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Clinical profile and complication of malaria hepatopathy

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Summary
Background: This study was designed to study the patient characteristics, presenting features and complications of malaria in patients with elevated liver enzymes and to compare these data to those of patients with normal liver enzymes.
Methods: A convenient sample of 100 patients with malaria was selected from three tertiary care referral hospitals. Study subjects were divided into two groups: (1) patients (controls) with normal liver enzymes and (2) patients (cases) with >3 times the normal liver enzymes in the absence of an alternate explanation for such elevation. Patient characteristics, presenting features and complications of malaria in these two groups were studied. Data were collected using a semi-structured pretested proforma and were analyzed using the statistical analysis program SPSS, version 11.5 (SPSS, Inc., Chicago, IL).
Results: The mean ages were 38.12 years for the cases and 35.20 years for the controls with a non-significant p value of 0.289. Males composed 82% of the cases that were diagnosed with malarial hepatopathy; the remaining 18% were females. Falciparum malaria was present in 56% of the cases, compared to 12% of the controls.

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Icterus was present in 66% of cases of malarial hepatopathy, compared to 32% of the controls. Of the 66% of these cases, 18.18% had serum bilirubin >3 mg%, whereas out of the 32% of the controls presenting with icterus, only 5.55% had serum bilirubin >3 mg% ($p = 0.003$). Of the cases with malarial hepatopathy, 38% suffered from hypoglycemia, compared to 0% of the controls ($p < 0.001$); 84% of the cases presented with thrombocytopenia, compared to 70% of the controls ($p < 0.001$); 12% of the cases suffered from renal failure with serum creatinine levels >2 mg%, compared to 2% of the controls ($p = 0.060$).

Conclusion: Plasmodium falciparum infection (either alone or along with *P. vivax*) is the leading cause of malarial hepatopathy. Jaundice is a common clinical manifestation among these patients. Patients with malarial hepatopathy have increased incidences of hypoglycemia and thrombocytopenia. Malarial hepatopathy occurs in relation to severe infection, most of which are treated with parenteral artesunate.

Introduction

Malaria is endemic in over 91 countries, setting at risk approximately 40% of the world population [1]. The disease accounts for 500 million clinical cases and more than a million deaths per year [2]; it is a major public health problem in developing countries and inflicts a huge health care burden in terms of morbidity and mortality [3—5].

Malarial hepatitis is characterized by hyperbilirubinemia (>3 mg/dl) and elevated transaminase enzymes of up to more than 3 times the normal levels [6]. Adherence of parasitized erythrocytes to the endothelial walls of liver capillaries leads to the blockade of intrahepatic channels, causing alterations in blood flow and, consequently, ischemia. As a result, complications such as hepatic encephalopathy, multiorgan failure and impaired protein synthesis occur. Histopathological studies have revealed hepatocyte necrosis, cholestasis, granulomatous lesions and malarial nodules [7].

According to the World Health Organization, signs of malarial hepatopathy are unusual in cases of malaria [8]. However, in recent years, signs of liver involvement have been increasingly reported in Asian countries, especially India, with a majority of cases suffering from falciparum malaria or mixed (both falciparum and vivax) malaria [8]. Cases with altered liver function tests and even fulminant hepatic failure have been reported [9,10]. A study conducted on Nigerian children concluded that the increased levels of liver enzymes are biochemical features of *Plasmodium falciparum* parasitemia [11]. However, the data on malarial hepatopathy is still sparse in the literature. This study was designed to evaluate the patient characteristics, presenting features and complications of malaria in patients with elevated liver enzymes and to compare these characteristics to those of patients with normal liver enzymes.

Materials and methods

This study was performed in three tertiary care referral hospitals in Mangalore, a malaria endemic coastal city in South India. These hospitals cater to a large number of patients with malaria. Adult patients presenting with fever who tested positive for malaria in a peripheral smear were enrolled in the study.

Inclusion criteria:

(1) The first group (controls) of patients included those suffering from malaria but who had normal liver enzymes.
(2) The second group (cases) included those patients who had elevated liver enzymes (>3 times the normal levels) due to malaria.

Exclusion criteria:

(1) Patients suffering from malaria and viral hepatitis A, B, C, D and E or viral hepatitis alone.
(2) Patients presenting with increased liver enzymes with conditions such as sepsis, drug-induced increase in liver enzymes or other similar conditions.
(3) Alcoholics.
(4) Patients <20 years old.

A convenient sample of 100 patients was considered. Institutional Ethics Committee approval was obtained at the first author's institute. Study subjects were divided into two groups as mentioned above under the inclusion criteria. They were