Original Research Article

Liver dysfunction in malaria – An observational study

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Abstract

Introduction: Malaria is associated with significant mortality and morbidity in India. Hepatic dysfunction in malaria is often under-diagnosed. Early identification of hepatic dysfunction is crucial for preventing complications.

Materials and methods: A prospective observational study was conducted in NRI Medical College and General Hospital, Chinakakani, Guntur District in Andhra Pradesh. A total of 50 patients with malaria were studied. Liver function tests were performed to assess the type of jaundice. The collected data was analysed.

Results: The incidence was P. Vivax and P. falciparum malaria were 64% and 34% respectively. The incidence of jaundice was 26%. All of them had predominantly conjugated hyperbilirubinemia. Around 14% had mixed jaundice, and 22% had hepatic jaundice. Only one case expired which had the highest level of serum bilirubin.

Conclusion: Hepatic involvement is more common among those with malaria. The incidence in vivax and falciparum malaria is comparable. Conjugated bilirubinemia with elevated liver enzymes is the most common manifestation. Early screening and identification of hepatic involvement in malaria are crucial. Initiation of treatment on time will aid in reducing mortality and morbidity.

Key words

Malaria, P. vivax, P. falciparum, Liver dysfunction.

Introduction

Malaria is an important infectious disease associated with mortality and morbidity in regions such as sub-Saharan Africa and tropical countries like India. According to the World Malaria report issued by the WHO in 2018, there were almost 219 million cases of malaria globally. India and sub-Saharan Africa contributed to 80% of the global burden of malaria [1].

Hepatic dysfunction is a feature of severe malaria mostly due to Plasmodium falciparum. Severe cases of falciparum malaria have been reported to have elevated liver enzymes and jaundice. Also, liver biopsies indicate the presence of necrosis of hepatocytes. One of the most common reasons for jaundice in malaria is intravascular hemolysis. There is increasing evidence indicating that there may be additional mechanisms contributing to liver dysfunction in malaria [2]. Additional mechanisms of liver injury include Kupffer cell hyperplasia, cholestasis, granuloma formations and malarial pigmentation [3, 4]. Plasmodium vivax has also been known to cause hepatic dysfunction [5, 6]. These manifest as elevated transaminase levels. The enzyme levels normalise after treatment. In most cases, the elevated enzymes levels are only incidental findings [7].

Other causes of jaundice may occur in malaria as well. Infectious such as Hepatitis E virus, chronic liver disease caused by pre-existing Hepatitis B infection, usage of anti-malarial drugs may also result in jaundice among those having malaria [3, 8].

The term ‘malarial hepatitis’ or ‘malarial hepatopathy ‘is used to describe liver dysfunction occurring in malaria. It has been described to be a heterogeneous syndrome with a spectrum of presentations, and severe disease has a better response to therapy compared to other causes of hepatic failure [9].

Knowledge of hepatic dysfunction in malaria is crucial since it is a reversible cause of liver injury. Early identification of liver dysfunction and determining the etiology are the key factors for successful treatment [10]. In a country like India, where the burden of malaria is high, there is a paucity of knowledge regarding liver dysfunction in malaria. This study seeks to assess the same. This study seeks to aims the prevalence and type of jaundice among those with malaria and the liver function parameters among those with malaria.

Materials and methods

A prospective observational study was conducted in NRI Medical College and General Hospital, Chinakakani, Guntur District in Andhra Pradesh. Data collection was done from October 2016 to September 2018.

The inclusion criteria comprised of

- All cases of malaria diagnosed by peripheral smear examination or by immunochromatographic test, either Rapid Card / Stick tests.

The exclusion criteria comprised of

- Intake of hepatotoxic drugs
- Pre-existing liver disease
- Previous history of blood transfusion
- History of alcoholism

A total of 50 patients were included in the study after applying inclusion and exclusion criteria. Laboratory investigations such as peripheral smear examination, liver function tests, complete blood count and renal function tests were performed. The algorithm (**Figure – 1**) was applied to classify patients based on their liver function test results.

The collected data was entered in MS Excel and analysed using SPSS version 23.0. The datawere summarised in tables and figures. Numerical variables were summarised as means with standard deviations. Categorical variables were summarised as a percentage.

Figure - 1: Algorithm for liver function tests.

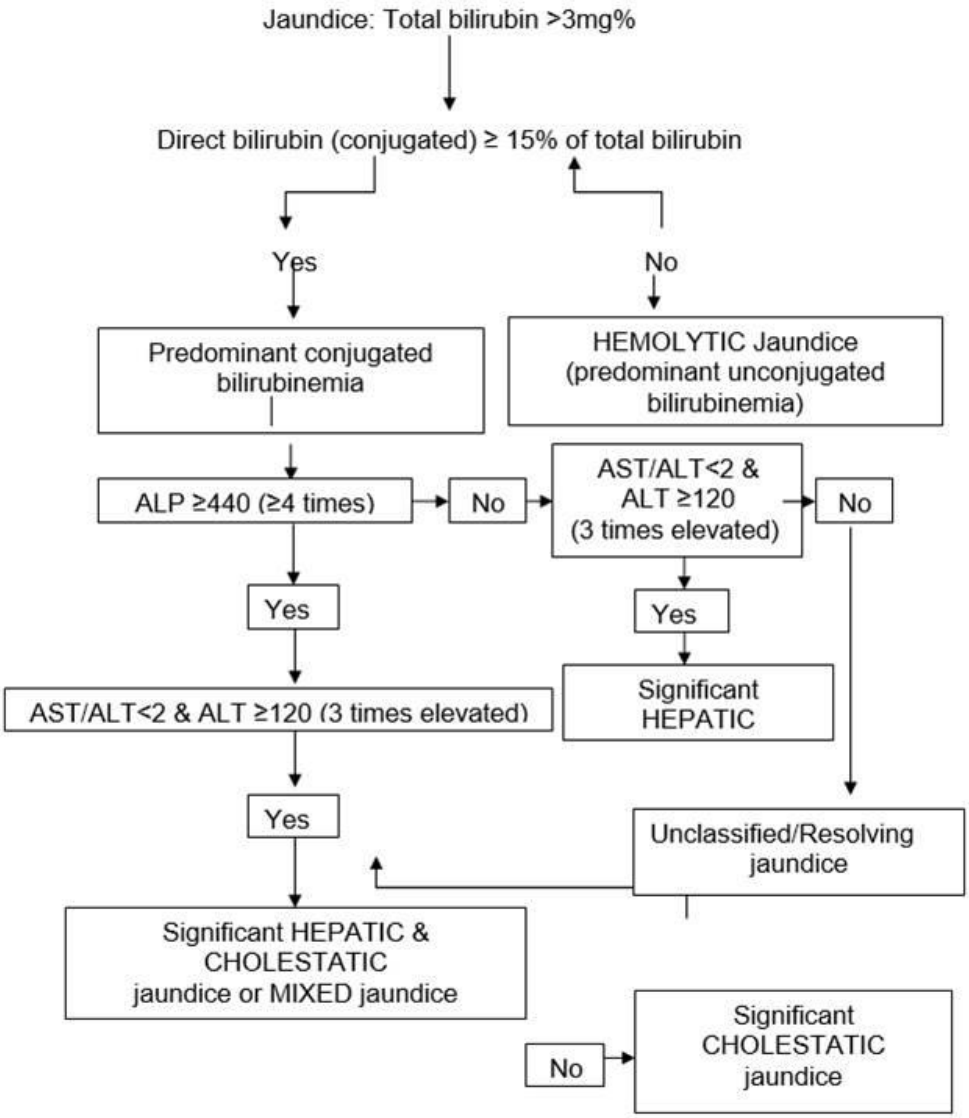

Figure - 2: Jaundice in Malaria.

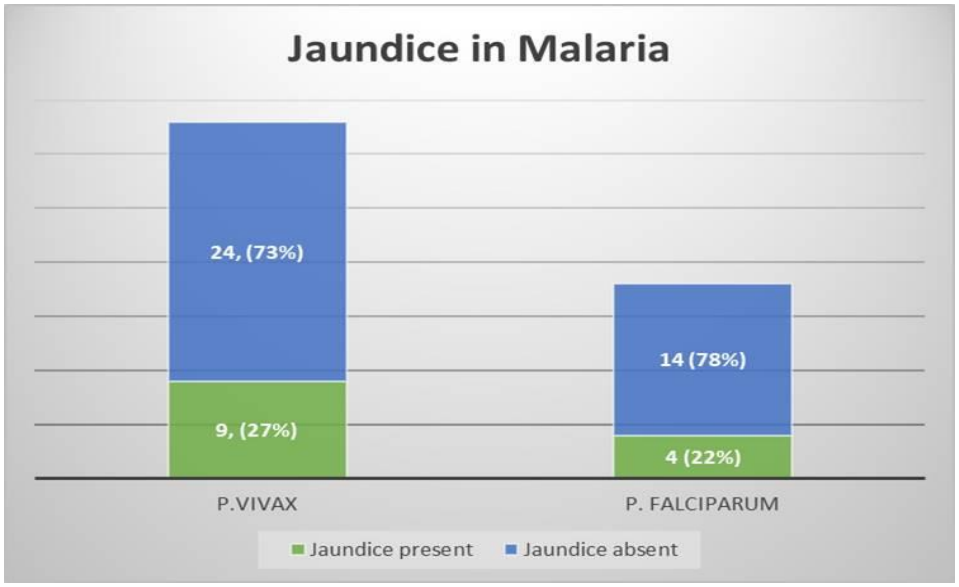

Table - 1: Liver function tests in Malaria.

Serum ALT (SGPT) IU/L	**No. of cases**	**%**
>120IU/L	10	20%
>1000	1	2%
>120 with AST/ALT <2	9	18%
>120 with AST/ALT <2 and total bilirubin>3mg/dl	5	10%
Serum AST (SGOT) IU/L		
>120	20	40%
>1000	1	2%
>120 with total Bilirubin >3 mg/dl	9	18%

Table - 2: Liver function and jaundice in malaria.

Jaundice	**No. of cases**	**The proportion of total (%)**
>3 mg/dl	13	26%
>3 mg/dl with predominantly conjugated jaundice	13	26%
Cholestatic jaundice (ALP>440IU/L) + Hepatic jaundice (ALT>120IU/L & AST/ALT<2) = Mixed jaundice	2	4%
Predominant hepatic jaundice (ALT>120IU/L and AST/ALT<2)	3	6%
Unclassified / resolving jaundice	8	16%

Results

A total of 50 patients were included in the study. Among them, 17(34%) had P. falciparum malaria, 32(64%) had P. vivax malaria, and only 1(2%) had mixed infection with both P. falciparum and P. vivax. Among the study population, 13(26%) had jaundice as defined by serum bilirubin of more than 3 mg/dL. All the individuals who had jaundice had conjugated hyperbilirubinemia. The incidence of jaundice based on parasite subtype is given in **Figure - 2**.

Serum Alkaline Phosphatase (ALP): ALP levels above 4 times the upper limit was taken to be suggestive of significant cholestatic jaundice. 3 (6%) cases had a serum ALP value above 4 times normal, i.e.>440 IU/L. But only two of these values were seen in jaundiced cases. Hence, 2 (4%) of 50 cases had a significant cholestatic component to jaundice. These two cases were caused by vivax malaria and had a significant hepatic component to jaundice seen in them. The one case without associated jaundice could signify transient cholestasis without bilirubinemia. This was a case of Falciparum malaria. The AST and ALT profile of the patients with jaundiceis given in **Table - 1**.

Classification of jaundice

Cases with total bilirubin> 3mg/dl and direct bilirubin (conjugated bilirubin) >15% of the total were classified into predominantly conjugated jaundice. All the 13 cases of jaundice had predominantly conjugated jaundice. No pure hemolytic (predominant unconjugated) jaundice was seen.

Of the 13 cases of predominantly conjugated jaundice, 2 had a significant cholestatic component with the additional hepatic component. Among the remaining 11 cases, 3 had significant hepatic component with no significant cholestasis.

The remaining jaundiced cases could not be categorised into having a predominant component of hepatic or cholestatic and were taken to be part of resolving hepatic dysfunction were the enzymes were returning to normal with bilirubin lagging. Hence, the proportion of hepatic jaundice among the study population was

22%. Around 14% had mixed jaundice and in the remaining 64%, the jaundice was unclassified. The patient liver function profile based on the liver function tests are given in **Table - 2**.

In the present study, 1 case died showing the highest bilirubin value died of respiratory distress. This was a case of vivax malaria and had mixed type of jaundice. Thus, the mortality in the icteric cases was ~7.7% while it was 0% in the non-icteric cases.

Discussion

The proportion of vivax and falciparum cases in the present study is 64% and 34% respectively. The proportion of falciparum cases was much lesser when compared with the study by Ramya M and Lakshmi M, et al. [11] (2018) where the proportion of vivax and falciparum cases were 33.80% and 66.15% respectively. According to the World Malaria report of 2017, the proportion of falciparum cases are a little above 30% in the South East Asian Region which is comparable to the current study.

In this study, the incidence of jaundice among those with malaria was 26%. This is slightly higher compared to the study by Ramya M and Lakshmi M, et al. [11] (2018) where the incidence of jaundice was 20.38%. In the study by TMV Rao, et al. [12] (2016), 51.4% had jaundice which is much higher compared to the current study. In the present study, the incidence of jaundice among P. vivax and P. falciparum was 27% and 22% respectively. This is much lesser compared to the study by Hazra, et al. [13] (1998) where the incidence of jaundice in vivax and falciparum malaria was 9.09% and 40% respectively. In the study by Ramya M and Lakshmi M, et al. [11] (2018), the incidence of jaundice among P. vivax and P. falciparum was 21.59% and 19.76% respectively which is lesser compared to the present study.

In the present study, all the patients with jaundice had conjugated hyperbilirubinemia. This is by the study by Bhalla, et al. [14] (2006) and Abro, et al. [15] (2009) where a majority of the patients with malaria had conjugated hyperbilirubinemia as well.

About liver enzymes in this study, 40% had elevated AST levels, and 20% had elevated ALT levels. In the study by Chawla, et al. [4] (1989), 21.8% had elevated serum transaminase levels. In this study, ALP was found to be elevated more than 440 IU/L in 6% of the cases, but the elevation was associated with conjugated bilirubinemia only in 4% of the cases. So, cholestatic component of jaundice was present in at least 4% of the total cases.

All the cases having jaundice in this study had predominantly conjugated bilirubinemia. No pure hemolytic (Unconjugated) jaundicewas seen. Jaundice in cases showing ALT >120IU/L and AST/ALT <2 had a significant hepatic component to jaundice. There were about 5 (10%) in such cases. Of these 5 cases, 2 (4%) cases also had ALP >440IU/L, implying additional cholestatic jaundice. So, three (6%) had only hepatic component, 2 (4%) had mixed (hepatic + Cholestatic) jaundice.

Other patients have jaundice, but no clear pattern of hepatic or cholestatic or hemolytic jaundiceprobably had a resolving hepatic dysfunction with conjugated bilirubinemia lagging behind the falling enzymes. There were 8 (16%) in such cases.

Cases with elevated liver enzymes without biochemical jaundice probably had early/ minimal hepatic injury or had hemolysis with good residual liver function that prevented a rise in bilirubin.

Conclusion and recommendations

There is a significant incidence of hepatic involvement among those with malaria. Hepatic involvement in vivax malaria is comparable to the involvement occurring in falciparum malaria. Hepatic involvement manifests as conjugated bilirubinemia with elevated liver enzymes. In

addition to hemolytic jaundice, cholestatic jaundice occurs as well. The risk of mortality is high among those with icterus. Hence, early suspicion and screening for hepatic involvement are necessary for those with malaria. This would aid in early diagnosis and prevent complications. Highest attention must be paid to those with elevated bilirubin levels since they are at the highest risk of mortality.

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