

Malaria Positive Cases with Reference to Liver Function Test among Patients Attending in Teerthanker Mahaveer Medical College and Research Centre, Moradabad, Uttar Pradesh, India

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Abstract

Introduction: Malaria is also an important infectious vector-borne disease caused by a *Plasmodium* species. According to the World Health Organization, involvement of liver in *Plasmodium Falciparum* malaria is not an uncommon presentation and presence of jaundice (bilirubin ≥ 3 mg/dl) is one of the signs of malaria. In severe and complicated malaria, a term “malarial hepatitis” is commonly used to describe hepatocytic dysfunction; however, actual inflammation is almost never seen in the liver parenchyma. An increased level of serum bilirubin along with increased level of serum glutamate pyruvate transaminase (SGPT) to more than three times the upper limit of normal, is main characteristics of malarial hepatitis.

Materials and Methods: This study was performed on 80 peripheral blood smear (PBS) confirmed cases of malaria. A collection of blood sample was done by venepuncture under aseptic conditions in the ethylenediaminetetraacetic acid tube for the diagnosis of malaria and in a plane vial to perform liver function test (LFT). Diagnosis of malaria was done by the microscopy of PBS and rapid malarial antigen test. The LFT was performed using autoanalyzer and Erba biodiagnostic kit, according to manufacturer instructions.

Results: Out of total 80 malaria positive patients, 60 patients (75%) had got deranged LFT in which 35 (70%) were males and 25 (83.33%) were females. According to serum bilirubin levels, patients were classified into three Groups A (59 patients, serum bilirubin < 3 mg/dl), B (21 patients, serum bilirubin 3-10 mg/dl), and C (no patient, serum bilirubin > 10 mg/dl). Total malaria positive patients had total bilirubin, direct bilirubin, indirect bilirubin, serum glutamic oxaloacetic transaminase, SGPT, and alkaline phosphatase levels in the range of 2.17 ± 1.78 mg/dl, 0.88 ± 0.77 mg/dl, 1.29 ± 1.12 mg/dl, 45.88 ± 28.99 IU/L, 41.04 ± 26.45 IU/L, and 104.48 ± 67.51 U/L, respectively.

Conclusion: Liver dysfunction in malarial infection ranged from mild elevation of liver enzymes and serum bilirubin (≥ 3 mg/dl) to acute hepatitis. It indicates severe illness with a high frequency of complications and mortality rates.

Key words: Liver function test, Malaria, Malarial hepatitis

INTRODUCTION

Malaria is responsible for infecting 300-500 million people and 1-3 million deaths annually in tropical areas.¹ Malaria is

also an important infectious vector-borne disease caused by a *Plasmodium* species. Malaria is caused by *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale*, *Plasmodium malariae*, and rarely *Plasmodium knowlesi* in human.² 90% of the deaths from malaria is caused by *P. falciparum* because *P. falciparum* is the most common cause of malarial infection.³

According to the World Health Organization, involvement of liver in *P. falciparum* malaria is not an uncommon presentation and presence of jaundice (bilirubin ≥ 3 mg/dl) is one of the signs of malaria.⁴ As highlighted in the

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world malaria report 2010, *P. vivax* malaria is a major public health problem, in which puts billions of the world's population at risk of infection.⁵ The transmission of malaria parasite to the human host occurs by sporozoites infection to the liver.⁶

Anemia, thrombocytopenia, and disseminated intravascular are the hematological alterations that are associated with malaria infection.⁷⁻¹⁰ After the bite of female Anopheles mosquitoes, the malarial sporozoites, once reaches in blood, are attached to hepatocytes through receptor for thrombospondin and properdin.¹¹ Then, these sporozoites become mature to form tissue schizonts or become dormant hypnozoites. The amplification of infection by tissue schizonts due to the production of large number of merozoites (10,000-30,000). Each merozoite, which is released from the liver, is capable to enter inside a human red blood cell (RBC) and performing the asexual cycle of replication in that RBC and release of 24-32 merozoites after 48-72 h of asexual cycle.¹²

In severe and complicated malaria, a term “malarial hepatitis” is commonly used to describe hepatocytic dysfunction; however, actual inflammation is almost never seen in the liver parenchyma.¹³ An increased level of serum bilirubin along with increased level of serum glutamate pyruvate transaminase (SGPT) to more than three times the upper limit of normal, is main characteristics of malarial hepatitis.¹⁴

Hepatic involvement in malaria has largely associated with severe infection of *P. falciparum*. Occasionally mixed infection with *Plasmodium vivax*¹⁵ and hepatitis E¹⁶ has been shown. The multiple factors leading to severe anemia in malaria are hemolysis, bone marrow dysfunction, etc., and are proportional to the level of parasitemia.¹⁷ A common feature of falciparum malaria is mainly unconjugated hyperbilirubinemia, and it is attributed to hemolysis of both parasitized and non-parasitized RBCs and partly due to liver damage.¹⁸

The observation of the presence of jaundice and renal failure is found more commonly in recent years in patients infected by *P. falciparum* in Thailand and Vietnam.¹⁹ The most common sign of hepatic dysfunction is jaundice in falciparum malaria, although the most common clinical finding in these patients is tender hepatomegaly. The resultant hemolysis and severe infestation of the RBCs by *P. falciparum* lead to rise in bilirubin level. Clogging of the capillaries in the important organ is caused by sequestration of the parasite - infested RBCs in the capillaries, which results ischemia and can lead to dysfunctioning of the organ system. When the same happens in the liver, it is called hepatic dysfunction.

The symptomatic stage of the infection begins, when the parasites reach densities of about 50/ μ l of blood. These symptoms are characterized by a headache, fatigue, abdominal discomfort, muscle pain, and fever.²⁰ Malaria results to systemic manifestations by affecting major organs such as kidneys and liver.^{21,22} Malarial infection also leads to pulmonary complications.²³ Hyperbilirubinemia often seen in association with other manifestations such as cerebral malaria or renal failure,²⁴ although it has linked with increased mortality related to malaria.²⁵

MATERIALS AND METHODS

This prospective study was conducted at the Department of Microbiology, Teerthanker Mahaveer Medical College Hospital and Research Centre, Moradabad, Uttar Pradesh over a period from March 2015 to January 2016.

Subject Selection

A total 80 samples were taken, after confirming by microscopic examination and rapid malarial antigen test. Patients of all age group with the history of fever, headache, vomiting, gastric, jaundice, chills, and malaise were included in this study. Those patients who were taking hepatotoxic drugs or any anti-malarial drugs were excluded from the study.

Collection of Sample

A volume of 5 ml of blood was collected from each patient under aseptic conditions by venepuncture in ethylenediaminetetraacetic acid vacutainer tube (2.5 ml) for the diagnosis of malaria and plain tube (2.5 ml) for liver function test (LFT). A thick and thin smear was prepared. Thick smears were dehemoglobinized and stained with Leishman's stain and examined under $\times 100$ oil emersion lens.

Methodology

Diagnosis of malaria was done by microscopy of peripheral blood smear (PBS) examination and rapid malarial antigen test. PBS remains gold standard for conformation to the diagnosis of malaria. Thick and thin blood smears were prepared and both are stained with Leishman's stain. Then, the smears were examined to the different stages of malaria parasites under oil immersion lens. Rapid malarial antigen test is performed by following the procedure given by the production company.

Diagnosis of liver function by the semi autoanalyzer of Siemens Company by the use of commercially prepared reagent of liver function (bilirubin, SGPT, serum glutamic oxaloacetic transaminase [SGOT], and alkaline phosphatase [ALP]) using Erba biodiagnostic kit, according to manufacturer instructions.

Statistical Analysis

Mean and standard deviation were calculated for quantitative variables, and Chi-square was used to calculate *P* value. *P* < 0.05 was considered as significant.

RESULTS

The present study was conducted to observe the impact of malaria on LFT. In this study, biochemical parameters (total bilirubin, direct bilirubin, indirect bilirubin, SGOT, SGPT, and ALP) were included. In our study, total 80 patients were taken which were confirmed as malaria positive, 50 patients (62.5%) were males and 30 patients (37.5%) were females (Table 1 and Figure 1). Out of total malaria positive patients, 60 patients (75%) had got deranged LFT (DLFT) in which 35 (70%) were males and 25 (83.33%) were females (Table 2 and Figure 2). In this study, the patients of age group more than 60 years have had major DLFT (100%) followed by the age group of 31-40 years (88.89%) and 21-30 (85%) (Table 3 and Figure 3).

In our study, out of 30 female positive patients, total bilirubin (TBIL), SGPT, SGOT, and ALP were out of

normal range in 18 (54%), 9 (30%), 16 (53.33%), and 16 (53.33%), respectively, while in 50 males TBIL, SGPT, SGOT, and ALP were 27 (54%), 18 (36%), 11 (22%), and 10 (20%), respectively (Table 4 and Figure 4). In our study, according to serum bilirubin levels, patients were classified in three Groups A (59 patients, serum bilirubin <3 mg/dl), B (21 patients, serum bilirubin 3-10 mg/dl), and C (no patient, serum bilirubin >10 mg/dl) (Table 5).

Total malaria positive patients had total bilirubin, direct bilirubin, indirect bilirubin, SGOT, SGPT, and ALP levels

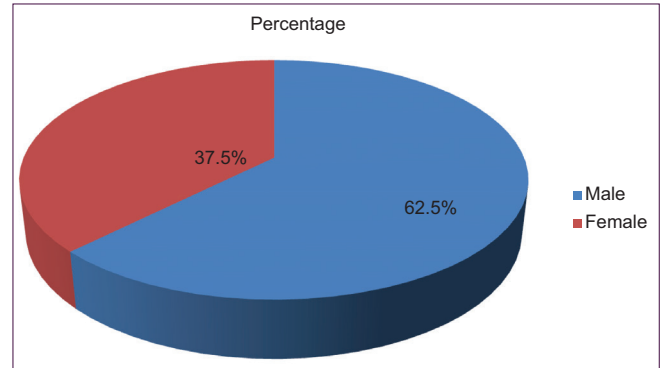


Figure 1: Sex wise distribution of total malaria positive patients

Table 1: Sex wise distribution of total malaria positive patients

Sex	Number of malaria positive patients	Percentage
Male	50	62.50
Female	30	37.50
Total	80	100

Table 2: Sex wise distribution of total malaria positive patients with abnormal and NLFT

Sex	Malaria positive	Percentage (n=80)	DLFT	Percentage	NLFT	Percentage
Male	50	62.5	35	70	15	30
Female	30	37.5	25	83.33	5	16.67
Total	80	100	60	75	20	25

DLFT: Deranged liver function test, NLFT: Normal liver function test

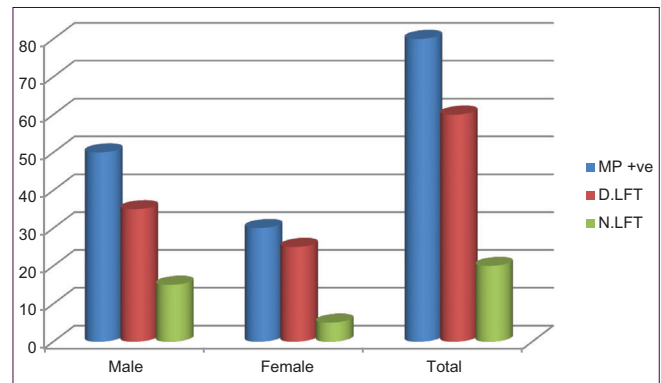


Figure 2: Sex wise distribution of malaria positive patients with abnormal and normal liver function test

Table 3: Age wise distribution of all malaria positive patients with abnormal and normal liver function test

Age	Malaria positive	% (n=80)	DLFT	%	NLFT	Percentage
1-10	8	10	4	50	4	50
11-20	29	36.25	22	75.87	7	25.13
21-30	20	25	17	85	3	15
31-40	9	11.25	8	88.89	1	11.11
41-50	6	7.5	3	50	3	50
51-60	6	7.5	4	66.67	2	33.33
>60	2	2.5	2	100	0	00
Total	80	100	60	75	20	25

DLFT: Deranged liver function test, NLFT: Normal liver function test

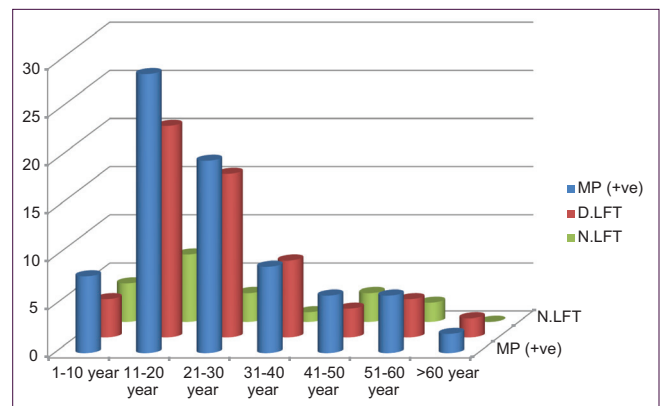


Figure 3: The age wise distribution of malaria positive patients with deranged and normal liver function test

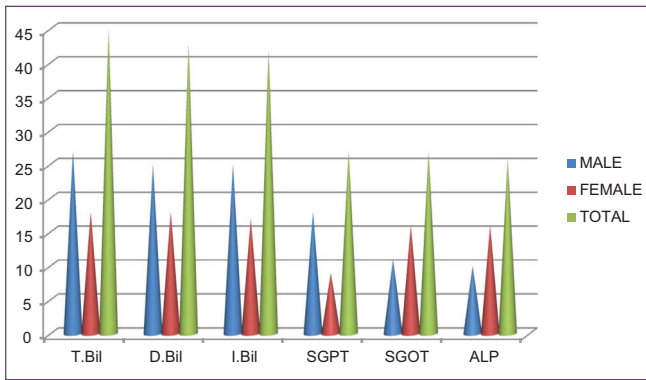


Figure 4: Sex wise distribution of malaria positive patients with increased level of liver function test markers

in the range of 2.17 ± 1.78 mg/dl, 0.88 ± 0.77 mg/dl, 1.29 ± 1.12 mg/dl, 45.88 ± 28.99 IU/L, 41.04 ± 26.45 IU/L, and 104.48 ± 67.51 U/L, respectively (Table 6).

DISCUSSION

In tropical areas, malaria is a major public health problem responsible for infecting 300-500 million people and 1-3 million deaths annually. Malaria involves liver where hepatocytes are invaded by sporozoites and multiply. In erythrocytic stage, the destruction of infected RBCs caused by merozoites. Molyneux *et al.* suggested that hemolysis is the most common cause of moderate elevation of hepatic enzymes than hepatic damage, which causes jaundice.²⁶

This study was performed to observe the impact of malarial infection on LFT. In our study, males 50 (62.5%) are more prone to malarial infection than females 30 (37.5%) out of total 80 positive patients. Our study is similar to the study of Abro *et al.*,²⁷ in which males 94 (91.5%) were more prone than female 9 (8.5%).

In our study, most of the malaria positive patients were in the age group of 11-20 years 29 (36.25%) followed by 21-30 years 20 (25%) and 1-10 years 8 (10%) while in the study of Rathod *et al.*²⁸ the age group 21-30 years 246 (32%) patients were more prone to malarial infection.

In our study, serum alanine aminotransferase (ALT or SGPT) level was above the reference range in 37.75% patients and serum bilirubin level above the reference range in 56.25% patients while in the study of Abro *et al.*²⁷ 67.6% patients had had ALT level above the reference range and in 81% patients serum bilirubin level was found to be higher than the normal level.

In this study, we observed <3 mg/dl serum bilirubin levels in 59 patients out of 80 patients while 20 patients out of

Table 4: Sex wise distribution of malaria positive patients with increased level of LFT markers

LFT parameters	n (%)		
	Male (n=50)	Female (n=30)	Total (n=80)
Total bilirubin	27 (54)	18 (60)	45 (56.25)
DBIL	25 (50)	18 (60)	43 (53.75)
IBIL	25 (50)	17 (56.66)	42 (52.5)
SGPT	18 (36)	9 (30)	27 (37.75)
SGOT	11 (22)	16 (53.33)	27 (37.75)
ALP	10 (20)	16 (53.33)	26 (32.5)

LFT: liver function test, SGPT: Serum glutamate pyruvate transaminase, ALP: Alkaline phosphatase, SGOT: Serum glutamic oxaloacetic transaminase, DBIL: Direct bilirubin, IBIL: Indirect bilirubin

Table 5: Classification of serum enzymes in patients as A, B, and C according to serum TBIL levels (n=80)

Groups	A	B	C
Serum bilirubin (mg/dl)	<3	3-10	>10
Number of patients	59	21	0
SGOT level (IU/L)			
<40	41	4	0
40-100	16	16	0
>100	2	1	0
χ^2 A with B=16.407, P<0.05			
SGPT level (IU/L)			
<40	40	9	0
40-100	19	11	0
>100	0	1	0
χ^2 A with B=6.064, P<0.05			

SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, TBIL: Total bilirubin

Table 6: The mean value and standard deviation of measured LFT markers in both male and female malaria positive patients separately

LFT parameters	Normal range	Mean±SD (n=80)
TBIL	0.2-1.0 mg/dl	2.17±1.78 mg/dl
DBIL	0.0-0.4 mg/dl	0.88±0.77 mg/dl
IBIL	0.0-0.7 mg/dl	1.29±1.12 mg/dl
SGOT	5-40 IU/L	45.88±28.99 IU/L
SGPT	5-40 IU/L	41.04±26.45 IU/L
ALP	50-126 U/L	104.48±67.51 U/L

SD: Standard deviation, LFT: Liver function test, TBIL: Total bilirubin, DBIL: Direct bilirubin, IBIL: Indirect bilirubin, SGOT: Serum glutamic oxaloacetic transaminase, SGPT: Serum glutamate pyruvate transaminase, ALP: Alkaline phosphatase

50 patients were having 3-10 mg/dl serum bilirubin level, in the study of Kochar *et al.*, 2003.²⁹

CONCLUSION

The results of our study provide valuable information and association between hepatic biochemical derangements in malarial patients. This study was conducted on a small sample size, and it provides basic information about patients

infected with the malaria parasite. Therefore, we suggested that same type of study should also be performed on large sample size, and early diagnosis of malarial infection should be performed with LFT to prevent complications and to reduce mortality. In malaria, severe hepatic dysfunction is usually related with the underlying chronic liver disease. The complications are more common in patients with malarial hepatopathy; that's why it should be recognized promptly.

Thus, in our opinion increased levels of bilirubin, SGOT and SGPT are the strong evidence of hepatic dysfunction in patients with malaria.

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