ABSTRACT

OBJECTIVE: To observe the correlation of hemoglobin versus liver function tests in patients of falciparum malaria

SETTINGS & DESIGN: A descriptive study conducted at Department of Biochemistry, Basic Medical Sciences Institute, JPMC, Karachi from August 2005 to July 2006.

PATIENTS AND METHODS: Total eighty-one patients of different ages ranging 3-56 years and both sexes suffering from acute malaria, confirmed by peripheral blood smear were selected by consecutive sampling. Nine out of eighty-one patients were infected by Hepatitis B and C infections and were excluded from the study. Out of seventy-two patients 48(70%) were suffering from malaria by Plasmodium falciparum and 24(30%) from Plasmodium vivax infection. The falciparum infected patients were equally segregated into two groups on the basis of duration of illness. Group 1 comprised of 24 patients complaining of fever with or without rigors ranging from 1 – 7 days. Group 2 also consisted of 24 patients with duration of illness lasting from 8-20 days.

RESULTS: The haematocrit percentage was showing a positive good correlation in these groups with hemoglobin, which is statistically significant (P<0.01). The bilirubin, SGPT and SGOT of group II were showing a weak negative correlation with hemoglobin but it is statistically significant (P<0.05). The other parameters of both groups were showing a non-significant correlation.

CONCLUSION: Because Falciparum can present like Fulminent hepatitis so liver function tests should be performed along with early diagnosis of Plasmodium falciparum malaria in order to prevent complications and to reduce mortality.

KEYWORDS: ALT, AST, Falciparum, Malaria, LFTS.

INTRODUCTION

Malaria, a major public health problem in tropical areas, responsible for 300-500 million infections and 1-3 million deaths annually. Majority of deaths occur due to severe malaria, having one or more complications in a patient of Falciparum infection. Malarial transmission to the human host is established by sporozoites infection to the liver. The malarial sporozoites once injected in blood by the bite of female Anopheles mosquitoes attaches to hepatocytes through receptor for thrombospondin and properdin. Hepatocyte invasion initiates the liver stage. Extensive differentiation and multiplication ensues, with each liver-stage parasite yielding tens of thousands of merozoites. The clinical manifestations of severe malaria are directly correlated with the induction of strong pro-inflammatory type-1 immune responses. Liver involvement is common in severe malaria and may manifest as jaundice i.e. raised serum bilirubin, hepatomegaly and elevated liver enzymes like aspartate and alanine transaminases. The pathogenesis of severe anemia in malaria may be due to factors as malnutrition, iron deficiency, bone marrow dysfunction and level of parasitaemia. The elevation of ALT and AST with conjugated hyperbilirubinaemia while prolonged duration of illness impairs consciousness with adverse outcome. Although hyperbilirubinemia has been linked with increased malaria related mortality, it is often seen in association with other complications such as acute renal failure or cerebral malaria. Alanine aminotransferase catalyze reactions in which the building block of protein(amino acid) is transferred from a donor molecule to a recipient molecule. It is found largely in the liver. Aspartate aminotransferase is found in a diversity of tissues including liver, muscle, heart, kidney, and brain. It is increased when any of these tissues is injured. Hence it is not highly specific indicator of liver damage. The increased serum alkaline phosphatase activity among the patients indicates...
that the liver stage of falciparum malaria infection is accompanied by a perturbation of the host hepatocytes drainage pathways and damage to hepatocytes membrane leading to leakage of the enzymes out of the liver cells. The present study was conducted on Plasmodium falciparum malarial patients to observe the correlation between liver enzymes and hemoglobin.

PATIENTS AND METHODS

This study was conducted in the Department of Biochemistry, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre Karachi. Total eighty-one patients of different ages ranging 3-56 years and both sexes suffering from acute malaria, confirmed by thick and thin peripheral blood smear were selected by consecutive sampling technique from Pediatrics Units in National Institute of Child Health, Malaria Control Program counter at Accident and Emergency Department, Medical Units I, II and III, Jinnah Postgraduate Medical Centre Karachi. Detail history and complete physical examination performed after taking consent. A proforma was filled while taking history beginning with name, age, address, and duration of illness, type of fever, drug history and history of jaundice in the past, history of diabetes or other diseases associated with this illness. If liver and spleen found enlarged, they were measured subcostly in the midclavicular line using a measuring tape (cm) while patient was lying supine. About 5 ml Venous blood taken and fractionated as: One m1 blood was transferred into a tube containing citrate for Prothrombin time, while another 1 m1 blood was transferred into other tube containing Ethylenediaminetetraacetic acid (EDTA) for hemoglobin and haematocrit estimation. A small drop of blood was also placed on the strip of glucometer (Optium, Abbott) to check the random blood glucose level. The tubes having blood were allowed to clot and then serum was pipette out after centrifugation, labeled and stored at -20°C in freezer for later analysis. Nine out of eighty-one patients were excluded by serological method having Hepatitis B and C infections. Out of seventy-two patients 48(70%) were suffering from malaria by Plasmodium falciparum and 24(30%) from Plasmodium vivax infection. The patients having Plasmodium falciparum infection were grouped on the basis of their duration of illness.

Group I: Plasmodium falciparum positive patients having illness of 1 to 7 days.

Group II: Plasmodium falciparum positive patients having illness of 8 to 20 days.

Exclusion Criteria:
1. Those patients having fever with or without rigors but were negative for falciparum malarial parasite.
2. Those who were taking hepatotoxic drugs.
3. Those that were having a mixed malarial infections.
4. Pregnant women.
5. On serology, if any patient was found positive for hepatitis.

Blood hemoglobin level was estimated by Cyanmat Hemoglobin method, Haematocrit values were estimated by microhaematocrit method on Microhaematocrit Machine, Serum Bilirubin (Total, Direct and Indirect) by JendrassikGrof Method. Serum glutamate pyruvate transaminase, Serum glutamate oxaloacetate transaminase and alkaline phosphatase estimated by enzymatic method. The statistics were applied by using SPSS version 10.0. The biochemical parameters compared between these groups. The p value was calculated. The correlation co-efficient among haemoglobin versus biochemical parameters observed. The Mean and SEM was found out and further statistical analysis performed.

RESULTS

All (100%) patients were having acute fever with or without rigors of moderate to high degree ranging from 100 to 104F. Fever was associated with headache, body ache and nausea in 95% patients and 5% were also having vomiting. In all patients the duration of illness was ranging from 1 to 20 days. There was no history of blood transfusion in the past four months. Pallor was present in 63.8% of patients, while 52.7% of patients were clinically jaundiced. None of them was having edema, ascites, or bleeding from any site. The liver was enlarged in 28 (38.9%) patients ranging from 0.5 cm to 4.0 cm, while spleen was found palpable in 27 (37.5%) of patients ranging from 0.5 cm to 3.0 cm. Ultrasound of abdomen especially for liver was performed on those patients who were having more than 2 cm of enlargement and found normal architecture without any dilation or obstruction in drainage pathway. All the patients were conscious and without any complications at the time of examination.

The results of our study are depicted in following Table # 1, 2 and figure 1 and 2.

Table 1 shows the distribution of only one specie Plasmodium falciparum malaria infected cases according to their duration of illness.
TABLE 1: DISTRIBUTION OF AGE AND SEX IN PATIENTS WITH FALCIPARUM MALARIA

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>NO. OF SUBJECTS</th>
<th>AGE</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Male No. (%)</td>
</tr>
<tr>
<td>Group 1</td>
<td>24</td>
<td>25.2 ± 3.33</td>
<td>14 (58.3)</td>
</tr>
<tr>
<td>Group 2</td>
<td>24</td>
<td>24.7 ± 2.71</td>
<td>16(66.7)</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SEM
Group I: Plasmodium falciparum +ve, having illness of 1 to 7 days.
Group II: Plasmodium falciparum +ve, having illness of 8 to 20 days.

In Group I age ranges from three years to fifty-six years. On peripheral blood smear examination only two (8.3%) gametes and twenty two (91.7%) rings or trophozoites were present. The liver was not palpable in seventeen (70.8%) patients and were palpable (ranging 0.5 cm to 4 cm) in seven (29.2%) patients, while spleen was not palpable in twenty-one (87.5%) patients and was palpable (ranging from 0.5 cm to 3 cm) in three (12.5%) patients. In Group II, The age ranges from five to fifty years. On peripheral blood smear examination, four (16.7%) patients were having gametes while rings or trophozoites were present in twenty (83.3%) patients. In five (20.8%) patients, the liver was not palpable, while in nineteen (79.2%), the liver was palpable subcostally. The spleen was not palpable in four (16.7%) and was palpable subcostally in twenty (83.3%) of the patients.

Table 2 shows the comparison of biochemical parameters between group I and group II.

TABLE 2: COMPARISON OF BIOCHEMICAL PARAMETERS BETWEEN GROUP I AND GROUP II

<table>
<thead>
<tr>
<th>Biochemical Parameters</th>
<th>Plasmodium falciparum +ve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I (n=24)</td>
</tr>
<tr>
<td></td>
<td>Mean ± SEM</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>9.2 ± 0.31</td>
</tr>
<tr>
<td>Haematocrit (%)</td>
<td>27.7 ± 0.97</td>
</tr>
<tr>
<td>Prothrombin time (Control: 11 to 16 sec)</td>
<td>14.4 ± 0.23</td>
</tr>
<tr>
<td>Random Blood Glucose (mg/dl)</td>
<td>93 ± 2.89</td>
</tr>
<tr>
<td>Bilirubin - Total (mg/dl)</td>
<td>1.4 ± 0.13</td>
</tr>
<tr>
<td>Direct (mg/dl)</td>
<td>0.6 ± 0.07</td>
</tr>
<tr>
<td>Indirect (mg/dl)</td>
<td>0.8 ± 0.08</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>27.5 ± 1.59</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>27.2 ± 1.19</td>
</tr>
<tr>
<td>Alkaline Phosphatase (U/L)</td>
<td>248 ± 11.6</td>
</tr>
<tr>
<td>Total protein (g/dl)</td>
<td>7.2 ± 0.14</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>4.3 ± 0.08</td>
</tr>
<tr>
<td>Globulin (g/dl)</td>
<td>2.9 ± 0.10</td>
</tr>
<tr>
<td>A/G ratio</td>
<td>1.5 ± 0.06</td>
</tr>
</tbody>
</table>
FIGURE 1: CORRELATION COEFFICIENT (r) AMONG HAEMOGLOBIN VERSUS HEMATOCRIT (HCT) IN GROUP II

![Graph showing correlation between haematocrit and haemoglobin.](image)

Plasmodium falciparum +ve, having illness of 1 to 7 days. Group II: Plasmodium falciparum +ve, having illness of 8 to 20 days.

The correlation co-efficient among haemoglobin versus biochemical parameters in both groups of falciparum performed. The \( r \)-value of haematocrit percentage in group 1 was 0.99 and in group 2 also 0.99 showing a positive good correlation with haemoglobin, which is statistically significant (\( P < 0.01 \)). The bilirubin, SGPT and SGOT of group II were showing a weak negative correlation coefficient \( r = -0.63 \) and \( r = -0.53 \) respectively (\( P < 0.01 \)) versus hemoglobin.

DISCUSSION

Among four species of malaria, Plasmodium falciparum and vivax are commonly observed in Pakistan. Malaria involves the liver where infective sporozoites invade and multiply in the hepatocytes and in erythrocytic stage the merozoites cause the destruction of infected red blood cells.\(^\text{15}\)

This study was performed to evaluate the acute hepatic damage by falciparum malaria. The physical parameters like fever, size of liver and spleen, and forms of parasites in peripheral blood smear, which were the criteria of subject selection while the biochemical parameters like bilirubin, enzymes and protein found to be highly significant and prove that subjects were of current cases of malaria rather than the chronic cases. In this study the liver was enlarged in 28 (38.9%) patients ranging from 0.5 cm to 4.0 cm, measured below the costal margin using measuring tape in mid clavicular line, while spleen was found palpable in 27 (37.5%) of patients ranging from 0.5 cm to 3.0 cm subcostly. Clinically pallor reflects low hemoglobin. In our study Pallor was present in 63.8% of patients, while 52.7% of patients were clinically jaundiced. In malaria, low hemoglobin may result from acute hemolysis or destruction of both infected and unininfected red blood cells, dyserythropoiesis and with nutritional deficiencies.\(^\text{1}\)

Table 2 shows Hemoglobin level with the mean value of 9.2 g/dl and 9.5 g/dl group I and group II respectively showed an anemic picture (<10 g/dl). These findings are in agreement to Bhalli and Samiuilah\(^\text{16}\) but do not match with the mean hemoglobin level of 13.78 g/dl as reported by Nadeem et al.\(^\text{4}\) The mean hemoglobin value has excellent positive correlation with haematocrit in both groups. In this study hyperbilirubinemia was present in 64.3% of cases which is close to the study result of Abro AH\(^\text{20}\) who found Serum bilirubin higher than normal level in 81%.The high mean value of indirect bilirubin in group II correlates with the duration of illness, which can be justified by the study of Irfan (2000)\(^\text{20}\). Coagulation abnormalities are not uncommon in falciparum malaria. In this study, mean values of the prothrombin time 14.4 in group I and 15.3 in group II (table 2). Only 4 out of 48 patients of Plasmodium falciparum infected group were having prolonged prothrombin time without any bleeding disorders. The results matches with the results of Abro AH but contradict with the results of Premaratna et al.\(^\text{19}\) showing a prothrombin time of 18 seconds. Our study results were also in accordance with the
Vogetseder et al showing an impairment of coagulation system with the severity of disease. It is well established that the erythrocytic stages of the malaria parasite rely mainly on glycolysis for their energy supply. Hypoglycemia may be due to decrease intake, depletion of liver glycogen, and glucose consumption by the large number of parasites. The results of random blood glucose were normoglycemic. The study of Van Thien et al contradicts the results of present study, who quantified gluconeogenesis in severe malaria. The increase serum level of hepatic enzymes, transaminases (SGOT and SGPT) and alkaline phosphatase are the markers of liver disorders. SGPT (ALT) is a specific enzyme of liver; in this study SGPT and SGOT were elevated in the group II. These results match with the results of Premaratna and Shah S. The rise in serum alkaline phosphatase shows leakage of this enzyme on the membranes of hepatic drainage system makes it a potentially important biomarker for the assessment of integrity of this system during malaria infection. The results of difference in mean value of this enzyme are statistical highly significant when group I and group II of Plasmodium falciparum infected were compared. This finding correlates with the results of Garba and Ubom. The results of total protein also showed a poor non-significant positive correlation coefficient with hemoglobin.

This study was performed on a small sample size and provides baseline information in these subjects, so we recommended that same type of study should be carried out on large sample size and liver function tests should be performed along with early diagnosis of Plasmodium falciparum malarial infections in order to prevent misdiagnosis, complications and to reduce mortality.

CONCLUSION

The results of our study provide valuable information and association between hepatic biochemical derangement and Falciparum malarial patients.

REFERENCES

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