Original Article

Clinical and laboratory findings in acute malaria caused by various plasmodium species

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Abstract

Objective: To find out clinical and laboratory findings in acute malaria caused by various plasmodium species.

Methods: This study was conducted in Department of Medicine and Pathology, Combined Military Hospital, Quetta, Balochistan, from August 2006 to December 2006. Five hundred and two subjects with positive malarial parasite slide were included in the study. Frequencies of alterations in clinical and laboratory parameters were determined in various plasmodium species and reported in percentage..

Results: Of 502 patients, 311 were Plasmodium (P.) falciparum, 100 were P.vivax and 91 were mixed infection. Triad of fever, chills and sweating was present in 91% of subjects with all three varieties of P. infection. Splenomegaly was detected in 59-73% individuals with malaria. Thrombocytopenia was the leading haematological alteration associated with various P. species, seen in almost 80% of infected patients. Anaemia and Jaundice were more common in P.falciparum and mixed infection as compared to P.vivax. Serum urea, creatinine and plasma glucose were within normal limits in all the patients with malaria.

Conclusion: Malaria must be considered as a leading differential diagnosis in an acutely febrile patient with one or more of abnormalities like splenomegaly, fall in blood counts or rise in bilirubin and serum alanine aminotransferase levels (JPMA 59:220; 2009).

Introduction

Malaria is the world's most important parasitic infection which poses major health challenges. Despite years of continual efforts, malaria is still a threat to over two billion people, representing approximately 40% of the world's population in about 100 countries. Geographical distribution of the disease is worldwide, being found in tropical areas, throughout Sub-Saharan Africa and to a lesser extent in Southeast Asia, South Africa, the Pacific Islands, India and Central and South America. Best estimates currently describe the annual global burden of malaria as 300-500 million cases and 1-2 million deaths.[1]

Malaria is caused by protozoan plasmodium (P.), transmitted by female anopheles mosquitoes, which typically bite between dusk and dawn. Four species of malarial parasite cause this disease (P. falciparum, P.vivax, P.malariae, P.ovale) but P.falciparum is the main cause of malaria and death. Malaria is not a uniform disease; it encompasses many manifestations and its impact varies on epidemiological setting. After P. falciparum, P.vivax is the next most significant malaria species; both often coexist in several parts of world.[2]

Malaria begins 8-30 days after infection. Clinical presentation of malaria caused by various species resembles each other. Clinical features include fever, chills, sweating, headache, vomiting, diarrhea, abdominal pain and distension, cough, splenomegaly and hepatomegaly.[3-5]

Laboratory alterations associated with malaria are well recognized but specific changes may vary with level of malaria endemicity, demographic factors and malaria immunity.[6]

The objective of this study was to determine the common clinical features and laboratory parameters in acute malaria caused by various P. species in this part of the world.

Patients and Methods

This prospective non-interventional descriptive study was conducted from September 2006 to December 2006 at a tertiary care hospital i.e. Combined Military Hospital, Quetta, Balochistan. Five hundred two subjects fulfilling inclusion criteria (i.e. between 12 to 60 years of age and positive malarial parasite slide) were enrolled in the study with non probability sampling technique after taking informed consent. Subjects with either pregnancy, history of antimalarial drug intake during the current disease or other co morbid preexisting conditions were excluded.

Blood samples of all suspected cases of malaria reported in the hospital were drawn for diagnosis and species of parasite by leishman stained blood smears following WHO recommendations.

After establishing the diagnosis, clinical evaluation was done and information regarding age, fever, chills, sweating, vomiting, headache, diarrhea, abdominal pain and distension, cough, Glasgow coma scale score, seizures, herpes labialis,

splenomegaly and hepatomegaly was recorded. Visceromegaly was confirmed by ultrasonography.

At the time of enrollment in the study, venous blood was obtained from each patient to assess complete blood count, bilirubin, alanine aminotransferase, urea, creatinine, and glycaemic levels.

Frequencies of various symptoms and signs of malaria caused by various P. species were determined. Mean, minimum and maximum values of laboratory alterations were calculated.

Results

Five hundred two male subjects with malaria were enrolled in the study. Their mean age was 28.2±7.0 years with the range of 12-60 years. Of the 502, 311 (62%) were P. falciparum, 100 (19.9%) were P. vivax while rest 91 (18.1%) showed mixed P. falciparum and P.vivax infection. None of the subjects had P. malariae or P. ovale infection. Fever was the leading symptom noted in both P. species and mixed infection, ranging from 97% to 100%. Other main symptoms were chills, sweating and headache particularly in P.falciparum and mixed infections. Splenomegaly was the leading sign in all three forms of P. infection ranging from 59% to 73%. The detailed account of clinical presentations is shown in Table 1.

Table 1: Clinical findings in various plasmodium species.

Parameters		P.falciparum n=311	P. vivax n=100	Mixed (P.falciparum & P. vivax) n=91
Age (years)	Mean	28.3±7.0	28.43±6.31	26.75±6.07
	Range	12-51	19-46	14-46
Evolution time (days)	Mean	2.5±1.5	3±1.6	2.6±1.4
	Range	1-13	1-9	1-10
Fever	(%)	99.04	97	100
Chills	(%)	91	81	91.21
Sweating	(%)	91.32	76	92.31
Headache	(%)	73.63	58	63.74
Vomiting	(%)	52.73	48	34.07
Diarrhea	(%)	4.5	2	2.2
Abdominal pain & distension	(%)	11.58	6	14.29
Dizziness	(%)	13.18	12	23.08
Cough	(%)	3.54	1	6.59
Sorethroat	(%)	0.64	0	2.2
Herpes labialis	(%)	2.89	3	2.2
Splenomegaly	(%)	68.81	59	73.63
Hepatomegaly	(%)	6.75	4	7.69
Glascow coma scale score <15	(%)	0.96	0	0

Thrombocytopenia (less than 150 x 10^9/l) was almost identical (approximately 80% subjects) in all three varieties but none of the subjects bled despite fall of platelets upto 16 x10^9/l. Anaemia was observed more frequently in P. falciparum (54.5%) and mixed infections (52.3%) as compared to P. vivax (29.5%). Leucopenia (less than 4 x10^9/l) was present in 22.1%, 20.9% and 18.4% subjects in P.vivax, P.falciparum and mixed infections respectively. High serum bilirubin was found more frequently in P.falciparum and mixed infections as compared to P.vivax infections while rise in serum alanine aminotransferase was almost identical in all three types of infections. Serum urea, creatinine and blood glucose were within normal limits in all individuals. The detailed account of laboratory parameters is shown in Table 2.

Table 2: Laboratory findings in various plasmodium species.

Parameters		P.falciparum n=311	P. vivax n=100	Mixed (P.falciparum & P. vivax) n=91
Platelets (10^9/l)	Mean	144.71±57.4	126.81±49.8	140.12±55.04
	Range	20-414	16-217	20-328
White blood cells (10^9/l)	Mean	5.9±1.69	5.8±1.75	5.71.60±1.60
	Range	1.7-11.5	2.6-11.6	2.2-10
Haemoglobin (g/l)	Mean	12.43±2.24	13.7±1.74	12.5±1.67
	Range	5.2-18	8.6-17	8.2-16
Bilirubin (mg/dl)	Mean	1.047 ± 0.86	0.85 ±0.56	1.01 ± 0.86
	Range	0.47-16.9	0.24-3.53	0.47-6.02
Alanine aminotransferase (u/l)	Mean	42 ± 28.01	36 ± 11.03	40 ± 24.43
	Range	22-278	22-174	22-229
Urea (mmol/l)	Mean	14.22 ± 3.06	13.19 ± 2.42	13.89 ± 2.76
	Range	7.22-17.22	8.33-21.67	8.89-19.16
Creatinine (mg/dl)	Mean	0.996 ± 0.15	0.97 ± 0.19	0.97 ± 0.15
	Range	0.77-1.37	0.76-1.67	0.76-1.42
Glucose (mg/dl)	Mean	98.17 ± 23.96	96.01±21.28	94.54±22.72
	Range	54.54-189	69.1-161.8	63.63-169.07

Discussion

This study demonstrates clinical and laboratory findings in various plasmodium species unlike available international and national data which either focused on one of the P. species[7-13] or few of the factors in different species.[14,15] All subjects were male in this study as it was carried out in a military hospital, which mainly treats soldiers.[9]

None of the subjects was found infected with P.ovale and P.malariae in this study. This observation is in line with the previous local data[5] and in contrast to outcome of some international studies.[14,15]

Fever, chills and sweating were the leading clinical presentations in the three forms and this triad was found in almost 91% of subjects with P.falciparum and mixed infection while in 76% of P.vivax subjects. This triad was less frequent in P.falciparum infections in previous studies.[5,9,10,14] This high frequency may be an incidental finding or that their temperatures were recorded more vigilantly and frequently.

Same triad was found in about 91% of subjects in P.vivax infection in Colombia.[7]

Vomiting was noted more commonly in 48% of subjects with P.vivax infection as compared to 39%[7] and 22%[14] in previous studies. Similar complaint was observed in 53% of P. falciparum infected subjects as compared to 37% in Western Thailand study.[14]

Herpes labialis was found in all three forms of plasmodium infections ranging from 2.2% to 3%. This finding was never reported in association with malaria previously in literature and requires further studies in future.

Splenomegaly was recorded in 59% of P.vivax, 68.8% of P.falciparum and 73.6% mixed P. infected patients. This high proportion of splenomegaly is in contrast to various international studies showing splenomegaly in 6.5% to 13% of the patients.[7,8,16] This unique finding may be due to the repeated plasmodium infection as most of the subjects in this study were from highly endemic malarious area.[5]

Hepatomegaly was detected in 4% of P.vivax infected individuals in our study. This data is similar to study in Surat-India[16] and dissimilar to data from Columbia (17%)[7] and Thailand (8.2%).[8]

Thrombocytopenia was detected in about 79-80% of subjects in various plasmodium infected patients in our study. This haematological alteration is a common finding in malaria and a result of peripheral destruction and consumption. Immune complexes generated by malarial antigen lead to sequestration of the injured platelets by macrophages in the spleen.[17] Frequency of this abnormality ranges from 8% to 89% in international literature.[7,13,14] This variation in thrombocytopenia may be an incidental finding or due to difference in sample size. However none of the subjects bled from any site despite significant fall in platelet count. This result is in contrast to one international study[18] in which two patients bled.

Anaemia has frequently been associated with malaria. The two common causes of anaemia are increased haemolysis and decreased rate of erythrocyte production from bone marrow[19] whereas the malnutrition and intestinal parasitic infections aggravate this problem in highly endemic areas. About 50% of the subjects with P.falciparum and mixed infection cases were anaemic while 29% of P.vivax infected cases had this abnormality. Anaemia was less frequently observed in various other studies.[14,20-23]

White cell counts are also found reduced in about 20% of the subjects infected with various plasmodium species. This haematological alteration is certainly not unprecedented, neither for P.falciparum[24,24] nor for P.vivax.[24]

Jaundice is a common feature attributed in part to liver damage and haemolysis of both parasitized and non-parasitized erythrocytes.[25] Serum bilirubin was found raised more frequently in P. falciparum (32%) and mixed infection (49%) as compared to P.vivax (9.4%). A study from Thailand[8] reported about 6.5% of P. vivax infected cases to be mildly jaundiced.

Clinical implication and limitations of study:

This study focuses on clinical and laboratory findings in various plasmodium species infection in this part of the world. Although these clinical and laboratory alterations in association with malaria are not new to the subject, this data adds more detailed information to the limited body of knowledge. Clinical presentation was almost identical in various species and in line with the existing data with few differences like herpes labialis that has never been reported in previous literature. Splenomegaly, fall in blood counts and rise in bilirubin were detected in higher number of subjects as compared to existing documented data.

The first limitation of this study was that all subjects were male which may alter various results.[7,14] Another limitation is that these cases were not followed for relapse and recrudescence.

The mechanism, aetiology, and clinical relevance of these findings deserve further studies.

Conclusion

Clinical presentation of various plasmodium species is almost similar with few differences. One must always keep malaria at the top in the differential diagnosis of an acutely febrile patient from a malaria endemic area with one or more of these abnormalities including splenomegaly, thrombocytopenia, leucopenia, anaemia, raised bilirubin and alanine aminotransferase levels.

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