosis (>4%) was seen in 10% and Prothrombin time was increased (>3 sec) in 8% of the patients.

Peripheral blood smear was evaluated for both the positively of parasite as well as for blood picture. The blood picture was normocytic normochromic in 58% (58), microcytic hypochromic in 22% and dimorphic in 18%. Peripheral blood smear was not done in two patients. Bone marrow aspiration was done in 14 patients. All had hypercellular marrow with erythroid hyperplasia and features of dual deficiency anemia, which was consistent with peripheral blood smear findings. One bone marrow picture was positive for gametocyte of plasmodium falciparum.

Liver function test shows that bilirubin was elevated in 28% of patients, of these 16% of patients had increased level of conjugated bilirubin. AST and ALT was elevated in 56% of patients. Hypoglycaemia (<40 mg/dl) was seen in two patients. On admission uraemia (urea >40 mg/dl) was seen in 39% and Serum Creatinine was elevated (>3 mg) in 16% of the patients.

Species identification:

Peripheral smear was evaluated for both the positively of parasite as well as for the blood picture. QBC was positive in 98% of cases when compared to peripheral blood smear, which was 78%. The commonest infecting species in this study was falciparum 72, 22% of the cases were vivax and 6% cases of mixed infection (Falciparum + Vivax). However, very high proportion of cases were with Falciparum were found.

Line of treatment of cases:

Out of 22 P. vivax cases 10 were initially treated with tab chloroquine of which 6 (60%) showed good response.; symptomatically improved and parasite count was also reduced (p=0.1). 4 (40%) cases showed resistance which were given inj. Artesunate.

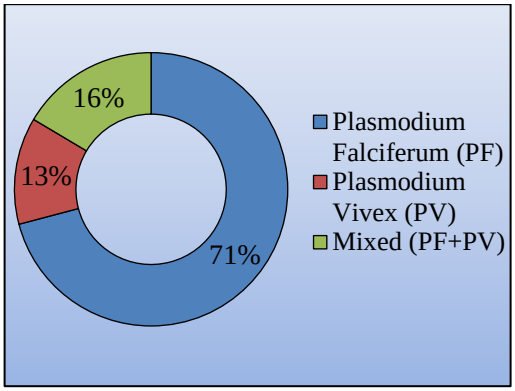

Figure 2: Species identification

All showed good response. Rest 12 cases were treated with tab artemether plus lumefantrine for three days. 9 (75%) cases showed good response (P=0.3). In rest 3 cases, tab doxycycline had to be added. In case of falciparum cases 78, 26 cases were treated with tab artemether + lumefantrine of which 15 (57%) showed sensitivity (P=0.007) rest 11 cases were treated with inj. Quinine 10 mg/kg 8 hourly.

Table 3: Line of treatment of cases

Cases	First Line Drug	Sensiti-vity	Second Line therapy (In case of Failure)
P. vivax Cases	Tab Chloroquine	60%	Inj. Artesunate
	Tab Artemether + Lumefantrine	75%	Tab Doxycycline
P. falciparum Cases	Tab Artemether + Lumefantrine	57.7%	Inj. Quinine
	Inj. Artesunate	80.8%	Inj. Quinine + Tab Doxycycline
	Inj. Quinine	69.2%	Inj. Artesunate + Tab Doxycycline

26 cases were treated with inj artesunate out of which 20 (76%) showed good response(P=0.05) rest 6 were added with inj quinine and tab doxycycline. Rest 26 cases were treated with inj quinine of which 18 (69%) showed sensitivity(P=0.06) rest 8 were treated with inj artesunate and tab doxycycline as second line therapy. All vivax cases were given tab primaquine 15mg for 2 weeks for radical cure and all P. falciparum cases were given single dose to prevent recurrence.

DISCUSSION

Today malaria is again a major health problem in many countries including India. Mortality as well as morbidity due to plasmodium falciparum is on increase, more so because of its complications. Rapid urbanization an increase in floating population due to better mode of transport, the highways connecting major cities which are the nature reservoirs of infection and ideal weather for vector multiplication, contribute to the rising incidence.

There was a clear male preponderance in this study with a male - females ratio of 4:1 (80/20), 84% of the cases were between 16-50 years of age with a peak of 54% in third decade. The incidence decreases as the age advances which correlates with study conducted by Mahakur et al[7]. The younger population is affected mainly because of no or partial immunity to plasmodium falciparum, compared to the older population group in this study. Males are more frequently exposed to the risk acquiring malaria than females because of the outdoor life they lead. Further, females in India are usually better clothed than males.

The range of fever in malaria can vary widely from apyrexial spells to the typical malignant tertian type. In this study all the patient (100%) had history of fever. Prodromal symptoms include malaise, anorexia, lassitude, body aches, headache and chills. Incidence of headache in this study is comparable to study by Mehta et al[8]. Only 8% of patients in this study had altered sensorium, compared to by Malhotra et al[9], who found a 22.7% incidence. All the patients with altered sensorium had history of severe headache, with history of convulsion in one patient.

Vomiting, loose stools and abdominal pain were present in 36%, 14% and 12% patients respectively. Among these three patients had gastroenteritis with signs of dehydration and acute renal failure. Mehta et al[8] in his study of 425 patients found abdominal pain (3.29%), loose stools (5.64%) and nausea, vomiting (8.47%). The pulmonary symptoms in malaria have been attributed to blockage of pulmonary capillaries by parasitized RBC's alveolar oedema, cell necrosis and IgE mediated hypersensitivity evoked by malarial toxins. The incidence of cough was 20% (20) in this study, when compared to Mehta et al[8] who found 4.47% among 425 patients. Rajput Singh et al[10] in his study concluded that, malarial atypical respiratory presentations are far higher in incidence than reported in literatures.

Though anemia is quite commonly seen in majority of the study population, patients did not present with symptoms of anemia. Similarly, 30% (30) of patients in the present study had thrombocytopenia, but none of them findings of Sharma S. K. et al[11] who also found that bleeding manifestations are rare though thrombocytopenia occurs commonly. In this study 32% of patients had icterus when compared to study by Nand et al[12] who found 46% in his study. All the patients with icterus had hepatomegaly.

Hepatomegaly was seen in 44% (44), which is comparable with the study by Malhotra et al[9], eight patients with hepatomegaly did not have jaundice. Hepatomegaly may be a result of visceral edema[13]. Spleen was palpable in 50% of patients. This is in correlation with study conducted by Mehta et al[8], who found 63% of incidence of splenomegaly. Incidence of splenomegaly is high in patients with anemia. All the cases with splenomegaly had anemia. This finding establishes that, in malaria as in certain other diseases, splenomegaly is associated with enhanced splenic filtration of parasitized RBC's.

In this study 56% (56) of the patient had anemia (<10gm%), out of which three had severe anemia (<5gm%), 80% anemia occurred in patients with falciparum malaria and in 11% of patients with vivax. Malhotra et al[9] found the incidence of anemia to be as high a 81.2%. This could be attributed to the cause of anemia, which is multifactorial. Degree of anemia varies with parasite load. Anemia was found to be associated with non-haematological complications like, renal failure and hepatic involvement. Presence

of anemia is also a significant predictor of mortality. This means that hemoglobin estimation can be used as a simple screening test for predicting an adverse outcome, for selecting patients for more intensive monitoring and possibly for referral to a tertiary care centre from a primary care level.

Thrombocytopenia seen in 30% patients in this study is comparable to study by Malhotra et al[9] (41%). 86.6% of thrombocytopenia was found in patients with falciparum malaria and 13.3% in patients with vivax malaria. In spite of thrombocytopenia none of the patients presented with bleeding manifestations. This is in concordance with the finding of Sharma S. K. et al[11] who also found only a 3.3% incidence of bleeding manifestations in spite of a 90% incidence of thrombocytopenia. Thrombocytopenia was not related to the infecting species. Prolonged PT was found in 8% of patients which is comparable to Sharma S. K. et al[11]study. All these patients had pernicious manifestations. Coagulopathy in falciparum malaria is usually of low grade but can come clinically important [14].

The peripheral blood smear findings in our study correlates well with the previous study by Sen et al[15]. Bone marrow aspiration was done in eight patients which showed hypercellular marrow with erythroid hyperplasia and one marrow showed gametocyte of falciparum. These findings were consistent with earlier studies.

Renal complications of malaria are life threatening. Three types of renal lesions are known in malaria: they are acute renal failure, glomerular nephritis (GN) and nephritic Syndrome (NS). Acute renal failure occurs commonly in P. falciparum malaria, though its rare occurrence has been reported in p. vivax malaria. Renal failure was seen in 38% of patients. Comparative studies show an incidence of 30% and 40.9% in Nand et al[12] and Malhotra et al[9] study respectively. All patients who had renal failure hade falciparum malaria. In this study the spectrum of abnormalities associated with acute renal failure were anemia (20%), thrombocytopenia (16%), hepatopathy (20%), gastroenteritis (6%) and altered sensorium (8%).

Incidence of hyperbilirubinemia was 28% in the present study when compared to study by Nand et al[12], who found a 50% incidence. There are studies like Sharma S. K. et al[11], who found an incidence of 23% which correlates with the present study. Elevated liver enzymes in our study and previous studies correlates well. In 12% of these patients the hyperbilirubinemia was predominantly unconjugated suggesting hemolysis as the cause for jaundice. The remaining had predominantly conjugated hyperbilirubinemia suggesting hepatic dysfunction.

Infection due to one or more species of malaria parasite are not uncommon, but they often overlooked. In endemic malarious areas mixed infections are particularly frequent. The most common type of mixed infection is PV and PF in tropical areas. World Health Organization has emphasized on early diagnosis and treatment as a major objective of the revised global malaria control strategy. This objective can only achieve diagnosis of malaria either clinically or through microscopic examination of blood slides[16]. Present study and previous studies show QBC to be a valuable new technology for routine clinical use and epidemiological survey.

According to Rober Hutagulung et al[16], artemether and lumefantrine is better option for P. vivax cases showing nearly 94 % sensitivity in P. falciparum and P. vivax cases. whereas in our study 75% and 57% sensitivity for vivax and falciparum respectively. Artemisinin combination treatment (ACT) regimens are now recommended as first-line treatment for falciparum malaria throughout the malaria-affected world. The artemisinin component is usually an artemisinin derivative (artesunate, artemether, or dihydro-artemisinin) given for 3 days, and the partner drug is usually slower acting antimalaria. Inj. Artesunate alone shows 90 % sensitivity.

CONCLUSIONS

Incidence of malaria was more in males than females due to their outdoor stay, travelling and more expose part of the body. Splenomegaly is the most common elicitable sign. Anaemia, thrombocytopaenia are found in falciparum malaria. Multidrug therapy like artemisinin combination therapy has more response in complicated and non-responding cases.

Complicated cases should be treated according to WHO treatment guidelines. Haematological and biochemical parameters should be meticulously checked and aggressive should be given to prevent deterioration.

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