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Original Research Article

Study of Clinical Profile of Malaria in Tertiary Referral Centre in Western Maharashtra

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ABSTRACT

Background: Several factors have been attributed to increased morbidity and mortality in malaria with altered hematological and coagulation parameters playing an important role.
Aims and Objectives: The present study is intended to study the clinical profile and haematological parameters as affected in P. falciparum, P. vivax and mixed infections and to observe any prognostic factor if present.
Materials and Methods: 100 cases of malaria (peripheral blood smears or rapid malaria antigen test positive) admitted from September 2011 to February 2013 at Krishna Institute of Medical Sciences, Karad (Maharashtra) were evaluated. Their case histories and clinical findings were recorded and haematological parameters measured, followed by monitoring the outcome.
Results: Of the 100 cases studied, 78 were males and 22 were females. Majority of patients were from age group of 20-40 yrs. 31% patients had anaemia (Hb <10 gm %) of either mild (54.84%) or moderate degree (29%). Severe anaemia was seen in 5% cases mainly with P. falciparum infections. Thrombocytopenia was seen in both vivax and falciparum malaria; with 79% of the cases showing platelet count less than 1.5/cumm. Bleeding conditions were not correlated to prothrombin time. Hypoglycemia was a significant predictor of mortality. 27% patients were admitted with deranged renal parameters and majority was due to pre-renal azotemia.
Conclusions: Various haematological changes can occur in both falciparum and vivax infections, most commonly normocytic hypochromic anaemia and thrombocytopenia. Degree of anaemia and thrombocytopenia usually correlate with parasite load. In a patient with febrile illness, observation of thrombocytopenia requires careful search for malarial parasite.

Key words: malaria, thrombocytopenia, leucopenia.

INTRODUCTION

Malaria is a public health problem in several parts of the country. About 95% population in the country resides in malaria endemic areas and 80% of malaria reported in the country is confined to areas consisting of 20% of population residing in tribal, hilly, difficult and inaccessible areas. Majority of studies of malaria are from endemic or hyperendemic areas of India. This study

shows presentation of malaria in Krishna Hospital, Karad (KIMS) from Satara district which is tertiary referral hospital of western Maharashtra from hypoendemic area.

The number of atypical presentations of malaria has gradually increased during the past few decades. [1] Several factors have been attributed to increased morbidity and mortality in malaria with altered hematological and coagulation parameters, playing an important role. So this study aimed to study the clinical profile and haematological parameters as affected in P. falciparum, P. vivax and mixed infections and to observe any prognostic factor if present.

MATERIALS AND METHODS

The present study was conducted in Krishna Institute of Medical Sciences (KIMS) Hospital and Research Centre, Karad. The study was carried out on 100 patients admitted during the period of September 2011 to February 2013 in this hospital. Detailed history regarding age, sex, nature and duration of illness, blood transfusion and history of antimalarial therapy were recorded in proforma. Every patient's written consent was taken prior to inclusion in this study. Clinical examination findings were noted. All the patients in this study were proved to be cases of malaria either by peripheral smear examination (both thick and thin smear) or Rapid Malaria Test (RMT).These investigations were ordered before the antimalarial treatment was started.

Investigations of haematological and coagulation parameters such as haemoglobin, total and differential WBC count, total platelet count, ESR, G6PD deficiency test was carried out. Bone marrow aspiration was considered in patients with pancytopenia only. Patients were enrolled in study with the following inclusion and exclusion criteria.

Inclusion Criteria: All adult male and female patients of age >15 years admitted in medical wards or MICU with peripheral smears being positive for malarial parasite (M.P) or Rapid Malaria Test (RMT) being positive were included in this study.

Exclusion Criteria: Patients presenting with fever with peripheral smear negative for MP and RMT Negative and patients of age < 15 yrs excluded from this study.

Cases characterized as chronic malaria (massive splenomegaly, anaemia, high titers of serum antimalarial antibody with or without peripheral smear showing malarial parasites) were not included.

Other investigations which were carried out were Random blood sugar (RBSL), Urine routine and microscopy, Renal function tests (RFT's), Serum electrolytes, Liver function tests (LFTs), Chest x-ray PA view, Electrocardiogram, USG Abdomen and pelvis. CT scan Brain / MRI brain/ CSF examination were done cases of altered consciousness or seizures with or without focal neurodeficit. All the investigations except bone marrow examinations were done before the treatment was started.

Once the patients were diagnosed to have malaria they were started on Anti-Malarial drugs according to the new Indian guidelines for treatment of Malaria. [1]

Statistical methods: Paired t test was applied for comparison of variables like age, hemoglobin, platelet count, creatinine, serum bilirubin levels. Chi square test was used for comparing proportions.

RESULTS

Out of 100 patients, 78 were males with mean age of 35.76 ± 15.25 years and 22 were females with mean age of 40.32 ±16.97 years.

Fever was present in 97 cases, while 93 patients presented with chills and rigors and 91% patients had easy fatigability.

Nausea and vomiting were a presenting complaint in 51% of the patients. It was seen in a significantly high percentage i.e. 71.43% (10) of patients with falciparum infection. Out of 100 patients, 29 patients had headache, 14 patients had abdominal pain and 8 patients had loose motions on admission. 21.43% (3) of P. falciparum had loose motions. Total 9 patients were admitted with decreased urine output in preceding few days. Bleeding tendency was noted only in the 7% of total patients. Total 16% of patients had cough as presenting symptom with other symptoms. Breathlessness was present in 31% of patients and most of time it was in individuals with anaemia and renal failure. Breathlessness was noted in 71.42% (10) cases of falciparum malaria. Total 4 patients had altered sensorium on admission. One patient of falciparum, 1.75% (1) of vivax and 6.90% (2) of mixed infection had altered sensorium on admission. Out of 4 patients 2 improved and were discharged, while 2 died during course of treatment.

Pallor was noted in 34 % of the total cases. It was seen in 78.57% (11) of the P. falciparum cases. Icterus was noted in 40 % of the total patients. Pedal oedema was noticed in 12% of the total patients. It was present in majority of patients with hypoproteinemia with deranged liver function tests, severe anaemia, and oligouric renal failure.

Out of 100 patients in the study, 46 patients had splenomegaly mainly on ultrasonography. About 42.86% (6) of the patients with falciparum malaria had splenomegaly. Incidence of splenomegaly was 40.35% (23) and 58.62% (17) with vivax malaria and mixed infection respectively. These observations show that splenomegaly is not species specific and is more often absent.

Total 30% of patients with malaria, had hepatomegaly either on palpation or on ultrasonography. On admission 10% patients admitted with hypotension (BP <100/70 mmHg).

CNS manifestations of coma and seizures were seen in 5% of total patients. Out of 5 patients, 2 patients had coma and 2 had seizures. One patient had neck stiffness without altered sensorium. CNS manifestations were seen in 3.51% (2) patient with vivax malaria. CNS manifestations were seen in 7.14% (1) patient with falciparum infections and 6.90% (2) patients with mixed infection respectively.

Out of 100 patients 6% patients had haemic murmur and were mainly present in patients with severe anaemia. Total 17% patients had respiratory manifestations. It includes rhonchi and crepitations on admission. In falciparum malaria 7 (50%) patients had respiratory manifestation.

Maximum infection was found with P. vivax consisting 57 cases with isolated P. vivax, while 29 patients were infected with both P. vivax and P. falciparum. Isolated P. falciparum infection was only in 14 patients. Thus it suggests that P. vivax infection was present in 86% patients i.e in isolated and mixed forms P. falciparum infection was present in total 43% patients. Out of 100 patients 6 (6%) patients PS for MP were negative for malaria parasite, while RMT was positive; hence they were treated with antimalarial treatment and well responded. Out of these 6 (6%) isolated RMT positive patients, 1 patient had P. falciparum antigens while remaining 5 had P. vivax antigen. Two patients were positive for PS for MP but were RMT negative. In both patients species was P. vivax.

Out of 100 patients 31 patients had hemoglobin less than 10 gm/dl. 5 patients (16.13%) patients were severely anaemic (Hb <6). Out of all (31) anaemic patients, 17 patients had splenomegaly consisting 54.84 % of anaemia. Thrombocytopenia (platelet

count <150000/cumm) was present in 79 patients of study of which 39 (49.37%) patients had splenomegaly. 12.66% (10) patients were infected by P. falciparum, 29.11% (23) contribution was of mixed parasite infection while 58.23% were infected with P. vivax. Total 16 patients had platelet counts between 1,00,000-1,50,000/cumm, 34 patients had platelet count between 50,000- 1,00,000/cumm. Remaining 29 patients had platelet count less than 50,000/cumm of which l4 patients had platelet count less than 25,000/cumm.

Mean infected RBC % of admitted patients was 2.32%. In fatal cases it was 20.67% and for discharged patients it was 1.71%. In the present study the degree of anaemia was not correlated with the parasite load using statistical analysis. Infected RBC % in patients with thrombocytopenia was 2.56% while in patients without thrombocytopenia it was 1.13%. This correlates platelet count with parasitaemia. The average leucocyte count was 7931/cumm. Leucocytosis (total leucocyte count >11,000/cumm) was seen in 14% of patients. Leucocytosis does not correlate with causative species of parasite. Leucopenia (total leucocyte count <4,000/cumm) was present in 17% patients.

Blood sugar 60 mg/dl or less on admission was recorded in 4 patients. Out of 4 patients 2 patients were discharged, while 2 died.

Serum creatinine was deranged (>1.5 mg/dl) in 27% of the total cases while blood urea levels were elevated (>45 mg/dl) in 31 patients of malaria. In 76% patients, direct bilirubin levels were increased (>0.4 mg/dl). In 46 patient direct bilirubin levels were mildly deranged (0.4-1mg/dl). In 53% patients, indirect bilirubin levels were increased (> 0.6 mg/dl). In 19 patients levels were between 1.1-2 mg/dl, while in 3 patients levels were >5mg/dl. Increased ESR (>20 mm/hr) was seen in 76% of the patients. Prothrombin time (INR) was deranged (>1.2) in 25 patients of this study.

DISCUSSION

Out of 100 patients 78 patients were male while 22 were female with male: female ratio of 3.54:1. Mean age in our study was 36.76 ± 15.67 years with the predominant age group of 20-40 years (as shown in Figure 1). Nearly 62% of the patients were from this age group.

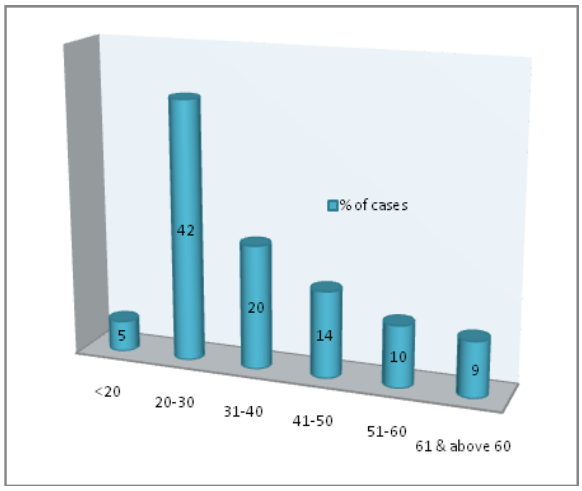

Figure 1: Age distribution in malaria patients (in years).

In the present study the percentage of isolated falciparum malaria was 14% and the incidence of isolated vivax and mixed infection was 57% and 29% respectively. In a study by Rojanasthien et al the prevalence of falciparum was 76.2% whereas vivax malaria was just 23.8%. [2] In the study by Reddy et al there was high incidence of vivax malaria i.e. 61.2% and falciparum was 36.8%, these observations suggest that the incidence of particular species varies with geographical area. [3]

In our study fever was the most predominant complaint i.e. 97% and 93% of the patients had chills and rigors (as shown in Table 1). In the study conducted by Mehta et al fever was present in 100% of the patients and it was present in 100% in the studies conducted by Malhotra et al. [4,5] It

was also noted that 91% of the patients in our study had easy fatigability as their presenting complaint. There was no mention regarding this in any other studies.

Nausea and vomiting was observed in 51% of the patients with our study. It was 37.36% and 4.35% in study of Muddaiah et al and Rathod et al respectively. [6,7]

Table 1: Showing various symptoms in malaria patients on admission according to plasmodium species.

Symptoms	P. falciparum	P. vivax	Mixed	Total
Fever	85.71 %	100%	96.55%	97%
Chills and Rigors	85.71%	96.49%	89.65%	93%
Easy fatigability	100%	87.72%	93.10%	91%
Nausea and vomiting	71.43%	45.61%	51.72%	51%
Altered sensorium	7.14%	1.75%	6.90%	4%
Headache	28.57%	29.82%	27.59%	29%
Abdominal pain	28.57%	14.04%	6.90%	14%
Loose motions	21.43%	5.26%	6.90%	8%
Oliguria	14.28%	5.26%	13.79%	9%
Cough	42.86%	14.03%	6.90%	16%
Breathlessness	71.42%	26.31%	20.69%	31%

Cough was a presenting complaint in 16% of the patients in our study. It was 11.57% and 2.04% in study by Muddaiah et al and Rathod et al respectively. [6,7]

In our study altered sensorium was in only 4% of patients. Muddaiah et al and Rathod et al reported 4.21% and 1.9% cases of altered sensorium in their studies respectively. [6,7]

Total 11.9% patients in the study of Rathod et al presented with complaint of oliguria while in our study 9% patients had oliguria on admission. [7] In our study majority of patients responded to hydration on admission and renal parameter improved, 3 patients required haemodialysis and recovered with treatment.

Pallor was noted in 34% of patients in our study (as shown in table 2). It correlates with study by Sharma et al. Icterus was noted in 40% of the patients in our study whereas it was seen in 25% of patients by Malhotra et al. [5]

Table 2: Showing different signs in different species of plasmodium at the time of admission.

Species	Pallor	Icterus	Pedal oedema	Splenomegaly	Hepatomegaly
P. falciparum	78.57%	50%	28.57%	42.86%	42.86%
P. vivax	26.32%	31.58%	10.53%	40.35%	21.05%
Mixed	27.59%	51.72%	6.90%	58.62%	41.38%
Total	34%	40%	12%	46%	30%

Thrombocytopenia was present in 79% of the cases in the present study (as shown in figure 2). It was comparable with study of Rathod et al who had incidence of 79.13%. [7] Thrombocytopenia was present in 12.66% of the cases with falciparum and 58.23% of vivax malaria in our study.

Thrombocytopenia is the most common finding, irrespective of the type of malaria seen in patients. Presence of thrombocytopenia in a patient of acute febrile illness in the tropics increases the probability of malaria and can be helpful clinical indicator for starting therapy. However thrombocytopenia is not a distinguishing feature between the two species of parasites. In the present study high parasitaemia was associated with marked thrombocytopenia. Degree of parasitaemia correlated with severity of thrombocytopenia.

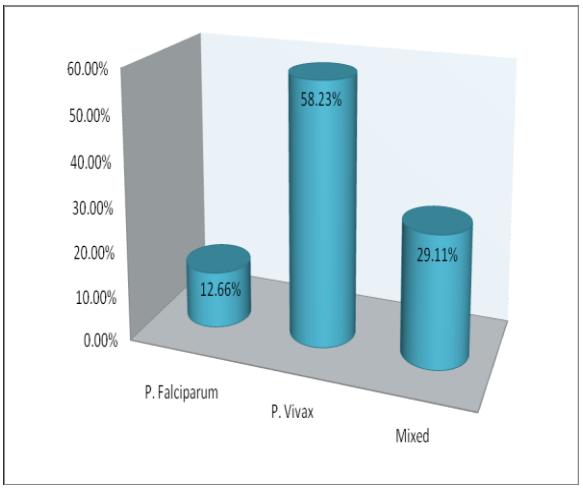

Figure 2: Thrombocytopenia in different species of plasmodium.

In our study 27 patients had raised serum creatinine levels (>1.5 mg/dl). A study by Rathod et al suggest 11.90% of raised serum creatinine levels and 11.57% in study by Muddaiah et al. [6,7] According to study of Muddaiah et al 14.21% patients had raised serum levels. [6] In our study 31% patients had raised blood urea levels on admission i.e. > 45 mg/dl. In our study renal parameters were deranged on admission mainly due to pre-renal azotemia. These parameters improved with hydration of patient, only 3 patients required haemodialysis on temporary basis, suggesting renal damage.

Splenomegaly was seen in 48% of the patients in our study. It was observed in 60% cases in study conducted by Nand et al. [8]

Hepatomegaly was noted in 30% of the patients in the present study. Coma, Seizures or altered sensorium was observed among 5% of the patients in our study which involved 2 patients of vivax, [9] one patient of falciparum and 2 patients of mixed infection.

Anaemia was present in 31% of patients in our study with 17 patients had splenomegaly. This indicates that there are other factors other than splenic sequestration which could lead to anaemia. The overall incidence of anaemia was higher in studies conducted by Sharma et al where the incidence was 86.7%. [10] The higher incidence could be explained by the fact that their study involved with cases of falciparum malaria only. The incidence of severe anaemia (Hb <6 gm %) was seen in 5% of the patients. In the present study the degree of anaemia was not correlated with the parasite load using statistical analysis (Chi-Square test).

Leucocytosis was seen in 14% of the total patients in our study while Leucopenia was seen in 17% of the overall cases in our study. Indirect bilirubin level which is more specific for haemolysis was raised in 36% of patients of present study.

Complicated Malaria:

As per WHO definition of complicated malaria, in present study we have observed 43 subjects suffered from complicated malaria. [11] Total 39.65% (23) patients of P. vivax infection, 41.38% (12) of mixed infection and 57.14% (8) of P. Falciparum infection had any one of complication according to WHO criteria. Many patients had more than one complication (as shown in table 3)

Three (3%) patients died during treatment course. Mean age of the fatal cases was 39 ± 18.68 years. Total 97 (97%) patients recovered and were discharged. The mean age of discharged patients was 36.69 ± 15.68 yrs. Mean duration of stay in succumbed patients was 2.67 ± 2.08 days, while mean duration of stay of discharged patients was 6.21 ± 4.78 days.

Total 7.14% (1) patients of P. falciparum succumbed during study while 1.75% (1) patients of P. vivax died. Out of mixed parasite infection 3.45% (1) died during treatment course. Out of these fatalities one was female and two males.

Table 3: Various complications in different species of plasmodium according to WHO's criteria of complicated malaria.

Complication	No of patients		
	P. falciparum	P. vivax	Mixed infection
Altered Sensorium	1	1	2
Severe Anaemia (Hb < 5 gm%)	2	2	0
Renal Failure (Sr. Creat >3 mg/dl)	3	0	3
Pulmonary Oedema	1	2	1
Hypoglycemia (RBSL <40 mg /dl)	2	1	0
Hypotension (SBP < 80 mm hg)	0	3	2
Bleeding	1	3	3
Convulsions	0	1	1
Hyperbilirubinemia (Total bil. >3 mg/ dl)	4	13	5
Hyperparasitemia (>5% parasitised RBCs)	1	0	3
Total	8/14 (57.14%)	23/ 58 (39.65%)	12/29 (41.38%)

CONCLUSIONS

P. vivax was more common (57%) species of plasmodium in this study. Fever is presenting symptom in almost all cases. There is no pathognomonic or specific symptom diagnostic of malaria, related to any particular organ system. When systemic symptoms like cough, breathlessness, diarrhea, impaired liver functions and renal failure are present, they favor P. Falciparum infection. Altered sensorium, generally considered a feature of CNS involvement by P. falciparum infection, may occur with isolated P. vivax infection. No sign in clinical examination is pathognomonic of malaria. Splenomegaly, traditionally considered a diagnostically useful sign may be absent in over 50% patients. No haematological abnormality is characteristic in malaria – particularly no definite pattern of leucocyte abnormality is found. Thrombocytopenia and prolongation of prothrombin time are generally modest and bleeding manifestations are rare. Thrombocytopenia is more common with P. vivax infection. Azotemia at admission may be pre-renal due to dehydration and hence rapidly correctible in majority of cases. Hypoglycemia and severe anaemia are risk markers for poor prognosis.

Thus, diagnosis of malaria is established on

a. High Index of suspicion in cases of fever in endemic areas.
b. Presence of the constellation of various systemic manifestations together,
c. Microbiological proof of presence of the causative Plasmodium, by reliable laboratory test/s.

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