

PREVALENCE OF HEPATIC DYSFUNCTION IN PATIENTS WITH PLASMODIUM FALCIPARUM MALARIA IN A TERTIARY CARE HOSPITAL

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DOI: <https://doi.org/10.5281/zenodo.15804197>

Keywords

Hepatic dysfunction, malaria, plasmodium falciparum, plasmodium vivax

Article History

Received on 29 May 2025

Accepted on 29 June 2025

Published on 04 July 2025

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Abstract

Objective: To determine the frequency of hepatic dysfunction in patients with plasmodium falciparum malaria visiting tertiary care hospital.

Study design: Cross sectional

Place & duration of study: Department of Medicine, Liaquat University of Medical & Health Sciences, Jamshoro.

Methodology: In this cross-sectional observational study, a total of 196 patients of either gender having age between 18-70 years presented with plasmodium falciparum malaria with duration ≤ 2 weeks were included. The blood samples of all the patients was collected in a sterile manner for serum ALT, AST and bilirubin levels to assess the outcome variable i.e. hepatic dysfunction. Data analysis were done using SPSS Version 26. The quantitative variables were presented as mean $\pm$ SD. Frequencies & percentages were calculated for qualitative variables.

Results: A total of 196 patients with plasmodium falciparum malaria were included in this study. The mean age of the patients was 36.14 ± 11.1 years and mean duration of malaria was 1 ± 0.5 weeks. Most of the patients were male 117 (59.7%) and 79 (40.3%) were female. 28 (14.3%) were hypertensive and 24 (12.2%) were diabetics. Out of 196 patients with plasmodium falciparum malaria, hepatic dysfunction found in 75 (38.3%).

Conclusion: Our study concluded that frequency of hepatic dysfunction in falciparum malaria is very high, though it is commoner and more severe in the former.

INTRODUCTION

Plasmodium falciparum is one of the main species that causes the majority of malaria infections in Pakistan, making the disease a serious health problem.¹ In 2021, there were 247 million instances of malaria, up from 245 million in 2020, according to the most recent World Malaria report. An estimated

619,000 people died from malaria in 2021, up from 625,000 in 2020, with Plasmodium (P.) falciparum accounting for 80% of these deaths.² Jaundice (bilirubin >3 mg/dl) is one of the WHO's criteria for severe malaria, and hepatic involvement in P. falciparum malaria is not an unusual manifestation.³

Falciparum malaria is linked to a high rate of complications and mortality, and jaundice can range from moderate to severe.⁴ However, unless there is concurrent viral hepatitis, clinical indications of hepatic encephalopathy are uncommon. Acute malaria typically recovers from jaundice and returns abnormal liver function tests to the reference range more quickly than acute viral hepatitis.⁵ In order to rule out acute malaria, patients with high bilirubin levels and an acute fever, whether or not they exhibit signs of hepatic dysfunction, should notify their doctor. This is especially important if the patient has recently traveled to an area where malaria is endemic.⁶ Malaria patients with hepatocellular dysfunction are more likely to experience problems, but if hepatic involvement is identified early and treated appropriately, they have a good prognosis.^{7,8} In areas like Pakistan, where *Plasmodium falciparum* is prevalent, malaria, which is mostly caused by *Plasmodium* parasites, continues to be a serious health concern.⁹ Despite the fact that the disease's clinical signs are well established, little is known about how these infections affect hepatic functioning. Considering the severe repercussions and high frequency of hepatic impairment linked to *Plasmodium falciparum* malaria,¹⁰ it is essential to determine the prevalence of this problem in a targeted study population. These kinds of studies are essential for improving clinical management and treatment procedures, which will enhance patient outcomes and help create improved public health policies. Thus, the purpose of this study was to ascertain the prevalence of hepatic dysfunction in tertiary care hospital patients with *Plasmodium falciparum* malaria.

METHODOLOGY:

This descriptive study was carried out over a period of six months in the Department of Medicine, Liaquat University of Medical & Health Sciences, Jamshoro. Patients were enrolled in this study after taking written informed consent. A total of 196 patients of either gender having age between 18-70 years presented with *plasmodium falciparum* malaria with duration ≤ 2 weeks were included via non-probability sampling technique.

Patients with malaria infections caused by *Plasmodium* species other than *P. Falciparum*, patients with fever and clinical symptoms caused by

etiologies other than malaria, including bacterial, viral, or non-infectious conditions, Patients who had already taken antimalarial treatment, patients with a history of severe cognitive impairment, pregnant patients assessed by history and confirmed by dating scan, patients with chronic conditions such as severe renal impairment, chronic liver disease, or severe immunosuppression (e.g., advanced HIV/AIDS), patients with a history of hepatotoxic drug intake during the last 3 months and Patients with a history of intake of herbal medicines were excluded.

A brief history of the duration of symptoms and demographic data was taken from each patient. Detection of species *P. falciparum* in the affected patient was done through a peripheral blood smear and antibody-based rapid malaria antigen test. All patients received anti-malarial medications as per the hospital policy.

The blood samples of all the patients was collected in a sterile manner for serum ALT, AST and bilirubin levels to assess the outcome variable i.e. hepatic dysfunction (Yes/No).

Hepatic dysfunction was categorized as positive by presence of any one or more of the following: Alanine transaminase (ALT) >100 IU/L, Aspartate transaminase (AST) >100 IU/L and Total bilirubin (TB) >2 mg/dl.

Data was analyzed using SPSS version-26.0. After checking the normality of data using Shapiro-Wilk test, mean and standard deviation was calculated for age and duration of malaria. Frequencies and percentages were calculated for gender, type II diabetes mellitus, hypertension and hepatic dysfunction. Effect modifiers were controlled through stratification of age, gender, duration of malaria, type II diabetes mellitus and hypertension. Post-stratification Chi-square / Fisher's exact test as appropriate was applied at a 5% level of significance.

RESULTS:

A total of 196 patients with *plasmodium falciparum* malaria were included in this study. The mean age of the patients was 36.14 ± 11.1 years and mean duration of malaria was 1 ± 0.5 weeks. Most of the patients were male 117 (59.7%) and 79 (40.3%) were female. 28 (14.3%) were hypertensive and 24 (12.2%) were diabetics, as shown in table # 1.

Out of 196 patients with plasmodium falciparum malaria, hepatic dysfunction found in 75 (38.3%), as shown in figure # 1. Further, frequency of hepatic

dysfunction was compared with respect to the baseline data, significant difference was observed except when same was compared with respect to gender, as shown in table # 3.

Table 1: Demographic data of the Patients

Demographic Data	(mean + SD) / n(%)
Age (years)	36.14 ± 11.1
Duration of Malaria (weeks)	1 ± 0.5
Gender	
• Male	117 (59.7%)
• Female	79 (40.3%)
Co-morbid	
Hypertension	
• Yes	28 (14.3%)
• No	168 (85.7%)
Diabetes Mellitus:	
• Yes	24 (12.2%)
• No	172 (87.8%)

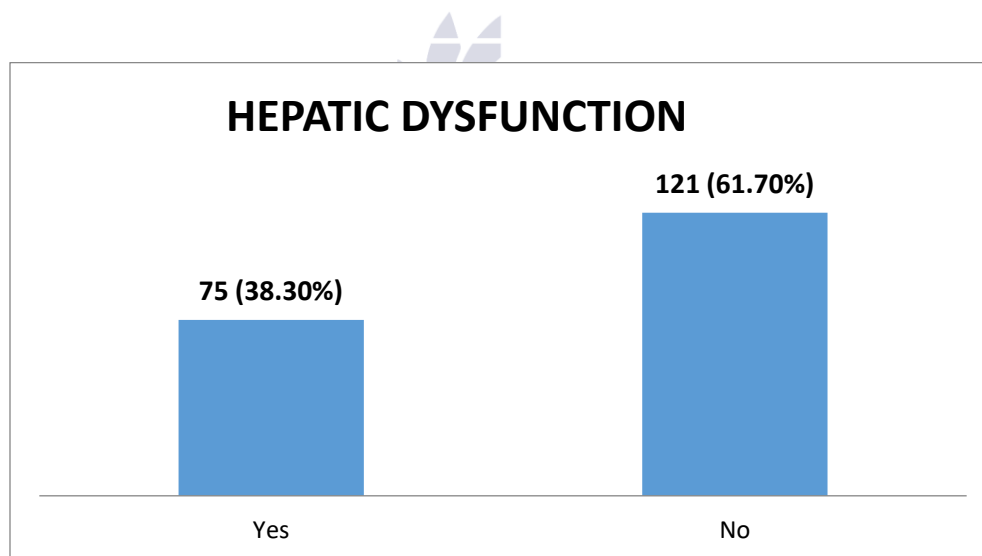


Figure 1: Frequency of Hepatic Dysfunction in Patients with Plasmodium Falciparum Malaria

Table 2: Comparison of Frequency of Hepatic Dysfunction with Respect to Demographic Data

Demographic Data	Hepatic Dysfunction		P-value
	Yes (n=75)	No (n=121)	
Age (years)			
• ≤35	47	51	0.004
• >35	28	70	
Duration of Malaria (weeks)			
• ≤1	43	86	0.035
• >1	32	35	
Gender			
• Male	44	73	0.467
• Female	31	48	
Hypertension			
• Yes	4	24	0.003
• No	71	97	
Diabetes Mellitus:			
• Yes	16	8	0.003
• No	59	113	

DISCUSSION:

Malaria is responsible for the illness or death of malaria sufferers worldwide, making it a major public health concern.¹¹ The World Health Organization (WHO) reports that it is most common in the Eastern Mediterranean and tropical sub-Saharan Africa. Malaria still contributes significantly to the global burden of infectious illnesses in terms of the mortality and disability rates among its victims, despite a strong focus on preventative and therapeutic efforts.¹² Hepatic issues and dysfunction are common in patients with mild to severe malaria, in addition to the involvement of other systems. These patients may also have hypoglycemia, or low blood sugar, multiorgan failure (MOF), and a pH problem that mimics a metabolic disease. The type of parasite, length of sickness, and when antimalarial treatment is started can all be used to forecast how severe malaria will be.^{13,14} The literature contains a variety of information regarding the prevalence of hepatic dysfunction and hepatitis in acute malaria because of variations in geographic location, age, malaria endemicity state, and coexistence with other local disorders.¹⁵

According to several research, the incidence of jaundice in falciparum malaria ranges from 2.5% to 20% to 30%.¹⁶ It is often modest in severity and is brought on by the intravascular destruction of red blood cells as well as the sequestration of parasitized cells in the spleen and other microcirculation components.¹⁷ Jaundice in certain people may be caused by hepatocellular dysfunction. It is generally regarded as mild, regardless of the source, and a bilirubin level over 51.3 $\mu\text{mol/L}$ has been observed to be uncommon.¹⁸ The study on jaundice and hepatomegaly in primary malaria found that the maximum bilirubin level was 8721 $\mu\text{mol/L}$.¹⁹ This analysis revealed that 38.3% of cases had malarial hepatopathy, which is consistent with other prior studies showing significant hepatic involvement in falciparum malaria cases. The results of the study showed that approximately one-third (34%) of people with malarial infections had hepatic impairment. This age group (25–35 years old) was the most frequently impacted by hepatic impairment (37%). Compared to 31% of males, 39% of females had hepatic dysfunction. The minimal duration of illness was 5-8 days, and 36% of the patients had hepatic impairment. Numerous studies have demonstrated

that malaria falciparum might have an impact on the liver.^{20,21}

Two examples of severe jaundice that resulted from a combination of hemolysis and hepatic damage caused by falciparum malaria were examined in a case study. Some writers have contested the idea of "malarial hepatitis," claiming that falciparum malaria did cause hepatic dysfunction that resulted in severe jaundice in their patients, as shown by the raised transaminases and liver histology.²²

CONCLUSION:

In conclusion, although it is more prevalent and severe in falciparum malaria, hepatic dysfunction is extremely common in the former. Hepatic dysfunction patients are more likely to experience complications and mortality. Understanding this entity is crucial for prompt and effective treatment in malaria-endemic areas. Disproportionate hyperbilirubinemia combined with only a slight increase of liver enzymes in a patient exhibiting fever and jaundice may help distinguish these symptoms from viral hepatitis.

ACKNOWLEDGMENT: We extend our sincere gratitude to our esteemed co-authors whose dedicated contributions were pivotal in shaping this manuscript.

CONFLICT OF INTEREST: NIL

FUNDING: NIL

ETHICAL DECLARATION:

Approval was obtained from the ethical review committee of the hospital. [NO. LUMHS/REC/-687]

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