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Original Research Article

Study of clinical presentation of malaria and the associated liver profile changes in various species of plasmodia

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ABSTRACT

Background: Malaria is one of the most common widespread infectious diseases in the tropical developing countries. It affects nearly 300-500 million cases every year with a mortality rate of 1.2-2.7 million deaths per year. Objectives of the study were to study the clinical presentation and liver profile changes in acute malaria caused by various plasmodium species. Medical college and Research centre, Bijapur, Karnataka, India.
Methods: One hundred subjects with peripheral smear positive for malarial parasite were included in the study. The alterations in liver profile laboratory parameters were determined in various plasmodium species and reported.
Results: Of 100 patients, 44 were *Plasmodium falciparum* (Pf), 51 were *Plasmodium vivax* (Pv) and 5 were mixed (Pf + Pv) infection. Fever (97%), chills (83.2%) and sweating (73.26) were the predominant presenting symptoms. Splenomegaly was detected in 78-80% individuals. Jaundice was more common in *P. falciparum* and mixed infection as compared to *P. vivax.*
Conclusions: Malaria is a potential cause of morbidity and mortality in the tropical countries. Jaundice is one of the common presentations of falciparum malaria. The raised serum bilirubin could be due to both hemolysis and hepatocellular dysfunction. Early diagnosis and treatment will help in reducing further complications like severe anaemia, hepatic encephalopathy, acute renal failure and disseminated intravascular coagulation.

Keywords: Jaundice, Liver function, Malaria, Plasmodium

INTRODUCTION

Malaria is one of the most common widespread infectious diseases in the tropical developing countries. It affects nearly 300-500 million cases every year with a mortality rate of 1.2-2.7 million deaths per year.[1,2] 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.[3,4] Laboratory alterations associated with malaria are well recognized but specific changes may vary with level of malaria endemicity, demographic factors and malaria immunity. Hepatic involvement is one of the cardinal manifestations of severe malaria.[5,6] The present study was done to evaluate the clinical and biochemical liver profile changes in patients with malaria, to study prevalence of jaundice in different species of *Plasmodium* (*falciparum* and *vivax*) and the type of jaundice (hemolytic or hepatic) in malaria.

METHODS

The present prospective study included 100 patients diagnosed as malaria by peripheral smear study admitted to BLDEU'S Shri BM Patil Medical College.

Institutional ethical committee clearance was obtained prior to conducting this study. Informed consent was also

obtained from patients for participation in the study. Alcoholics, cirrhosis, hepato cellular carcinoma unexplained hepatomegaly and patients with hepatitis B and C viral infections were excluded from the study.

All patients were evaluated clinically for history of fever with chills and sweating, headache, pain abdomen, vomiting, pallor, icterus, hepatomegaly, splenomegaly, altered sensorium, convulsions and coma. Both thick and thin smears were prepared and examined for malarial parasite. Quantitative buffy coat study was done to confirm the presence of malarial parasite.

The laboratory investigations for assessment of liver function included serum bilirubin (total, direct and indirect), serum proteins (total, albumin), SGOT, SGPT and ALP. Hepatitis B and C infection were also tested to rule out concomitant viral hepatitis.

Statistical analysis

The data obtained were analysed using the student's t-test, chi-square test and Fisher's exact test. A P value of <0.05 was considered statistically significant. SPSS software package version 10 was used. Results were expressed as Mean±Standard Deviation (SD) and percentage.

RESULTS

The age group was in the range of 11-70 years, among which maximum was seen in 31-40 year (Table 1). 59 were males and 41 females. Of the 100 patients, 44 were Pf, 51 were Pv while 5 showed mixed infection (Table 2).

Table 1: Age distribution.

Age (years)	No. of patients
0-10	-
11-20	13
21-30	20
31-40	24
41-50	19
51-60	15
61-70	6
>70	3
Total	100

None of the subjects had *P. malariae* or *P. ovale* infection. Fever was the leading symptom noted, ranging from 98% to 100%. Other main symptoms were chills, sweating and headache particularly in Pf and mixed infections.

Hepatomegaly was seen in 50-60% of patients. Splenomegaly was the leading sign ranging from 78% to 80%. Icterus and High serum bilirubin was found more frequently in *P. falciparum* and mixed infections (40%) as compared to *P. vivax* infections (20%). Hyper-bilirubinaemia was predominantly unconjugated bilirubin (Table 2 and 3).

Rise in serum liver enzymes was significant with SGOT ($\chi 2$ 8.63, $p<0.05$) and SGPT ($\chi 2$ 5.985, $p<0.05$) in all three types of infections (Table 4, 5). Out of 48 patients with jaundice SGPT was raised in 17 patients ($\chi 2$ 13.197; $p<0.001$) indicating hepatic cause of jaundice. There was a decrease in serum albumin in all the three groups (Table 3).

Table 2: Clinical features in different *Plasmodium* species.

Parameters	P falciparum (Pf) n=44	P Vivax (Pv) n=51	Mixed infection (Pf + Pv) n=5
Age (years) (mean + standard deviation)	41.93±14.98	37.56±16.49	35±7.905
Fever	44 (100)	50 (98%)	5 (100%)
Chills	40 (91.2%)	40 (78.4%)	4 (80%)
Sweating	40 (91.2%)	35 (68.6%)	3 (60%)
Headache	38 (86.6%)	35 (68.6%)	3 (60%)
Vomiting	25 (57%)	20 (39.2%)	1 (20%)
Pain abdomen	20 (45.6%)	10 (19.6%)	2 (40%)
Cough and sore throat	10 (22.8%)	10 (19.6%)	3 (60%)
Pallor	40 (91.2%)	45 (88.2%)	5 (100%)
Icterus	18(41.04%)	12 (23.52%)	2 (40%)
Hepatomegaly	30 (68.64%)	25 (49%)	3 (60%)
Splenomegaly	35 (79.8%)	40 (78%)	4 (80%)
Glass gow coma scale < 10	4 (9.12%)	0	1 (20%)

Table 3: Liver function test results (mean + standard deviation).

Parameters	P falciparum (Pf) n=44	P Vivax (Pv) n=51	Mixed infection (Pf + Pv) n=5
Total bilirubin (mg/dl)	2.86±4.22	1.26±0.83	1.14±0.20
Conjugated bilirubin (mg/dl)	1.21±1.37	0.78±0.60	0.7±0.14
Unconjugatd bilirbin (mg/dl)	1.65±3.04	0.47±0.45	0.44±0.32
T.protien (gm/dl)	5.8±0.48	5.84±0.56	6.08±0.52
Albumin (gm/dl)	3.26±0.466	3.41±0.55	3.56±0.70
A/G ratio	0.94±0.122	0.97±0.106	0.96±0.11
SGOT (AST)	52.38±67.45	29.43±8.81	29.55±8.79
SGPT (ALT)	40.79±22.05	29.06±9.14	28.88±8.89
Alkaline Phosphatase	142.81±70.14	57.31±48.72	133.6±37.29

Table 4: Alterations in the liver function tests in various plasmodium species.

Parameter		Pf (n=44)	Pv (n=51)	Pf + Pv (n=5)	Total	X2 (chi square)	p value
Total bilirubin (mg/dl)	≤1 mg/dl	26	23	3	52	1.988	0.370
	>1 mg/dl	18	28	2	48		
Conjugated bilirubin (mg/dl)	≤0.4mg/dl	21	42	4	67	13.211	0.001
	>0.4 mg/dl	23	9	1	33		
Unconjugated bilirubin (mg/dl)	≤0.6mg/dl	16	25	2	43	1.563	0.458
	>0.6 mg/dl	28	26	3	57		
SGPT (ALT)	0-40 IU/L	30	46	5	81		
	>40 IU/L	14	5	0	19	8.673	0.02
SGOT (AST)	0-40 IU/L	31	46	4	81		
	>40 IU/L	13	5	1	19	5.985	0.05
Alkaline Phosphatase (ALP)	<100U/L	08	12	01	21		0.03
	>100U/L	36	39	04	79	8.606	
Total Proteins (gm/dl)	<6 mg/dl	22	22	02	46	1.551	0.46
	>6mg/dl	22	29	03	54		
Albumin (gm/dl)	≤3 gm/dl	05	07	00	12	8.891	0.01
	>3gm/dl	39	44	05	88		

Table 5: Comparison of serum bilirubin with SGOT, SGPT and ALP in the study subjects.

Total bilirubin	SGOT		SGPT		ALP	
	0-40 IU/L	>40 IU/L	0-40 IU/L	>40 IU/L	<100u/L	>100u/L
≤1 mg/dl -52 patients	46	06	50	02	08	44
> 1 mg/dl- 48 patients	35	13	31	17	13	35

4 patients with falciparum infection and 1 patient with mixed infection had features of cerebral malaria with altered sensorium. The serum bilirubin in these patients was between 12- 16 mg/dl with elevated liver enzymes. One patient who developed convulsions and died had Pf infection with cerebral malaria, serum bilirubin of 15 mg/dl and SGPT>500 IU/L.

DISCUSSION

This study demonstrates clinical and laboratory findings in malaria due to various plasmodium species. Fever was the predominant presenting symptom (98-100%). Chills and sweating were present in 91% of Pf, 68-78% of Pv and 60-80% of patients with mixed infection.[7] Abdul Rashid et al study found these symptoms in almost 91% of subjects with *P. falciparum* and mixed infection while in 76% of *P. vivax* subjects. Headache was seen in 86% of Pf, 68% of Pv and 60% of mixed infection. Vomiting was seen in 57% of Pf, 39% of Pv and 20% of mixed infection. Jaundice is one of the manifestations of severe malaria. It results from the intravascular haemolysis of parasitized erythrocytes, hepatic dysfunction and microangiopathic haemolysis associated with disseminated intravascular coagulation.[8,9] The histopathological changes reported in the malaria patients include hepatocyte necrosis, cholestasis, bile stasis, granulomatous lesions and malarialnodules.

The bile stasis is due to impairment of bilirubin transport because of reticulo-endothelial blockage and disturbance of hepatocyte microvilli.[10,11,18]

Icterus was seen in 32 patients of whom 18 had Pf, 12 had Pv and 2 had mixed infection. This contributed to 40% of Pf and mixed infection and 23% of Pv. Serum bilirubin was found raised (> 1mg/dl) more frequently in Pf (59%) and mixed infection (60%) as compared to P.vivax (45%). Adbul rashid et al study found raised serum bilirubin in 32% of Pf 49% of mixed and 9.4% of Pv infection.[7]

The incidence of jaundice was found to be more in adults than children and ranged from 32-37% with predominant unconjugated hyperbilirubinemia as reported by Harris et al.[4] In patients with severe malarial infection, the incidence of jaundice is reported to be 2-57% Devar bhai et al.[12] According to the WHO, in severe falciparum malaria patients, serum bilirubin levels remain in the range 7–10 mg%, but in our study 13 patients (out of 44) had serum bilirubin levels >3 mg%. The maximum value of serum bilirubin observed in this study was 23 mg/dl.

Liver enzymes (SGPT and SGOT) were elevated in 31% of Pf and 9% of Pv ($p< 0.05$, $\chi 2 =8.673$) indicating hepatic dysfunction more frequent in Pf than Pv. Liver abnormalities are relatively common findings in severe P. falciparum malaria and it has been demonstrated that abnormal liver function profile return to normal a few weeks after treatment (Wilaratna et al).[5]

According to world health organization (WHO), apart from jaundice, other signs of hepatic dysfunction are unusual. In recent years, there has been increasing number of reports favoring existence of malarial hepatopathy, from Asian countries, especially from India. The majority of the cases have either isolated infection with *P. falciparum* or a mixed infection with both P. falciparum and *P. vivax*. The extent of liver involvement varies from a minimal abnormality in liver function tests to hepatic encephalopathy.[13-15]

Chawla et al studied 31 patients, of whom 14 had serum bilirubin>10mg%, with predominantly conjugated hyper-bilirubinaemia.[16] They attributed these elevated serum bilirubin levels to intravascular haemolysis and associated renal failure, leading to decreased excretion of bilirubin.[17-19]

Murthy et al in their study of 95 patients observed that high serum bilirubin levels in malaria were associated with a more severe course of illness, and with higher incidence of complications and poor prognosis because of histopathological changes to the liver.[11]

CONCLUSION

Malaria is a potential cause of morbidity and mortality in the tropical countries. Jaundice is one of the common presentations of falciparum malaria. The raised serum bilirubin could be due to both hemolysis and hepatocellular dysfunction. Early diagnosis and treatment will help in reducing further complications like severe anaemia, hepatic encephalopathy, acute renal failure and disseminated intravascular coagulation.

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