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Original Article

Age, Gender and Length of Illness's Relation with Hepatic Dysfunction in Individuals Having Malaria: A Cross-sectional Study

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ABSTRACT

With almost 200 million medical cases occurring each year, malaria is the most common vector-borne disease worldwide. **Objective:** To ascertain the relationship of hepatic dysfunction with age, gender, and length of illness in individuals with malaria. **Methods:** Data were gathered using a non-probability consecutive sampling method. A total of 270 patients are selected for a sample using the Open Epi program, ranging in age from 25 to 65 and of either gender. Patients who tested positive for malarial parasites and had fever >104°F for longer than 4 days accompanied with chills, and rigors were selected. Patients with undiagnosed hepatomegaly and hepatic cirrhosis were excluded. Samples of blood were gathered and delivered to the pathology lab for biochemical evaluation. SPSS version 16.0 was used for data entry and analysis. For the numerical variables (such as age of the patients and disease duration), means and standard deviations were computed. The subjective variables (gender, age groups, length divisions, and hepatic dysfunction) were evaluated as percentages and frequencies. **Results:** A total of 270 individuals with confirmed cases of malaria were examined, having a mean age of 39.97 $\pm$ 8.91 years. There were 70 (27.5%) women and 185 (72.5%) men. A total of 100 (37.3%) individuals with malaria had hepatic impairment. The only factor that significantly correlated (p0.03) to hepatic dysfunction was the length of the illness, whereas gender and various age categories did not. **Conclusions:** Only the length of the illness revealed a strong relationship between malaria and hepatic dysfunction in our research's findings (p 0.03).

INTRODUCTION

With almost 200 million medical cases occurring each year, malaria is the most common vector-borne disease worldwide [1]. Every year, 0.6 million infant and pregnant fatalities are attributed to malaria [2]. Worldwide, there are now 214, 217, and 219 million occurrences of malaria, up from 2015, 2016, and 2017, correspondingly [3-5]. Every year, 3.5 million probables and verified cases of malaria are reported. The newest WHO study on malaria revealed that the estimated number of infections were 241 million and 627 000 deaths from the disease globally year 2020 [6]. This amounts to 69 000 more fatalities and approximately 14 million greater occurrences in 2020 relative to 2019. Inadequate malaria control, diagnosis, and management during the pandemic were responsible for about 27% of these excess deaths (47 000). Intravascular hemolysis is relevant to the pathogenesis of malaria. A patient is more vulnerable to systemic consequences with mild to extreme hemolysis (the breakdown of red blood cells or erythrocytes), which can lead to organ impairment or multi-organ failure. Jaundice (a spike in bilirubin level

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beyond usual; >1 mg/dL) and elevated liver enzymes as a result of intravascular hemolysis or the disintegration of red blood cells have been more frequently linked to Plasmodium falciparum. The proof for additional liver damage pathways related to malaria is also changing [7]. These include Kuepfer cell hyperplasia, cholestasis, malarial coloring, and granuloma forms [8]. A medical condition known as hyperbilirubinemia occurs when the serum bilirubin content is greater than 3 mg/dL in the plasma and the serum aminotransferase amount is also raised. This disease is regarded as hepatopathy or liver or hepatic involvement in malaria. Additional problems include cerebral malaria, shock, acute renal damage, or renal failure including blood urea nitrogen values above 40 mg/d and creatinine values above 1.5 mg/dL [9]. Malarial hepatitis or hepatocellular jaundice caused by Plasmodium falciparum is a serious illness with a greater frequency of abnormalities and a bad prognosis [10]. Malaria's evolution exemplifies our inability to tackle global outbreaks because it continues to pose the biggest danger to public healthcare, economic progress, and growth in a number of developing nations [11]. Five Plasmodium species, including P. vivax, P. falciparum, P. ovale, P. malaria, and P. knowlesi, are responsible for human malaria (zoonotic infection) [12]. Malaria has resurfaced as a severe health issue in Asia despite the extensive and expensive measures used to eliminate it over many years. A total of 60% of people reside in areas where malaria is prevalent. Plasmodium vivax accounts for 81.3% of malaria cases, P. falciparum for 14.7%, and mixed species account for 4%. Cytoadherence of parasitized red blood cells, or erythrocytes (RBCs), to the endothelium of arteries and platelet-induced agglutination, are both symptoms of Plasmodium falciparum infection [13]. Malaria-induced hepatocellular jaundice/ hepatopathy manifests as flu-like signs such as headaches, fever accompanied by chills, exhaustion, muscle pain, nausea, or stomach pain, and this patient's appearance is similar to those of viral infections, gastroenteritis, or sepsis. Jaundice (an elevated bilirubin level greater than 3 mg/dl or hyperbilirubinemia), can cause an abnormal state of consciousness, and renal damage in more extreme cases. Individuals typically exhibit fever, anemia, jaundice, hepatomegaly, or splenomegaly as their main clinical symptoms. As per endemic sensitivity patterns, management focuses mainly on the malarial parasite, and hepatitis diminishes when the organism leaves the body. Hypoglycemia, thrombocytopenia, as well as renal failure, are among the main systemic problems or organ failures that these individuals are more likely to experience [14]. In one study, it has been noted that there are varying proportions of hepatic dysfunction in these individuals, ranging from 32% to 37% in adults [15]. The purpose of this research was to examine the relationship between hepatic dysfunction in malaria patients and their age, gender, and length of illness.

METHODS

After receiving authorization from the Ethics Committee, written informed consent was obtained from the 270 admitted individuals. Data were gathered from hospitalized patients between the ages of 25 and 65 who had symptoms suggestive of malaria, such as a temperature over 104°F for longer than 4 days accompanied by chills, and rigors, as well as a positive malaria pathogen immune chromatographic test (MP-ICT). Individuals having liver cirrhosis, portal hypertension, unknown hepatomegaly, ascites, a history of alcohol abuse, a background of using hepatotoxic drugs, a record of positive viral markers for hepatitis, and blood films negative for malaria (even though they displayed clinical symptoms of malaria) were exempted. Patients with other conditions such as dengue, sepsis, liver infection, typhoid, or even leptospirosis were also not considered. An overview of the patient's medical background was obtained. For the liver function tests (serum transaminase and bilirubin levels), blood samples were sterilely taken from the hospitalized and recruited malaria patients in this research. The hospital's pathology division and laboratory received the samples which are recorded for biochemical examination. Variable results were recorded and data were kept in a self-designed manner. When the level of the enzyme alanine aminotransferase in the serum rises, patients are labelled as possessing hepatic dysfunction (ALT)>100 IU with hyperbilirubinemia or jaundice >3 mg/dL. Patients' ages were divided into ranges, such as 25-35, 36 to 45, 46 to 55, and 56 to 65 years old, while the length of the disease was categorized as 5-8 days, 9-12 as well as 13–16 days. The information gathered was recorded utilizing computers and statistical software, Version 16.0 of SPSS. Age of the individual and length of illness was determined as means and standard deviations (quantitative variables). As for the gender, age in various groupings, length of illness into divisions, and hepatic dysfunction, frequencies and percentages were computed (qualitative variables). Segmentation by age, gender, and length of illness to determine how these factors affect the final variable, hepatic dysfunction. The chi-square test was used after stratification, and a p-value of 0.05 or less was regarded as statistically important, while a p-value of more than 0.05 was regarded as statistically non-significant.

RESULTS

A total of 270 individuals with malarial infection who had been diagnosed were considered, with a mean age of 39.97

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+ 8.91 years. The average number of days spent unwell was 6.23 + 3.35. According to the table I, there were 68 (25.5%) women and 202 (74.8%) men. A total of 100 (37.3%) patients with malaria had hepatic impairment. Only the length of the disease emerged as statistically important when it was evaluated according to age groups, gender, and other factors.

Variables	Mean ± SD
Age (years)	39.97±8.91
Length of illness (days)	6.23±3.35

Table 1: Demographic profile of the participants

Table 2's gender stratification results revealed that 25 (39%) of females and 69 (31%) of males experienced liver dysfunction.

Variables	Hepatic dysfunction		Total	P-value
	Yes	No		
Age (Years)				
25-35	45 (37%)	70 (63%)	115 (100%)	0.50
36-45	39 (33%)	56 (66%)	95 (100%)	
46-55	11 (27%)	29 (73%)	40 (100%)	
56-64	05 (26%)	15 (74%)	20 (100%)	
Gender				
Male	69 (31%)	133 (69%)	202 (100%)	0.12
Female	25 (39%)	43 (61%)	68 (100%)	3
Length of illness (days)				
5-8	66 (36%)	113 (64%)	179 (100%)	
9-12	19 (31%)	42 (69%)	61 (100%)	
13-16	06 (11%)	24 (89%)	30 (100%)	

Table 2: Age and gender stratification results of study participants

Figure 1 reveals disease distribution according to various age groups.

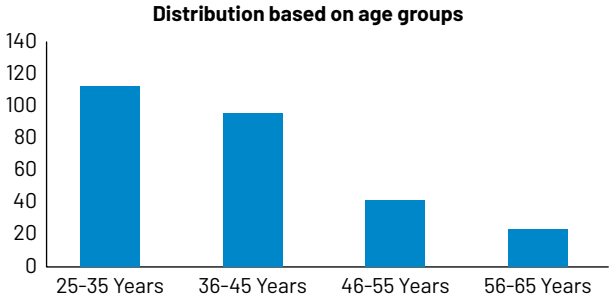

Figure 1: Distribution based on age groups n=270

Figure 2 reveals disease distribution according to a length of illness.

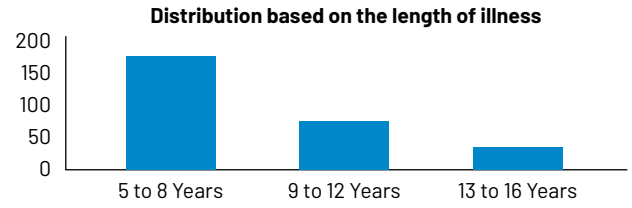

Figure 2: Distribution based on the length of illness n=270

DISCUSSION

Malaria continues to be a serious public health concern throughout the world, where it is to blame for the illness or death of malaria patients [16]. It is especially prevalent in tropical sub-Saharan-African and Eastern Mediterranean regions as reported by the world health organization (WHO). Despite a sizable emphasis on preventative and curative measures, however, malaria still accounts for a sizable portion of the load of infectious diseases worldwide in terms of it resulting in disability and mortality among malaria patients [17]. Hepatic complications and dysfunction are frequently seen in malaria patients with medium to severe malaria in addition to the engagement of other systems. These patients may also experience difficulties like lowered serum sugar levels (hypoglycemia), pH disorder similar to a metabolic disorder, as well as multi-organ failure (MOF). The type of parasite, length of the disease, and when antimalarial medication first started can all be used to forecast the intensity of malaria [18]. Due to differences in geographic area, age, malaria endemicity condition, and cohabitation with other illnesses indigenous to that area, there is a wide range of information in the literature about the prevalence of hepatic dysfunction and hepatitis in acute malaria [19]. According to the study's findings, hepatic impairment affected roughly one-third (34%) of individuals with malarial infections. The most often affected age cohort (25–35 years) by hepatic dysfunction was this one (37%). Hepatic dysfunction affected 39% of females relative to 31% of males. Hepatic dysfunction occurred in 36% individuals with the minimum illness length 5-8 days. There is a lot of evidence in the literature that malaria falciparum can affect the liver [20]. According to one study, 21% and 4% of malaria infected individuals had high serum transaminases and 4% had raised serum bilirubin [21]. According to another study, up to 34% of the malaria victims had increased serum bilirubin. In their study, Singh et al. found that 14% of malaria patients had serum transaminases that were more than thrice the usual limit [22]. Another study they conducted revealed that 56% of patients had significantly elevated blood bilirubin levels (>10 mg/dl) and that 55% of patients acquired jaundice [23]. Regarding hepatic consequences from malaria, there hasn't been a noticeable variation in ages of the patients; however, instances have been noted in the literature to be older than control. The gender disparities were contrary, as they were in our research, with more females receiving a diagnosis of malarial hepatopathy. The majority of the literature particularly from India has noted that men are more likely than women to experience malaria-induced hepatic dysfunction, albeit the causes are yet unknown [24]. The age of the participants and gender-based contrast did not

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demonstrate a substantial (p>0.05) relationship with hepatic dysfunction in infected individuals, according to our study's findings. The underlying pathophysiology of hepatic dysfunction in patients affected with malaria in the hepatocytes is result of systemic inflammation (pro inflammatory response and anti-inflammatory reaction) which ultimately injures the liver. The relationship between oxidative stress and liver harm develops due to inflammation. The oxidative stress and inflammation are the main culprits of mitochondrial dysfunction in the host and apoptosis of hepatocytes. It has a strong or prospective impact on serious disease (pathogenesis) occurring as a result of simple hepatic malaria. Hepatic dysfunction was significantly (p 0.05) correlated with the length of illness (measured in days) of the selected patients who had malaria. Similar outcomes to ours were seen in one study. Malaria frequently involves hepatic involvement. It might even show very early on in the illness. Therefore, it is crucial to check for hepatic dysfunction in infected patients even in the early stages of the disease. Early detection, prompt investigations, and therapies are essential for preventing or reducing death rates and multi-organ failure, as well as for guaranteeing a positive disease outcome (MOF). The single-centered study design and small quantity of selected patients are this study's limitations. It is advised that the study should be multi-centered hence its scope be broadened.

CONCLUSIONS

In our study only the length of the illness in malaria revealed a strong correlation with hepatic dysfunction. One-third of infected individuals may exhibit hepatic impairment, which is a frequent consequence. It is crucial for treating doctors in malaria-endemic regions to take hepatic problems into account even in the initial stages of the illness.

Conflicts of Interest

The authors declare no conflict of interest.

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