A Correlation of Cerebral Malaria with Different Changes in Hepatitis: A Hospital Based Study

Pratap Singh

ABSTRACT

**Background:** Ventilator associated pneumonia (VAP) is a type of nosocomial pneumonia occurring in patients who are mechanically ventilated for more than 48 hours. VAP is the most common nosocomial infection occurring in the intensive care units and its incidence varies from 8% to 28%.

**AIMS & OBJECTIVES:** This study was done to determine the bacteriological profile and antibiotic sensitivity pattern of the isolates obtained from the endotracheal aspirates of the clinically suspected patients of VAP in ICU. **Materials & Methods:** The study was conducted in the department of general medicine of the Haridev Joshi Hospital, Dungarpur, Rajasthan, India. The present study included 52 patients who had serum bilirubin > 3 mg%. So, after excluded patient the study group included 45 patients. All patients were underwent set of investigations, including conjugated and unconjugated bilirubin, and serum AST and ALT levels. All the patients with cerebral malaria underwent detailed ultrasonography to check the size and echo-texture of the liver. **Results:** A total of 45 patients with malaria were included in the study. The mean serum bilirubin level was 11.23±6.8 mg %, mean AST levels was 298.42±242.21 IU/l and mean ALT levels was 382.21±298.12 IU/l. 17 patients were diagnosed having cerebral malaria. The patients with cerebral malaria were directed to undergo USG abdomen. Enlarged size if liver was seen 14 patients. **Conclusion:** Within the limitations of our study we conclude that significant hepatitis findings are seen in patients with cerebral malaria. Required supportive and anti-malarial treatment should be provided to the patients with specially taking care of the hepatic health.

**Key words:** Ventilator associated pneumonia, Intensive care unit, Multi drug resistant, Endotracheal aspirates

INTRODUCTION

Malaria is a devastating parasite transmitted by the bite of infected Anopheles mosquitoes. It is responsible for infecting 300-500 million and 1-3 deaths annually. In humans malaria is caused by Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, and rarely Plasmodium Knowlesi. Plasmodium vivax is the most common of the malaria species. Malaria can be transmitted by three known ways; vector transmission, blood transfusion and congenital transmission. The malaria parasite interferes with 3 major organs in the body, namely: the brain, kidney and liver. The liver is an important organ involved during the hepatic stage of the malaria parasite’s life cycle, where malaria sporozoites develop into merozoites. The merozoites are then released into the circulation and enter the erythrocytic stage. In the erythrocytic stage, parasitized red blood cells (PRBCs) become sequestered in small blood vessels. The degraded haemozoin pigment is then engulfed by local tissue macrophages, such as Kupffer cells and alveolar macrophages. Common histopathological findings of the liver in P. falciparum malaria include reactive Kupffer cells, retention of haemozoin pigment and minimal PRBC sequestration. An ultrastructural study reported an association between high PRBC load in the livers of malaria patients with jaundice, hepatomegaly and liver enzyme elevation. Hence, the present study was planned to study the correlation of cerebral malaria with different changes in
hepatitis.

METHODS

The study was conducted in the department of general medicine of the Haridev Joshi Hospital, Dungarpur, Rajasthan, India. The ethical clearance for the study was obtained from the ethical board of the institute prior to commencement of the study. The present study included 52 patients who had serum bilirubin > 3 mg%. Any patient with evidence of liver disease (e.g. viral hepatitis, cirrhosis liver, portal hypertension, amoebic liver abscess, unexplained hepatomegaly, ascites, history of alcoholism, taking hepatotoxic drugs, past history of jaundice) were excluded. Three patients had a history of regular consumption of alcohol over > 10 years and two patients were on antitubercular drug: all five were also excluded. So, after excluded patient the study group included 45 patients. All patients were underwent a set of investigations, including conjugated and unconjugated bilirubin, and serum AST and ALT levels. All the patients with cerebral malaria underwent detailed ultrasonography to check the size and echo-texture of the liver. All patients received specific treatment in the form of i.v./oral quinine using the standard regimen, along with the usual specific supportive care. The data was tabulated and subjected to statistical analysis.

The statistical analysis of the data was done using SPSS version 20.0 for windows. The Student’s t-test and Chi-square test were used to check the significance of the data. The p-value less than 0.05 was predetermined as statistically significant.

RESULTS

A total of 45 patients with malaria were included in the study. Table 1 shows the mean values of different blood parameters in the study group. The mean serum bilirubin level was 11.23±6.8 mg%, mean AST levels was 298.42±242.21 IU/I and mean ALT levels was 382.21±298.12 IU/I. On comparing the results statistically, non-significant results were observed [Fig 1]. 17 patients were diagnosed having cerebral malaria. The patients with cerebral malaria were directed to undergo USG abdomen. Table 2 shows USG findings in patients with cerebral malaria. Enlarged size if liver was seen 14 patients, altered echo pattern was seen in 4 patients, normal architecture was seen in all the patients, mid grey scale was seen in 11 patients, low grey scale was seen in 4 patients and normal grey scale was seen in 1 patient. The highest frequency of patients was seen in enlarged size of liver followed by mid grey scale.

Table 1: Mean values of different blood parameters in study group

<table>
<thead>
<tr>
<th>Blood parameters</th>
<th>Mean values</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum bilirubin levels (mg %)</td>
<td>11.23±6.8</td>
<td>0.1</td>
</tr>
<tr>
<td>AST levels (IU/I)</td>
<td>298.42±242.21</td>
<td>0.09</td>
</tr>
<tr>
<td>ALT levels (IU/I)</td>
<td>382.21±298.12</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Table 2: USG findings in patients with cerebral malaria

<table>
<thead>
<tr>
<th>USG findings in liver</th>
<th>Frequency of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size enlarged</td>
<td>14</td>
<td>86</td>
</tr>
<tr>
<td>Altered echo pattern</td>
<td>4</td>
<td>23.5</td>
</tr>
<tr>
<td>Normal architecture</td>
<td>17</td>
<td>100</td>
</tr>
<tr>
<td>Mid grey scale</td>
<td>11</td>
<td>64.7</td>
</tr>
<tr>
<td>Low grey scale</td>
<td>4</td>
<td>23.5</td>
</tr>
<tr>
<td>Normal grey scale</td>
<td>1</td>
<td>5.8</td>
</tr>
</tbody>
</table>

DISCUSSION

In tropical areas, malaria is a major public health problem responsible for infecting 300-500 million people and 1-3 million deaths annually. Malaria involves liver where hepatocytes are invaded by sporozoites and multiply. In erythrocytic stage, the destruction of infected RBCs is caused by merozoites. Molyneux et al. suggested that hemolysis is the most common cause of moderate elevation of hepatic enzymes than hepatic damage, which causes jaundice. [7,8] The present study was conducted to study the correlation of cerebral malaria with different changes in hepatitis. We observed that about 86 % of the patients had enlarged liver. Normal architecture of the liver was seen in 100% patients. The results were compared to previous studies from the literature and results were found to be consistent. Viriyavejakul P et al investigated the liver pathology of severe P. falciparum malaria as well as the regulation and occurrence of apoptosis in cellular components of formalin-fixed, paraffin-embedded liver tissues. The liver tissues used in the study came from patients who died from P. falciparum malaria with hyperbilirubinaemia (12 cases), P. falciparum malaria without hyperbilirubinaemia (10 cases); and patients who died due to accidents, whose liver histology was normal (the control group) (10 cases). The histopathology of the liver tissue was studied by routine histology method. Caspase-3 and nuclear factor kappa B (NF-κB) p65 expressions were determined using immunohistochemistry. The severity of liver histopathology, occurrence of apoptosis and NF-κB p65 activation in P. falciparum malaria were associated with higher TB level. Significant correlations were found between NF-κB p65 expression and apoptosis in Kupffer cells and lymphocytes in the portal tracts. They concluded that hyperplastic Kupffer cells and portal tract inflammation are two main features found in the liver tissues of severe P. falciparum malaria cases. In addition, NF-κB is associated with Kupffer cells and lymphocyte apoptosis in severe P. falciparum malaria. Kochar DK et al identified the evidence for hepatocyte dysfunction and/or encephalopathy in jaundiced patients with falciparum malaria. They studied 86 adult patients of both sexes who had malaria with jaundice (serum bilirubin > 3 mg%). The main outcome measures were: flapping tremor, deranged psychometric test, level of consciousness, serum bilirubin level, serum aspartate transaminase (AST) and alanine transaminase (ALT) levels, blood ammonia level, viral markers for hepatitis, ultrasonography of liver and gall bladder and electroencephalography (EEG). The range of serum bilirubin
was 3–48.2 mg%. The ranges of AST and ALT levels were 40–1120 IU/I and 40–1245 IU/I, respectively. Evidence of hepatic encephalopathy was seen in 15 patients. Asterixis was observed in 9 patients, impaired psychometric tests in 12 and altered mental state in 13. Arterial blood ammonia level was 120–427 μmol/L. EEG findings included presence of large bilateral synchronous slow waves, pseudo burst suppression and triphasic waves. Four patients died due to multiple organ dysfunction; the others made rapid recoveries. They concluded that there is strong evidence of hepatocyte dysfunction and hepatic encephalopathy in some of these patients, with no obvious non-malarial explanation.

Andrade BB et al conducted study to evaluate whether areas that are endemic for malaria are also highly endemic for hepatitis B virus (HBV) infection. An observational study of 636 individuals was performed in Rondônia, western Amazon, Brazil between 2006 and 2007. Active and passive case detections identified Plasmodium infection by field microscopy and nested Polymerase Chain Reaction (PCR). HBV infections were identified by serology and confirmed by real-time PCR. Epidemiological information and plasma cytokine profiles were studied. The data were analyzed using adjusted multinomial logistic regression. Plasmodium-infected individuals with active HBV infection were more likely to be asymptomatic, present with lower levels of parasitemia and demonstrate a decreased inflammatory cytokine profile. Nevertheless, co-infected individuals presented higher HBV viremia. Plasmodium parasitemia inversely correlated with plasma HBV DNA levels. They concluded that HBV infection diminishes the intensity of malaria infection in individuals from this endemic area.

Enemchukwu BN et al conducted liver function assessment on 90 volunteer patients; comprising (30) patients with malaria only, (30) with typhoid only and (30) with malaria-typhoid co-infection randomly selected from Abia State University Teaching Hospital, Aba, Abia State, Nigeria and (20) healthy individuals were used as control. Blood samples collected from these subjects were screened for malaria parasite and Staphylococcus typhi using standard methods. Mean serum levels of ALP, AST, ALT, TB, CB and ALP, AST, ALT, TB, CB were obtained for those subjects with malaria and typhoid respectively and subjects with malaria-typhoid co-infection recorded the following; ALP, AST, ALT, TB, CB while the control subjects had mean serum levels of ALP, AST, ALT, TB and CB. The mean values were subjected to a statistical test using students t-test which revealed a significant increase. The results suggest that malaria, typhoid and malaria-typhoid co-infection can elevate ALP, AST, ALT, TB and CB serum levels and can lead to liver damage if not properly treated.

CONCLUSION
Within the limitations of our study we conclude that significant hepatitis findings are seen in patients with cerebral malaria. Required supportive and anti-malarial treatment should be provided to the patients with specially taking care of the hepatic health.

REFERENCES