Section: Pathology

Original Research Article

A STUDY ON MALARIAL HEPATOPATHY AMONG PATIENTS WITH FALCIPARUM MALARIA

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Abstract

Background: Malaria impose a major health challenge in many parts of the world. Jaundice is usual accompaniment of malaria. There are reports of a continuum of hepatic dysfunction ranging from those describing liver failure as a side effect of falciparum malarial infection to those describing modest derangements of liver function tests. Present study was aim to evaluate the clinical, biochemical and ultrasonographic changes in patients with falciparum malaria with jaundice. **Materials and Methods:** Total 42 patients having falciparum malaria with jaundice were recruited in this study. Detailed medical history, clinical examination, biochemical parameters for liver function tests and blood tests for hepatitis B and hepatitis C were done in all patients. **Result:** Hepatopathy occurred in 35% of patients with falciparum malaria and jaundice. It is a heterogenous syndrome with at least two clinical subsets. **Conclusion:** Malarial hepatopathy is associated with severe dysfunction of other organs. Patients presenting with cerebral malaria can be misdiagnosed as fulminant hepatic failure, therefore, need to be diagnosed carefully.

INTRODUCTION

In many regions of the world, malaria continues to be a serious health issue. Humans get malarial parasites from female anopheles' mosquitoes. The liver is crucial to the life cycle of the malarial parasite and can be severely harmed in some situations. Although hemolytic jaundice is a typical side effect of malaria, reports of a variety of hepatocellular dysfunction, from moderate changes in liver function tests to those reporting liver failure as a falciparum malarial infection consequence, have been made.[1-3] According to several old articles, liver illness has been linked to malaria for more than a century.[4] The host-mosquito-host cycle of avian malaria was clarified by Ronald Ross in 1898.[5] The fact that malarial parasites invade and grow in liver hepatocytes was originally identified in 1948.[6]

The liver is affected in two stages in the life cycle of the malarial parasite [Figure 1]. Initially the pre-erythrocytic cycle and then in the erythrocytic phase. The clinical symptoms of malaria are a result of the erythrocytic phase. The sporozoite, an invasive type of malarial parasite, is injected into the dermis when a female Anopheles mosquito bites a human host. These sporozoites infect the hepatocytes after travelling through the bloodstream to the liver. The sporozoite proceeds through schizogony in the hepatocytes to create a schizont, which then splits to create tens of thousands of merozoites. Despite having no apparent impact on its function, the liver experiences schizogony. Merozoites are released into the bloodstream by the rupture of an infected hepatocyte, where they infiltrate red blood cells to start the erythrocytic phase.[7] The infection is maintained by the merozoites' ability to replicate inside parasitized RBC to create new merozoites that burst from the RBC and invade fresh RBC. The gametocytes of a few merozoites can be classified as male or female. These gametocytes are consumed by a feeding mosquito, where they are fertilized in the midgut to create a zygote, which then develops into an ookinete, which then reproduces into hundreds of sporozoites. Sporozoites go to a mosquito's salivary

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glands. The cycle is continued when the mosquito bites a different human host.[8]

The diagnosis of malarial hepatopathy is made when P. falciparum infection is present, transaminase levels have increased by at least thrice, whether or not there is conjugated hyperbilirubinemia, and there is no clinical or serological indication of viral hepatitis. There is a lack of information on malarial hepatopathy on a worldwide scale, thus research of this kind will be helpful in revealing the severity and consequences of the condition so that early interventional measures may be taken.[9] In view of the above, present study was conducted to evaluate clinical, biochemical and ultrasonographic changes in patients with falciparum malaria and jaundice.

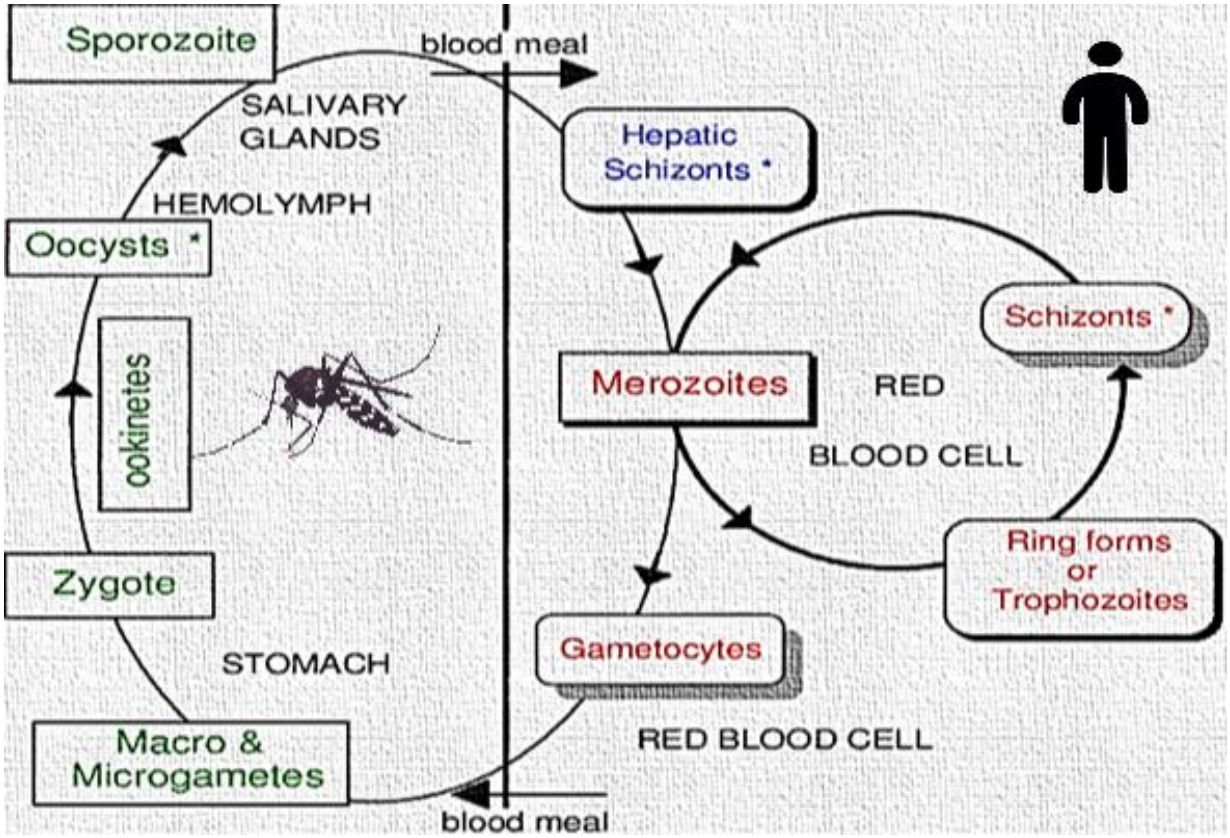

Figure 1: Malarial life cycle with two phases occurring in mosquito and human.

MATERIALS AND METHODS

Study design: Total 42 patients with peripheral blood film evidence as well as positive for falciparum malaria on malaria antigen test who had jaundice were included in the study. Based on their medical history, pertinent clinical examinations, and other investigations, patients with evidence of Plasmodium vivax infection or other liver diseases (such as viral hepatitis, cirrhosis of the liver, portal hypertension, amoebic liver abscess, unexplained hepatomegaly, ascites, a history of alcoholism, a history of using hepatotoxic drugs, or a history of jaundice) were excluded.

Biochemical investigations: Complete blood counts, peripheral blood films for RBC morphology, 6-9 thick and thin blood films for malarial parasites, bleeding time, clotting time, prothrombin time, total serum bilirubin, conjugated and unconjugated bilirubin, and serum AST and ALT levels were among the tests performed on all patients. Urobilinogen, bile pigment, and bile salt were all tested in the urine.

All patients had blood tests for leptospirosis, hepatitis A, B, C, and E, as well as blood testing for blood culture and sensitivity. Comprehensive serological tests were performed to rule out the potential of acute viral hepatitis. These tests included IgM anti-hepatitis A virus (IgM anti-HAV), hepatitis B surface antigen (HBsAg), IgM anti-hepatitis B core antibody (IgM anti-HBc), and IgM anti-hepatitis E virus antibody (IgM anti-HEV).

Ultrasonography: A thorough ultrasound was performed to examine the liver's size and echotexture as well as to look for abnormalities in the gallbladder, intrahepatic or extrahepatic biliary ducts, and symptoms of portal hypertension. The presence of Plasmodium falciparum infection, a minimum three-fold increase in transaminases (especially ALT), shown in two samples taken 24 hours apart, with or without conjugated hyperbilirubinemia, absence of clinical or serological evidence of viral hepatitis, and

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response to anti-malarial therapy were used to diagnose malarial hepatopathy.

RESULTS

Age of the patients ranged from 15 to 51 years. All patients had fever, icterus. Pallor was present in 65%, hepatomegaly in 28%, splenomegaly in 7% and impaired consciousness in 15 % patients [Table 1].
Serum bilirubin levels ranged from 3.5 to 25 mg%. ALT levels ranged from 22 to 880 IU /l. AST levels ranged from 24 to 1180 IU /l. INR ranged from 1 to 1.13 [Table 2].

Ultrasonography showed hepatomegaly with decreased echogenicity of liver in 12 (35%), splenomegaly in in 29 (71%) and both hepatomegaly and splenomegaly in 5 (12%) of patients (Table 3).
Gallbladder wall thickness was increased in 4 (9.5%) of patients. There was no evidence of biliary dilatation. 20 (48%) of the patients had predominantly conjugated or mixed hyperbilirubinemia and serum transaminases were more than three times normal. After viewing peripheral blood smear under microscope, multiple thin, delicate rings of plasmodium falciparum seen inside the infected RBC's along with the gametocytes [Figure 2].

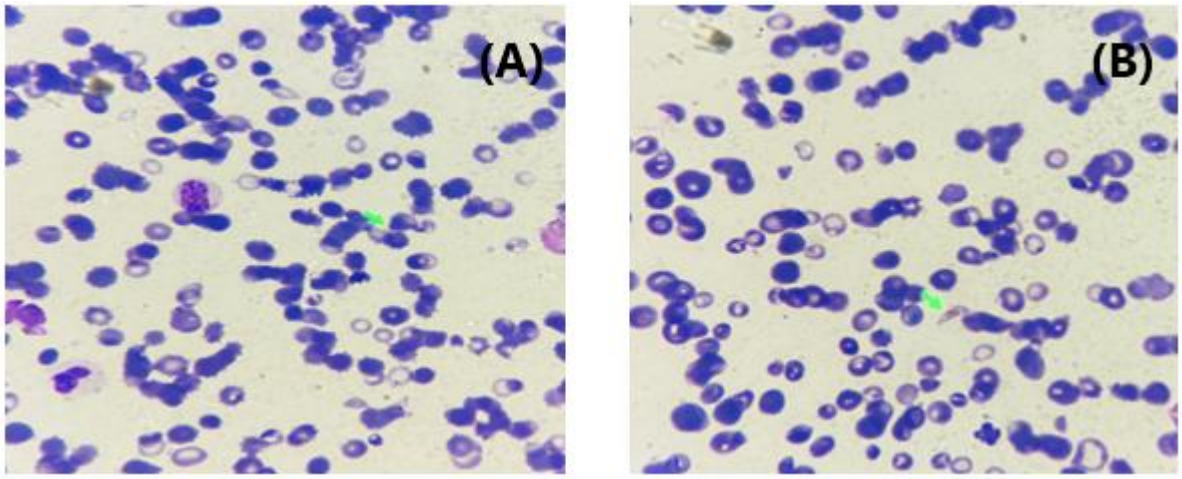

Figure 2: (A) Multiple thin, delicate rings of Plasmodium Falciparum seen inside the infected RBC's. Ring shows 1 to 2 chromatin dots. (B) Gametocytes of Plasmodium Falciparum (Oil immersion - 1000X).

Table 1: Clinical parameters of the patients.

Clinical parameters	N (%)
Fever	All (100%)
Icterus	All (100%)
Pallor	27 (65%)
Hepatomegaly	12 (28%)
Splenomegaly	30 (70%)
Impaired consciousness	6(15%)

Table 2: Biochemical parameters of the patients.

Biochemical parameters	Range
Serum Bilirubin	3.5 to 25 mg%
ALT	22 to 880 IU/l
AST	24 to 1180 IU/l
INR	1 to 1.13

Table 3: Ultrasonography findings of the patients.

Ultrasonography Parameter	N (%)
Hepatomegaly	12 (35%)
Splenomegaly	29 (71%)
Hepatomegaly and splenomegaly	5 (12%)

DISCUSSION

Falciparum malaria's hepatic dysfunction may have several causes. Hepatocellular dysfunction, disseminated intravascular coagulation (DIC), or intravascular hemolysis might be the culprits. In falciparum malaria hepatocellular jaundice should be referred to as malarial hepatopathy rather than malarial hepatitis.[10]
If a patient meets the following criteria, they can be diagnosed with malarial hepatitis.
i) Laboratory evidence of P. falciparum shown ii) Two consecutive blood samples obtained more than 24 hours apart showed at least a three-fold increase in transaminases, notably ALT, with or without

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conjugated hyperbilirubinemia. iii) Lack of any clinical or serological evidence of viral or drug-induced hepatitis; iv) Clinical response to antimalarial medication; or, v) Postmortem evidence of widespread falciparum infection.[10] Falciparum malaria does not produce hepatitis, but rather a suppression of bilirubin excretion caused by endotoxemia, metabolic acidosis, the action of parasitemia on the hepatocytes, or a combination of these abnormalities. The cause of coma in a patient with cerebral malaria may be different from the cause of hepatic encephalopathy.[11]

Although significant liver illness, one of the criteria for the diagnosis of fulminant hepatic failure, has not been demonstrated on post-mortem examination, hepatocellular jaundice can develop in severe or complex malaria.[10] Most patients with malarial hepatopathy show signs of additional organ failure. A heterogeneous condition with two clinical subgroups is malarial hepatopathy. Hepatic failure might be mistaken for the fulminant clinical disease (Type A) with coma, severe jaundice, purpura, and renal failure. Patients with a relatively milder disease (Type B) simply have fever, headaches, and vomiting. Hepatocellular jaundice is an indication of severe malaria, although therapy for the disease shouldn't change under these circumstances. Even mild instances would get better with antimalarial medication. When treating falciparum malaria, Ghoda discovered that the liver function tests of 56 individuals with falciparum hepatopathy quickly returned to normal.[12] At 8 weeks and 6 months after the initial treatment, Anand et al. discovered no signs of persistent liver damage in the survivors.[13]

Like the current study, Saya et al. found that 34% of patients had clinical jaundice in addition to all patients having fever. In 13 cases, splenomegaly alone was detected by ultrasound, while hepatosplenomegaly was detected in 63 cases.[9] In the research by Shah et al., ultrasonography indicated splenomegaly in 48 (77.3%) patients, hepatomegaly in 22 (35.4%) patients, and both hepatomegaly and splenomegaly in 16 patients (25.8%). Five (8.06%) of the patients had thicker gallbladder walls. No signs of biliary dilation were present.[14] Similar results were found in present study.

The results of this hospital-based study cannot be applied to the wider public. The basic healthcare system may overlook mild cases of malarial hepatopathy because the illness pattern and complications may be different there. Due to practical limitations, liver biopsy and histology were not performed on these participants. Despite these drawbacks, the study offers useful information that the relevant healthcare system authorities may use to implement the proper interventional actions.

CONCLUSION

A sizable portion of patients with falciparum malaria and jaundice develop malarial hepatopathy. Malaria-induced hepatopathy is linked to severe organ dysfunction. It is possible to misdiagnose patients with cerebral malaria as having fulminant liver failure. To understand the causes of malarial hepatopathy and to stop the consequences and death, further research is needed. In order to lessen the burden of malarial hepatopathy and associated sequelae, secondary prevention by early detection and treatment of P. falciparum malaria is also crucial in the primary healthcare system.

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