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ASSOCIATION OF BILIRUBIN WITH LIVER ENZYMES IN FALCIPARUM MALARIA AFFECTED PATIENTS

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Abstract:

Introduction: *Malaria Falciparum is responsible for 1-3 million deaths annually worldwide. Liver involvement is common and can occur as high serum bilirubin, liver enlargement and high liver enzymes. It has been observed that unconjugated hyperbilirubinemia usually causes increased mortality. Alanine aminotransferase (SGPT) is an indicator of liver damage. This study was conducted to observe a correlation between liver enzymes and bilirubin in patients with Plasmodium falciparum malaria.*

Aim: *To observe the correlation coefficient of bilirubin with liver enzymes (SGPT, SGOT and alkaline phosphatase) in patients with falciparum malaria.*

Study Design: *A descriptive study*

Place and duration: *In the Department of Pathology, Sir Gangaram Hospital, Lahore for one year duration from March 2019 to March 2020.*

Materials and methods: *A total of 81 patients of different ages and both genders suffering from severe malaria were selected with non-probable sampling. Nine patients with hepatitis B and C infection were excluded from the study. Of the remaining 72 cases, 48 (70%) had Plasmodium falciparum infection and 24 (30%) had Plasmodium vivax infection. Falciparum infected patients were divided into two groups equally depending on the duration of the disease. In Group I; the disease continued for 1 to 7 days, in group II lasted for 8 to 20 days. Patients suffering from plasmodium vivax infection had a duration of 1 to 20 days and were placed in group III.*

Results: *Group I, SGPT and alkaline phosphatase showed a statistically significant positive correlation with bilirubin ($r = 0.50$ and $r = 0.054$), and SGPT showed a perfectly positive correlation in group II ($p < 0.05$). $r = 0.88$; $P < 0.01$), SGOT and alkaline phosphatase also showed a statistically significant positive correlation. In group III, both transaminases and alkaline phosphatase showed a statistically significant positive correlation $r = 0.82$, 0.63 and 0.69, respectively.*

Conclusion: *Positive correlation of liver enzymes and bilirubin suggests that liver function tests should be performed with early diagnosis of malaria infection Plasmodium falciparum to prevent complications and reduce mortality.*

Key words: *malaria, liver enzymes, bilirubin, malaria falciparum*

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INTRODUCTION:

Malaria, which is an important public health problem in tropical regions, is responsible for the transmission of 300-500 million people and 1-3 million deaths annually[1-2]. Most deaths occur due to severe malaria with one or more complications in a patient with Falciparum infection. Transmission of malaria to the host depends on infection of the sporozoites in the liver[3-4]. Malaria sporozoites are injected into the blood once by the bite of female Anopheles mosquitoes, binding to hepatocytes via the thrombospondin receptor and properdin. Here sporozoites mature or become hidden hypnosis, creating tissue patterns[5-6]. Tissue patterns increase the infection by producing a large number of merozoites (from 10,000 to 30,000). Any merozoite released from the liver can attack human red blood cells and form asexual replication cycle in this red blood cell with the release of 24 to 32 merozoites at the end of the 48-72 hour asexual cycle[7]. Malaria causes liver abnormalities, but opinions on the clinical significance of this damage vary. Liver involvement in malaria is common in patients with severe malaria and jaundice, liver enlargement and elevated liver enzymes such as aspartate and alanine transaminase. There are many factors that cause severe anemia in malaria like hemolysis, bone marrow dysfunction etc. Essentially unbound hyperbilirubinemia is a common feature of malaria falciparum and is caused by hemolysis of parasitic and non-parasitic erythrocytes and partly liver damage[8]. Although hyperbilirubinemia is caused by an increased mortality from malaria, it is often associated with other complications such as acute renal failure or cerebral malaria. Alanine aminotransferase catalyzes reactions in which the building blocks of the protein (amino acid) are transferred from the donor molecule to the receptor molecule that occurs mainly in the liver[9-10]. Therefore, serving as a marker for liver damage, aspartate aminotransferase is found in a variety of tissues, including the liver, muscles, heart, kidneys and brain. It increases when any of these tissues is damaged. Therefore, this is not a very specific indicator of liver damage[11]. This study was conducted to observe a correlation between liver enzymes and bilirubin in patients with malaria Plasmodium falciparum.

PATIENTS AND METHODS:

This study was conducted at the Department of Pathology, Sir Gangaram Hospital, Lahore for one year duration from March 2019 to March 2020. A total of 81 uncomplicated and symptomatic patients (confirmed by thick and thin slip) were selected. Nine patients were positive for hepatitis B and hepatitis C and were therefore excluded from the study. The remaining 72 patients were included in the study. The inclusion criteria for patients of all ages and sexes with all symptoms were confirmed by thick and thin film. A detailed history was collected and a full physical examination was performed. Exclusion criteria. Patients with fever with or without stiffness, but negative for malaria interference. People with jaundice for reasons other than malaria. Those who take hepatotoxic drugs or pregnant woman were excluded. About 5 ml of venous blood was drawn through the vein of the elbow and fractionated by a single-use syringe: another tube containing EDTA for hemoglobin and hematocrit, while another 1 ml of blood was transferred to a tube containing 1 ml of citrate. A small drop of blood was also placed on the meter strip (Optium, Abbott) to randomly check blood sugar levels. Blood tubes were allowed to clot and then pipetted after centrifugation of the serum, labeled and stored in the freezer at -20 ° C for further analysis. Selected patients were grouped by species type and disease duration. Group I: Plasmodium falciparum positive and disease lasting from 1 to 7 days. Group II: Plasmodium falciparum positive and disease lasting 8 to 20 days. Group III: Plasmodium vivax positive and disease from 1 to 20 days. The level of hemoglobin in the blood was calculated by the Cynamet hemoglobin method, hematocrit values were calculated by the Microhaematocrit method, serum bilirubin method (total, direct and indirect) and by the method of Jendrassik Groff. Serum glutamate pyruvate transaminase, serum glutamate oxaloacetate transaminase and alkaline phosphatase were estimated by enzymatic method. Biochemical parameters were compared between three groups. A correlation between bilirubin and liver enzymes was observed using regression analysis using SPSS version 10, with a significant P value less than 0.05.

RESULTS:

The total number of patients included in the study was 72. Patients from all age groups and both sexes were included. They were divided into three groups. Group I (Plasmodium falciparum + and disease lasting from 1 to 7 days): the total number of patients in this group is 24 years. The age range is 3-56 years and the average age is 25.2 ± 3.33. 14 (58.3%) were men and 10 (41.7%) were women. In the peripheral blood smear study, gametocytes were observed in 2 (8.3%) cases, rings or trophozoites in 22 (91.7%) cases. The liver was palpable in 7 (29.2%) patients, while the spleen was palpable in 3 (12.5%) patients. Group II: (including 24 positive cases of Plasmodium falciparum with a disease duration of 8-20 days. Their age ranged from 5 to 50 years. The average age was 24.7 (16.7%) cases, while ringtocyte was observed during the game in a circle.20 (83.3%) patients were trophozoites, 19 (%) 79.2) the patient may be palpated in the liver, sub-epidermis and spleen in 20 (83.3%) patients. Group III: (24 Plasmodium vivax, the disease ranges from

1 to 20 days. SD was ± 2.75 years. 15 (62.5%) men and 9 (37.5%) cases were women. Examination of the peripheral blood smear showed that in 6 (25%) cases gametocyte forms were present and in 18 (75%) ring or trophozoite forms. The liver can be felt in 2 (8.3%) cases, and the spleen in 4 (16.7%) cases. There was a statistically significant difference in liver and spleen size at P <0.001.

Table 1: Comparison of Biochemical Parameters between Groups of Plasmodium Falciparum and Plasmodium Vivax Malaria

Biochemical Parameters	**P. Falciparum**		**P. vivax**	**P value**
	Group I (n=24)	**Group II** (n=24)	**Group III** (n=24)	
	Range(Mean ± s.e.m)	Range(Mean ± s.e.m)	Range(Mean ± s.e.m)	
Bilirubin – Total (mg/dl)	0.63 - 2.89 (1.4±0.13)	3.34 – 19.12 (7.1 ± 0.83)	0.30 – 3.9 (1.6 ± 0.17)	0.001***
Direct (mg/dl)	0.20 - 1.60(0.6 ±0.07)	1.20 – 10.56 (3.1 ± 0.49)	0.08 – 2.00 (0.7 ± 0.11)	0.001***
Indirect (mg/dl)	0.41 - 1.87(0.8± 0.08)	0.32 – 8.56(4.0 ± 0.43)	0.20 – 2.00 (0.9 ± 0.10)	0.001***
SGPT (U/L)	15 - 46 (27.5 ± 1.59)	34 – 210(67.9 ± 7.72)	28 – 44 (35.4 ± 1.10)	0.001***
SGOT (U/L)	20 - 38 (27.2 ± 1.19)	30 – 100(52.1 ± 4.21)	25 – 40 (32.9 ± 0.95)	0.001***
Alkaline Phosphatase (U/L)	98 - 340 (248 ± 11.6)	260 – 480 (352 ± 10.7)	100 – 603 (273 ± 27.1)	0.001***

Table 1 shows the difference in the results of the mean bilirubin values: total, direct, indirect, SGPT, SGOT and alkaline phosphatase. Table 2 shows the correlation coefficient between bilirubin and hemoglobin, SGPT, SGOT and alkaline phosphatase in three groups. In group I, especially SGPT and alkaline phosphatase enzymes show a statistically significant positive correlation with bilirubin, respectively (r = 0.50 and r = 0.54).

Table 2: Correlation Coefficient (r) among bilirubin and biochemical parameters

Biochemical Parameters	**Group I P. falciparum <7 days**	**Group II P. falciparum >7 days**	**Group III P. vivax 1 to 20 days**
Haemoglobin (g/dl)	- 0.13	- 0.59*	- 0.46
SGPT (U/L)	0.50*	0.88**	0.82**
SGOT (U/L)	0.24	0.75*	0.63*
Alkaline Phosphatase (U/L)	0.54*	0.62*	0.69*

Hemoglobin shows a weak negative correlation with bilirubin. Hemoglobin shows a statistically negative correlation (r = -0.59; P <0.05), SGPT shows an excellent positive correlation (r = 0.88; P <0.01), SGOT and alkaline phosphatase show a statistically significant positive correlation. Transaminases and alkaline phosphatase show a statistically significant positive correlation r = 0.82, 0.63 and 0.69, respectively.

DISCUSSION:

Of the four malaria species, Plasmodium vivax is the most common species in Pakistan, followed by Plasmodium falciparum. Malaria attacks the liver, where infectious sporozoites attack and multiply in hepatocytes and at the stage of red blood cells, merozoites cause the destruction of infected red blood cells. Molyneux et al. It is suggested that deep jaundice is often accompanied by a moderate increase in liver enzymes and is caused by hemolysis rather than liver damage[11]. The study was conducted to assess acute liver damage caused by malaria falciparum. In addition, cases infected with Plasmodium vivax were included in the comparative analysis. History has shown that the subjects are more cases of acute malaria than chronic. In acute malaria, both liver and spleen enlargement are caused by reticulo-endothelial cell hyperplasia[11]. In this study, the liver was enlarged in 28 (38.9%) patients in the range of 0.5 cm to 4.0 cm, the spleen was palpable in 27 (37.5%) patients. It ranges from 0.5 cm to 3.0 cm. In malaria, low hemoglobin may

be due to acute hemolysis or destruction of infected and uninfected red blood cells, dys-erthropoiesis and nutritional deficiencies[12]. Table 2 shows the anemic picture (<10 g / dl) of the hemoglobin level, group I and group II, respectively, with an average of 9.2 g / dl and 9.5 g / dl. These findings are consistent with Bhalli and Samiullah, but Nadeem et al. As reported, the average hemoglobin level does not coincide with 13.78 g / dl. The mean hemoglobin value has an excellent positive correlation with hematocrit in both groups. Anemia and hyperbilirubinemia (mainly unconjugated) are common features of malaria falciparum and are associated with the hemolysis of parasitic and non-parasitic erythrocytes.[13] In this study, 64.3% of the cases in which the level of hemoglobin correlated with bilirubin showed hyperbilirubinemia, showed a significant negative correlation with the unconjugated type of hyperbilirubinemia, reflecting mild to moderate anemia. Coagulation abnormalities in Falciparum infection are not uncommon and impaired coagulation is associated with the severity of the disease. Increased serum liver enzymes, transaminases (SGOT and SGPT), and alkaline phosphatase levels are markers of liver damage. SGPT (ALT) is a liver-specific enzyme. In this study, SGPT and SGOT increased in group II. These enzymes did not increase in patients with Plasmodium vivax group III positive and showed statistically significant differences in mean values ($p < 0.001$)[14]. These results overlap with the Premaratna results. Similarly, SGPT and SGOT showed a correspondingly good negative correlation coefficient $r = -0.63$ and $r = -0.53$ ($p < 0.01$), compared to hemoglobin, while SGPT showed an excellent positive correlation coefficient ($r = 0.88$ and $r = 0.82$) relative to bilirubin. In II and group III ($P < 0.01$). An increase in serum alkaline phosphatase indicates that the leakage of this enzyme into the membranes of the liver drainage system is a potentially important biomarker to assess the integrity of this system during malaria infection[15]. The results of the difference in the average value of this enzyme are very important when comparing group I and group II patients infected with plasma falciparum. This finding is related to the results of Garba and Ubom.

CONCLUSION:

The results of our study provide valuable information and a relationship between liver biochemical disorders in patients with Falciparum malaria. This test was performed on a small sample and contains basic information on these issues, therefore we recommend performing the same type of tests on large samples and performing liver function tests with early diagnosis. Treatment of malaria infection Plasmodium falciparum to prevent complications and reduce mortality.

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