

ORIGINAL ARTICLE

Clinical and Laboratory Profile of Hospitalized Malarial Patients: An Agra-Based Study

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Abstract

Objective: The clinical presentations and laboratory profile of malaria has been changing over the years. Therefore this study was undertaken to study the clinical profile and laboratory parameters of malarial patients.

Methods: This prospective observational study was undertaken in military hospital with high prevalence of malaria. A total of 320 patients were studied. All patients tested positive by peripheral blood smear or rapid diagnostic test were included. Clinical presentations, hematological and biochemical parameters were noted.

Results: Of the total 320 patients, 249 had *P. vivax*, 43 had *P. falciparum* and 28 had mixed malaria. 79% patients were male. Maximum (51.56%) patients were in 21-30 age group. The mean duration of symptoms was 2.54 days in *vivax* to 3.03 days in mixed malaria. Fever was observed in 97.8% of patients of *vivax*. Thrombocytopenia was observed in 99% of all patients. Splenomegaly was noticed in 24.84% patients of *vivax* and 34.5% of *falciparum* malaria. Herpes labialis was observed in 23.64% patients of *vivax* and 5.94% had urticaria.

Conclusion: High index of suspicion should be maintained in picking up the diagnosis. Any patient with thrombocytopenia, leucopenia, headache, herpes labialis, pain epigastrium and urticaria deserves exclusion of malaria.

Editorial Viewpoint

- Malaria has protean manifestation.
- High index of suspicion should be maintained to pick up diagnosis.
- This study finds conditions such as herpes labialis, epigastrium pain and urticaria also associated with malaria.

myalgia, chills, and/or cough. The diagnosis of malaria should also be considered in any person with fever of unknown origin regardless of travel history.³ *Vivax* malaria is no longer regarded as benign species as was believed earlier.⁴

This study was designed to assess the clinical features and laboratory parameters in hospitalized patients of malaria in this part of India and world.

Introduction

Malaria is a major public health problem in India and one which contributes significantly to the overall malaria burden in Southeast Asia. The National Vector Borne Disease Control Program of India reported 1.6 million cases and 1100 malaria deaths in 2009. Some experts argue that this is a serious underestimation and that the actual number of malaria cases per year is likely between 9 and 50 times greater, with an approximate 13-fold underestimation of malaria-related mortality.¹ In 2011, 2.15 million parasitologically confirmed malaria cases were reported, with 3 countries accounting for 95%

of confirmed cases: India (61%), Myanmar (22%) and Indonesia (12%). Both cases and deaths are substantially underreported, but these proportions are indicative of the geographical distribution of malaria in the Region.²

Symptoms of malaria are generally non-specific and most commonly consist of fever, malaise, weakness, gastrointestinal complaints (nausea, vomiting, and diarrhea), neurologic complaints (dizziness, confusion, disorientation, and coma), headache, back pain,

Material and Methods

This was a prospective observational study undertaken in the medical wards of a 450 bed military hospital. Patients admitted from June 2012 to October 2013 were included in the study. All patients who tested positive for malaria parasite (peripheral smear positive or rapid diagnostic test positive) were included. Pregnant females with malaria were not included in the study. Rapid diagnostic kit from Bio Standard Diagnostics Pvt. Ltd. was used. After establishing

Table 1: Age and sex distribution

Age (yrs.)	<i>P. vivax</i>		<i>P. falciparum</i>		Mixed malaria		Total
	Male	Female	Male	Female	Male	Female	
11-20	27	05	04	01	00	01	38
21-30	110	23	16	04	07	04	164
31-40	33	07	06	03	06	02	57
41-50	16	06	05	01	01	01	30
51-60	09	03	01	01	02	00	16
61-70	06	01	00	00	03	00	10
>71	02	01	01	00	01	00	05
Total	203	46	33	10	20	08	320

Table 2: Clinical features

Parameters	<i>P. vivax</i> n=249	<i>P. falciparum</i> n=43	Mixed malaria n=28
Age (years)			
Mean	31.497±13.065	31.790±13.044	35.357±14.241
Range	12-92	16-86	16-75
Duration of illness (days)			
Mean	2.556±1.446	2.790±1.582	3.107±1.571
Range	1-9	1-8	1-8
Fever (%)	97.8	99.2	99.6
Chills/Rigors (%)	84	87.4	92.37
Sweating (%)	68.6	73.86	78.42
Headache (%)	82.26	46.6	53.86
Vomiting (%)	12.5	24.54	10.6
Abdominal pain (%)	19.4	4.05	9.5
Myalgia (%)	72.4	38.28	63.4
Fatigue (%)	26.48	45.38	17.4
Cough (%)	7.08	3.49	5.94
Urticaria (%)	5.94	1.6	2.86
Sore throat (%)	1.2	0.34	2.54
Herpes labialis (%)	23.64	12.98	8.5
Splenomegaly (%)	24.84	34.5	28.86
Hepatomegaly (%)	4.56	8.34	7.75
Loose stools (%)	12.3	4.68	2.36
Altered sensorium (%)	0.46	2.84	0
Jaundice (%)	0.54	0.87	0.36

*Data are presented as % or mean ± SD (range) unless otherwise specified

the diagnosis, detailed clinical evaluation with information about age, duration of illness, fever, chills/rigors, sweating, headache, vomiting, abdominal pain, myalgia, fatigue, cough, urticaria, sore throat, herpes labialis, splenomegaly, hepatomegaly, loose motions, altered sensorium and jaundice were noted. Ultrasound scan of abdomen was done to confirm organomegaly. Laboratory investigations done in each patient included hemoglobin, WBC count, platelet count, serum bilirubin, serum transaminases, blood urea, serum creatinine, blood glucose and pH. Optional investigations as

required to exclude other diagnosis (Blood culture, Dengue serology, Widal, Leptospira, Urine culture, Radiological investigations) were done on case to case basis. Frequencies of occurrence of various symptoms and signs of malaria were determined. Mean, standard deviation and range of laboratory parameters were calculated. A total of 320 patients were studied. Formal approval of the hospital ethics committee was obtained.

Results

A total of 320 patients were admitted during the study period

of which 249 had *P. vivax* malaria, 43 had *P. falciparum* and 28 had both vivax and falciparum (mixed malaria) as diagnosed by peripheral blood smear and rapid diagnostic tests (RDT). The gender distribution showed a male preponderance (79%). The average age was 31.49 years in vivax malaria, youngest being 12 yrs and oldest was of 92 yrs (Table 1). Maximum (51.56%) patients were in 21-30 age group. The mean duration of symptoms was 2.54 in vivax to 3.03 days in mixed malaria. Fever was observed in 97.8% of patients of vivax. Four patients (1.25%) presented only with pain epigastrium without any history of fever. Only two had urticaria as the presentation. Splenomegaly was noticed in 24.84% patients of vivax and 34.5% of falciparum malaria. Herpes labialis was observed in 23.64% patients of vivax and 5.94% had urticaria. Other main symptoms and signs were chills/rigors, sweating, headache, vomiting, myalgia, fatigue, cough, abdominal pain, sore throat, hepatomegaly, diarrhea, altered sensorium and jaundice. The detailed account of clinical features is shown in Table 2.

The mean platelet count was 72,036/mm³ in vivax and 84,389/mm³ in mixed malaria with minimum being 16,000/mm³ (Table 3). Thrombocytopenia (<1,50,000/mm³) was noticed in 99% of all patients. Leucopenia (<4,000/mm³) was observed in 56.56% of all patients. The hemoglobin values ranged from 4.5 gm% to 16 gm%. The mean serum bilirubin levels were 1.42 mg% in falciparum and 2.04 mg% in mixed malaria (range 0.6-5.8 mg%). Serum aspartate transaminase values were higher (mean 83.92 mg% for mixed malaria) for all 03 groups as compared to alanine transaminase levels (mean 52.68 mg% for falciparum). Blood urea levels ranged from 5-98 mg/dl across all groups while the maximum serum creatinine levels were 2.6 mg/dl in falciparum malaria. Minimum blood glucose

Table 3: Laboratory parameters

Parameters	<i>P. vivax</i> n=249	<i>P. falciparum</i> n=43	Mixed malaria n=28
Platelets (/mm ³)			
Mean	72,036±29,503	82,748±38,544	84,389±38,781
Range	16,000-1,80,000	16,000-1,96,000	34,000-1,96,000
White blood cells (/mm ³)			
Mean	4520±2196	4362±2006	4406±2011
Range	1,700-9,800	2,500-9,800	2,478-9,800
Hemoglobin (g/l)			
Mean	11.41±2.13	11.97±2.29	11.87±2.46
Range	4.5-16	6.7-15	6-15
Bilirubin (mg/dl)			
Mean	1.56±0.90	1.42±0.91	2.04±1.45
Range	0.6-3.6	0.6-5.6	0.6-5.8
Alanine transaminase (IU/L)			
Mean	46.60±14.65	52.68±19.68	45.35±10.40
Range	23-98	28-108	34-78
Aspartate transaminase (IU/L)			
Mean	65.71±41.08	75.51±52.62	83.92±43.71
Range	22-265	22-271	34-198
Blood urea (mg/dl)			
Mean	20.73±13.22	23.53±15.30	23.04±18.07
Range	5-93	12-98	7-75
Serum creatinine (mg/dl)			
Mean	1.08±0.30	1.11±0.38	1.08±0.31
Range	0.5-1.9	0.5-2.6	0.6-1.9
Blood glucose (mg/dl)			
Mean	86.58±19.86	88.11±22.35	89.35±23.31
Range	45-154	59-170	59-154
Blood pH			
Mean	7.33±0.10	7.31±0.13	7.34±0.09
Range	6.9-7.48	6.6-7.46	7-7.48

*Data are presented as % or mean ± SD (range) unless otherwise specified

recorded was 45 mg% in vivax malaria. Lowest blood pH was noted in falciparum malaria (6.6). Eight (2 vivax, 4 falciparum and 02 mixed) patients had evidence of acute respiratory distress syndrome (ARDS) on chest radiograph. The mortality rate was 1.25% (4/320, 02 falciparum, 01 vivax and 01 mixed malaria). All those who expired had duration of illness of more than 7 days prior to reporting to hospital. All patients were treated with artemisinin based combination therapy. Patients requiring ICU care were managed accordingly and blood transfusions were used on as and when required basis. Radical cure with primaquine was given to all vivax malaria patients who were having normal G6PD levels.

Discussion

The classical triad of fever, chill/rigors and sweating was found in 68.6% of vivax malaria and 78.42% of mixed malaria cases. This finding is in divergence from other similar studies which reported higher percentage.⁵⁻⁷ Headache was noted in 82.26% of vivax patients and 46.6% of falciparum patients while Abdul Rasheed et al documented headache in 73.63% of vivax and 58% of falciparum patients⁷ and a study from Colombia showed 99% of patients with vivax had this symptom.⁸ Vomiting was noticed more commonly in falciparum (24.54%) as against vivax (12.5%), other studies have shown a frequency of 35%⁸ in vivax and 53% in falciparum subjects.⁷

Epigastric pain as a symptom

was recorded in 19.4% of all vivax patients, in fact 03 of the patients presented only with this symptom without any history of fever. A study from Pakistan has documented pain abdomen in 6% of vivax and 11.58% of falciparum patients.⁷

Herpes labialis was another significant finding in almost 23.64% patients of vivax and 12.98% of falciparum. This finding has been noticed in 2006⁷ ranging from 2.2% to 3% among various plasmodium species. Herpes labialis has been reported in 17% cases of falciparum malaria by Mehta SR¹⁷ and 10% patients of falciparum malaria in a rather recent study from Mysore.¹⁸

Splenomegaly was recorded in 24.84% patients of vivax, 34.5% of falciparum and 28.86% of mixed malarial patients. Various international studies have shown splenomegaly in 6.5% to 13% of their patients.^{5,8,9} Splenomegaly was reported in 59% of vivax, 68.8% of falciparum and 73.6% in a study from South East Asia.⁷ Hepatomegaly was noticed in 4.56% of vivax, 8.34% of falciparum and 7.75% patients of mixed malaria. This data is similar with some other studies^{5,7} and dissimilar to studies from Colombia (16%)⁸ and Thailand (8.2%).⁹

Thrombocytopenia was extremely important finding seen in more than 99% of all patients. A recent study from Mumbai has shown thrombocytopenia in 89.13% of vivax and 79.82% of falciparum patients.¹⁰ A study from Baluchistan had earlier documented thrombocytopenia in 79-80% of their patients.⁷ International literature documents this finding in ranges from 8% to 89%.^{8,11,12} None of the patients had any bleed from any site due to thrombocytopenia. The mechanism of thrombocytopenia in malaria is not clearly understood. Immune-mediated lysis, sequestration in the spleen and a dyspoietic process in the marrow with diminished platelet production have all been

postulated. Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malarial parasites themselves. Fajardo and Tallent in 1974 demonstrated *P. vivax* within platelets by electron microscopy and suggested a direct lytic effect of the parasite on the platelets.¹³ Tumour necrosis factor and interleukin-10 have been implicated in the development of *P. falciparum* anemia, but the role of these cytokines has not been studied in the development of thrombocytopenia in patients of acute malaria.¹⁴

The mean hemoglobin was around 11 gm% in various plasmodium species. Around 21% of all patients had hemoglobin of less than 10 gm% and almost all of them were either females or elderly males. Common causes of anemia in malaria are increased hemolysis and decreased rate of erythrocyte production from bone marrow,¹⁵ but in highly endemic areas malnutrition and intestinal parasite infections boost this problem. Leucopenia was demonstrated in 56.56% of all malarial patients. This data is definitely higher than figures mentioned in earlier studies⁷ and literature.¹⁶

The mean blood glucose was 86.58 mg% in vivax malaria with lowest recordable blood sugar being 45 mg%. Three patients reported with hypoglycemic coma while rest of the patients didn't reveal any signs of hypoglycemia. In a similar study in 2001 in Colombia involving vivax malaria,

41% of the study population have had hypoglycemia.

Conclusion

Most of the cases of malaria are likely to be missed if the clinicians keep on looking for the typical intermittent fever with chills/rigors and a palpable spleen. A high index of suspicion should be the "order of the day". Any patient with thrombocytopenia, leucopenia, headache, herpes labialis, pain epigastrium and urticaria deserves exclusion of malaria. An early diagnosis and treatment goes a long way in preventing avoidable deaths due to malaria.

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