Original Article

Association of Age, Gender, and Duration of Illness with Hepatic Dysfunction in Patients with Malaria

Muhammad Saqib ur Rehman[1], Adil Khan[1], Ali Shan[1], Jamal Ara[2], Saleem Ullah Abro[3] and Masooda Fatima[1]

ABSTRACT

Objective: To determine the association between age, gender, and duration of illness with hepatic dysfunction in patients with malaria.

Study Design: Observational / cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Medicine in Baqai Medical University Fatima Hospital, Karachi from February to July 2021.

Materials and Methods: A non-probability consecutive sampling technique was used to collect data. A sample of 255 is taken by using Open Epi software with age of patient's ranges from 25-65 years with either gender. Patients with having fever >1040F for more than four days with chills and rigors and positive Malarial parasite tests were included. Patients with liver cirrhosis, and unexplained hepatomegaly were excluded. The blood samples were collected and sent to the pathology laboratory for biochemical analysis. Data were entered and analyzed in SPSS version 16.0. Mean and standard deviations were calculated for the quantitative variables (like age of the patient and duration of illness). Frequencies and percentages were calculated for the qualitative variables (gender, age groups, duration categories, and hepatic dysfunction).

Results: A total of 255 diagnosed patients of malarial infection with a mean age of 38.87 ± 9.94 years were included. There were 185 (72.5%) males and 70 (27.5%) females. Hepatic dysfunction was found in 85 (33.3%) patients with malaria. Only duration of illness showed significant association ($p<0.03$) with hepatic dysfunction, while the different age groups, gender did not showed significant association.

Conclusion: In our study results, only duration of illness showed significant association ($p<0.03$) with hepatic dysfunction.

Key Words: Hepatic dysfunction, malaria, age

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INTRODUCTION

According to World Health Organization's (WHO) World Malaria (infectious disease caused by mosquito) Report 2020, there was an estimate of 229 million diagnosed cases of malaria and 409,000 malarial multi-systemic failure induced deaths reported worldwide in 2019 with an incidence of 57 per 1000 population at risk and a mortality rate of 10 per 100,000 population at risk.[1]

[1.] Department of Medicine, Fatima Hospital, Baqai Medical University, Karachi.
[2.] Department of Medicine, KMDC, Karachi.
[3.] Department of Physiology, Baqai Medical University, Karachi.

Correspondence: Dr. Saleem Ullah Abro, Assistant Professor, Department of Physiology, BMU,/CMO in CHK Karachi.
Contact No: 0333-7541063
Email: drsaleemullah@baqai.edu.pk

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According to Pakistan Annual Malaria Report 2019, there were 374,513 malaria cases reported during the year with 84% Plasmodium vivax (tertian fever) cases and 15% Plasmodium falciparum cases.[2]. Pertinent to malaria pathology is intravascular hemolysis. Moderate to severe hemolysis (breakdown of red blood cells or erythrocytes) renders a patient susceptible to systemic complications and may result in organ damage or multi organ failure – including kidneys (heamoglobinurea), liver (hepatomegaly, jaundice), spleen (splenomegaly), lungs, vessels, brain (convulsions or cerebrovascular accidents or CVA, altered level of consciousness), blood (hemolytic anemia or Hemoglobinb level <7.0 g/dL, thrombocytopenia or platelets <150,000 /μL) and gastrointestinal tract involvement (vomiting, loose motions).[3] Plasmodium falciparum has more commonly been associated with hepatic dysfunction leading to jaundice (increased bilirubin level above normal; >1 mg/dL) and raised liver enzymes (SGPT or ALT) secondary to intravascular hemolysis or breakdown of red blood cells (erythrocytes). The evidence regarding other mechanisms of liver injury in malaria is also evolving.[4]. These include granuloma formations, cholestasis, malarial pigmentation, and Kupffer cell

hyperplasia.[5] Hyperbilirubinemia is a pathological condition in which serum bilirubin concentration more than 3 mg/dL in plasma, and serum aminotransferase level also increased above thrice in blood or elevated aminotransferases (alanine aminotransferase ALT levels >39 U/L). This condition is considered as liver or hepatic involvement/ hepatopathy in malaria. It is further associated with complications such as shock, acute renal injury or Renal dysfunction in which creatinine i-e >1.5 mg/dL and Blood urea nitrogen i-e >40 mg/d levels, and cerebral malaria.[6] Plasmodium falciparum induced hepatocellular jaundice or malarial hepatitis causes severe illness with higher incidence of complications with poor outcome or poor prognosis. Plasmodium falciparum is associated with cyto-adherence of parasitized red blood cells or erythrocytes (RBCs) to the endothelium of vessels, and platelets induced agglutination. This was observed by Murthy et al. Malarial induced hepatocellular jaundice or hepatopathy in mild cases (flue like symptoms) presents with headache, fever with chills, fatigue or muscle pain and vomiting or abdominal discomfort and this presentation of patients resembles with viral infection or gastroenteritis or sepsis. It was observed in more severe cases, patients can present with jaundice (increased bilirubin level more than 3mg/dl or hyperbilirubenemia), altered level of consciousness (ALOC), and kidney injury. Fever, anemia, jaundice, hepatomegaly, and splenomegaly are core clinical findings in patients. Management is focused primarily on the malarial parasite (according to endemic sensitivity pattern) and hepatitis subsides as the organism clears from the system. These patients are more prone to other systemic complications or various organs failure – hypoglycemia, thrombocytopenia, and renal failure.[6,7.] Literature has reported variable frequencies of hepatic dysfunction in these patients ranging from 32%–37% in adults in one review article.[8]. In a landmark study by Murthy et al., 62% of patients with falciparum malaria had jaundice, and 21% malarial hepatitis.[9] This study aimed to determine the Association of age, gender, and duration of illness with hepatic dysfunction in patients with malaria.

MATERIALS AND METHODS

This study was done at Fatima hospital (medicine department) of baqai Medical University Karachi. It was observational cross-sectional study, from February to July (six months) was duration of study, and the sample size of study was calculated by using Open Epi software version 3.01 taking the margin of error as 5%, confidence level 95%, and estimated prevalence from the literature as 21%, which came out to be 255. [9] Written informed consent was taken from the admitted patients after having permission from the Ethics Committee of Baqai medical university, Karachi with reference no: BMU-EC/01-2021. A non-probability consecutive sampling technique was used to collect data from admitted patients of 25-65 years of age presenting with illness suggesting malaria i.e. having fever $>104^0$F for more than four days with chills and rigors and positive Malarial parasite immuno-chromatographic test (MP-ICT). Patients with liver cirrhosis, portal hypertension, unexplained hepatomegaly, ascites , history of alcoholism, history of taking hepatotoxic drugs, history of positive viral markers for hepatitis (A, B, and C), blood film negative for malaria (even if having clinical features of malaria) were excluded. Patients having other causes of deranged liver function tests like dengue, sepsis, liver abscess, typhoid, and leptospirosis were also not taken into consideration. A brief history of the duration of illness was taken. The samples of blood were collected from admitted and enrolled patients with malaria of this study in a sterile manner for liver functions test (serum transaminase and bilirubin levels). The collected samples were sent to the pathology department and laboratory of Fatima hospital for biochemical analysis. The findings of variables were entered in a self-designed proforma and information saved. Patients were diagnosed with having hepatic dysfunction if there is a rise in serum alanine aminotransferase level (ALT) >100 IU and Jaundice or hyperbilirubinemia >3 mg/dL. Patients Age were categorized into groups like 25-35 years, 36-45 years, 46-55 years, and 56-65 years, while the duration of illness was grouped as 5-8 days, 9-12 days, and 13-16 days. The collected data was entered in computer and statistical analysis was done by using SPSS version 16.0® Mean and standard deviations were calculated for the age of the patient and duration of illness (quantitative variables). Frequencies and percentages were calculated for the gender, age in different groups, duration of disease into categories, and hepatic dysfunction (qualitative variables). Stratification according to age groups, gender, and duration of illness to see the effect of these on the outcome variable i.e. hepatic dysfunction. Post-stratification, the chi-square test was applied and a p-value of ≤ 0.05 was considered as statistically significant, and p-value of >0.05 was considered as statistically non-significant.

RESULTS

A total of 255 diagnosed patients of malarial infection with a mean age of 38.87 ± 9.94 years were included. The mean duration of illness was 7.22 ± 2.55 days. There were 185 (72.5%) males and 70 (27.5%) females as shown in table I. Hepatic dysfunction was found in 85 (33.3%) patients with malaria. When it was assessed according to the age groups, gender, and duration of illness, only the latter came out to be statistically significant ($p<0.03$). Stratification for gender showed that 57 (30%) of males and 28 (40%) of females developed hepatic dysfunction as shown in table 2.

Distribution according to different age groups and duration of illness is given in Figures 1 and 2.

Table No.I: Demographic profile of the participants.

Variables	Mean	±SD
Age (years)	38.87	±9.94
duration of illness (days)	7.22	± 2.55

Table No.2: Association of age, gender, and duration of illness with hepatic dysfunction in patients with malaria.

Varia-bles	Hepatic (liver) Dysfunction		Total	P-Value
	Yes (with)	No (without)		
Age (in years)				
25-35	39(36%)	69(64%)	108(100%)	0.65
36-45	30(34%)	57(66%)	87(100%)	
46-55	10(26%)	28(74%)	38 (100%)	
56-65	06(27%)	16(73%)	22 (100%)	
Gender				
Male	57(30%)	128(70%)	185(100%)	0.164
Female	28(40%)	42(60%)	70(100%)	
Duration of illness (in days)				
5-8	65(37%)	109(63%)	174(100%)	
9-12	17(30%)	39(70%)	56(100%)	
13-16	03(12%)	22(88%)	25(100%)	

p-value< 0.05-statistically significant

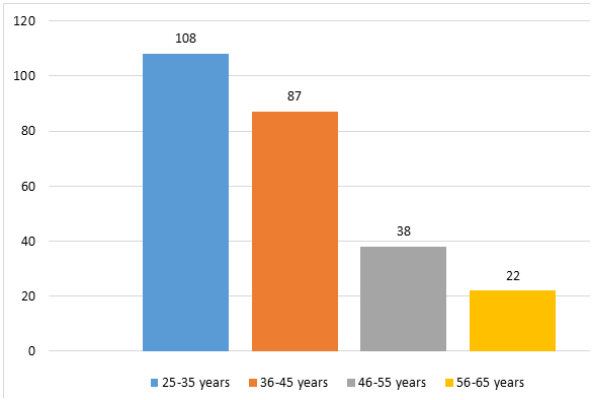

Figure No.1: Distribution according to age groups (n=255)

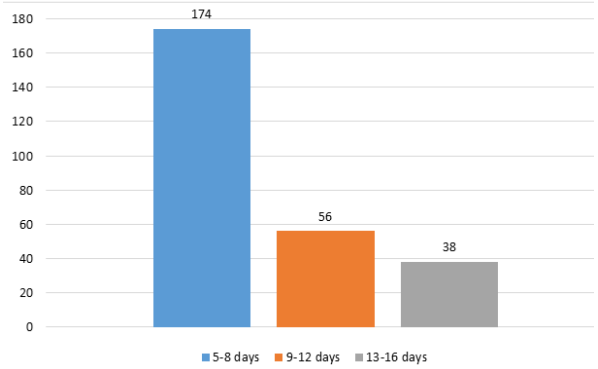

Figure No.2: Distribution according the duration of illness (n=255)

DISCUSSION

Malaria has remained a major public health though out the world and responsible for causing morbidity or mortality in malarial patients, especially in tropical sub-Saharan African and Eastern Mediterranean regions as reported by world health organization (WHO). Even with a substantial focus on preventive and curative programs, malaria still forms a significant chunk of the global infectious disease burden in terms of causing disability and deaths in malarial sufferers. [1] Along with the involvement of other systems, hepatic involvement and hepatic dysfunction are commonly observed in malarial sufferers with moderate to severe malaria with different complications like decreased serum sugar level or hypoglycemia, pH disorder like metabolic disorder, and multi-organ failure (MOF). The severity of malaria can be predicted by parasite species, duration of illness, and time of onset of antimalarial treatment.[10]. Literature pertinent to the incidence of hepatic dysfunction and jaundice in severe malaria is variable owing to the difference in geographic location, age, the status of malarial endemicity, and coexistence with other infections endemic to that region.[11,12] The results of this study indicated that almost one-third of patients (33%) with malarial infection was complicated with hepatic dysfunction. The youngest age group (25-35 years) suffered from hepatic dysfunction most frequently (36%). As far as gender was concerned, 40% of women suffered from hepatic dysfunction as compared to 30% of men. Patients with the shortest duration of illness (5-8 days) suffered from hepatic dysfunction most frequently (37%). Literature has shown extensive evidence of hepatic involvement with malaria falciparum.[13-14] Chawla et al. showed that 45% of patients with malaria had elevated serum bilirubin and 22% had elevated serum transaminases.[13] Anand et al. showed that as many as 33% of their malaria patients had elevated serum bilirubin. [15] Singh et al., in their work, showed 13% of malaria patients with serum transaminases more than thrice of the normal range.[15] Ahsan et al., in their work, showed that 46% developed jaundice and 57% had serum bilirubin severely raised (>10mg/dl).[16] There has been no significant difference in age of patients in terms of hepatic complications in malaria, however, literature has reported cases to be older than controls. As with our study, the gender differences were opposite with more females being diagnosed with malarial hepatopathy. Although the reasons remain unclear, most literature, especially from India, has reported a higher incidence of malarial induced hepatic dysfunction in males as compared to females.[17,18] According to our study results, the age of the patients and gender based comparison did not showed significant (p>0.05) association with hepatic dysfunction (yes or with and without or no Liver function test abnormalities) in patients with malaria.

Like our results, similar findings were observed in study, which is done by I.J. Reuling et al.[10] The pathophysiological basis for hepatic dysfunctioning in malarial patients is due to systemic inflammation (pro-inflammatory response and anti-inflammatory response) in liver hepatocytes, and ultimately injury occurs in liver cells. The oxidative stress is associated with inflammation, and develops liver injury. The inflammatory process and oxidative stress are causing malfunctioning of the host's mitochondria and hepatocyte apoptosis. It plays a vital or potential role in developing (pathogenesis) severe disease due to uncomplicated malaria in liver.[10] The Duration of illness (in days) of the admitted patients showed significant ($p<0.05$) association with hepatic dysfunction (yes or with and without or no Liver function test abnormalities) in patients with malaria. Like our results, similar findings were observed in study.[19] Hepatic involvement in malaria is a common entity. It may even present in an earlier course of illness. Therefore, it becomes critical to evaluate patients of malaria for hepatic dysfunction even in the early course of illness. Early screening, timely investigations, and interventions are very crucial in ensuring a good disease outcome and for prevention or decrease in mortality rate and multi-organ failure (MOF).[5,19,20] This limitation of this study is single centered study and limited number of admitted patients. It is recommended that study should be multi-centered and number should be increased.

CONCLUSION

In our study results, only duration of illness showed significant association ($p<0.03$) with hepatic dysfunction. Hepatic dysfunction in malaria is a common complication and as many as one-third of patients may present with it. In malaria-endemic areas, it is essential for managing physicians to consider hepatic complications even in the early course of illness.

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Author's Contribution:

Concept & Design of Study:	Muhammad Saqib ur Rehman
Drafting:	Adil Khan, Ali Shan
Data Analysis:	Jamal Ara, Saleem Ullah Abro, Masooda Fatima
Revisiting Critically:	Muhammad Saqib ur Rehman, Adil Khan
Final Approval of version:	Muhammad Saqib ur Rehman, Saleem Ullah Abro

Conflict of Interest: The study has no conflict of interest to declare by any author.

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