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ASSOCIATION OF BILIRUBIN LEVELS WITH LIVER ENZYMES IN FALCIPARUM MALARIA AFFECTED PATIENTS

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Abstract:

Introduction: *Malaria Falciparum is responsible for 1-3 million deaths worldwide each year. Liver involvement is common and may occur as high serum bilirubin, liver enlargement and high liver enzymes. Unconjugated hyperbilirubinemia has often been shown to increase 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 malaria Plasmodium falciparum.*

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

Project: *A Descriptive study*

Place and duration of the study: *In the Medicine department of Akhtar Saeed Trust Teaching Hospital, Lahore for one year duration from January 2019 to January 2020.*

Materials and methods: *81 patients of both sexes and acute malaria were selected by appropriate sampling. Nine patients with hepatitis B and C infection were excluded from the study. In the remaining 72 cases, 48 (70%) had Plasmodium falciparum infection and 24 (30%) had Plasmodium vivax infection. Falciparum infected patients were divided equally into two groups depending on the duration of the disease. Group I lasted from 1 to 7 days, group II from 8 to 20 days. Patients with Plasmodium vivax infection lasted from 1 to 20 days and were placed in group III.*

Results: *Group I showed a statistically significant positive correlation with SGPT and alkaline phosphatase bilirubin ($r = 0.50$ and $r = 0.054$), and SGPT showed excellent 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, while in group III both transaminase and alkaline phosphatase showed a statistically significant positive correlation $r = 0$, 82, 0.63 and 0.69.*

Conclusion: *A positive correlation between liver enzymes and bilirubin suggests that an early diagnosis of Plasmodium falciparum malaria infection should be made to prevent complications and reduce mortality.*

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

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INTRODUCTION:

Malaria, an important public health issue in the tropics, is responsible for the transmission of 300-500 million people and 1-3 million deaths annually. Most deaths occur due to severe malaria, which has one or more complications in a patient with Falciparum infection. The transmission of malaria to humans is determined by infection of the sporozoites in the liver. Malaria sporozoites bind to hepatocytes once by the bite of female Anopheles mosquitoes and their receptors and thrombospondin properties. Here sporozoites ripen to form tissue patterns or become latent hypnosis. Tissue models increase infection, producing a large number of merozoites (from 10,000 to 30,000). Any merozoite released from the liver can release 24-32 merozoids at the end of the 48-72-hour asexual cycle, attacking human red blood cells and forming asexual replication cycle in these red blood cells. However, malaria causes liver abnormalities; Opinions differ in the clinical significance of this injury.

Liver involvement in malaria is common in severe malaria and jaundice, liver enlargement, and liver enzymes such as aspartate and alanine transaminase. There are many factors that cause severe anemia in malaria. Hemolysis, bone marrow dysfunction etc. Is proportional to the level of interference. Mainly unconjugated hyperbilirubinemia is a common feature of malaria falciparum and is caused by hemolysis of parasitic and non-parasitic erythrocytes and partly liver damage. Although hyperbilirubinemia is caused by increased malaria mortality, it is often associated with other complications such as acute renal failure or cerebral malaria. Alanine aminotransferase catalyzes reactions in which protein building blocks (amino acids) are transferred from the donor molecule to the acceptor molecule. It is mainly visible in the liver. Therefore, as a sign of 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 fairly specific indicator of liver damage.

Increased serum alkaline phosphatase activity in patients indicates that the hepatic stage of falciparum malaria infection is accompanied by impaired drainage pathways of the host hepatocytes and damage to the hepatocytic membrane. leakage of this enzyme from liver cells. This study was conducted to observe a correlation between liver enzymes and bilirubin in patients with malaria Plasmodium falciparum.

PATIENTS AND METHODS:

The study was conducted at the Medicine department of Akhtar Saeed Trust Teaching Hospital, Lahore for one-year duration from January 2019 to January 2020. A total of 81 uncomplicated and symptomatic patients (confirmed by thick and thin slip methods) were selected. Nine patients were positive for hepatitis B and hepatitis C. The remaining 72 patients were enrolled.

Accept the terms

All symptomatic patients of all ages and sex were included in the study, whose diagnosis was confirmed by a thick, thin smear film. A detailed date was developed and a full physical examination was performed.

Exclusion criteria

1. Patients with fever with or without stiffness, but negative in the case of malaria intervention.
2. People with jaundice for reasons other than malaria.
3. Those who take hepatotoxic drugs.
4. Mixed patients with malaria infection.
5. Pregnant women.
6. Serological tests, if any patient has had positive tests for hepatitis.

About 5 ml of venous blood was drawn from a vein into the elbow of a disposable syringe and separated as follows:

During the prothrombin period, one ml of blood was transferred to a tube containing citrate, and 1 ml of other blood was transferred to another tube containing EDTA to assess hemoglobin and hematocrit. 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, labeled and stored in a freezer at -20 ° C for further analysis after centrifugation of the serum. Selected patients were grouped by type and duration of illness.

Group I: Plasmodium falciparum positive and lasting from 1 to 7 days.

Group II: Plasmodium falciparum positive and lasting from 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 Jendrassik Groff method in a micro-hemocrit, and serum bilirubin (total, direct and indirect) was determined. 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 with SPSS version 19 was observed with a significant P value less than 0.05 based on regression analysis.

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 + ve with disease from 1 to 7 days):

The total number of patients in this group is 24. Their age was 3-56 years, their average age was 25.2 ± 3.33, 14 were men (58.3%) and 10 were women (41.7%). In the study with peripheral blood smears, gametocytes were observed in 2 (8.3%) cases, rings or trophozoites in 22 (91.7%) cases. The liver was felt in 7 (29.2%) patients and the spleen in 3 (12.5%) patients.

Group II: (including 24 positive cases of Plasmodium falciparum with disease duration from 8 to 20 days. Their age ranged from 5 to 50 years. The average age was 24.7 ± 2.71 SD. 16 (66.7%) men and 8 (33.3%) women, peripheral blood test. During the study 4 (16.7%) cases with gametocyte, 20 (83.3%) cases with rings or trophozoites were observed.

Group III: (24 cases of Plasmodium vivax + and diseases from 1 to 20 days). The age is 3.5 to 50 years and the average age is 23.3 ± 2.75 years SD. 15 (62.5%) are men and 9 (37.5%) are women. Examination of the peripheral blood membrane showed that gametocyte forms and 18 (75%) ring or trophozoite forms occurred in 6 (25%) cases. 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: 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*

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). Hemoglobin has 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.

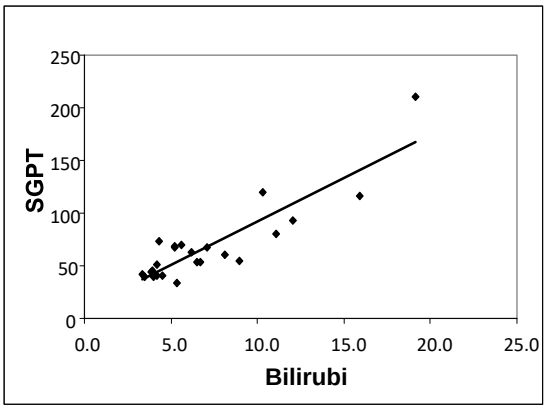

Figure1: **Correlation Coefficient of bilirubin and SGPT in Group II**

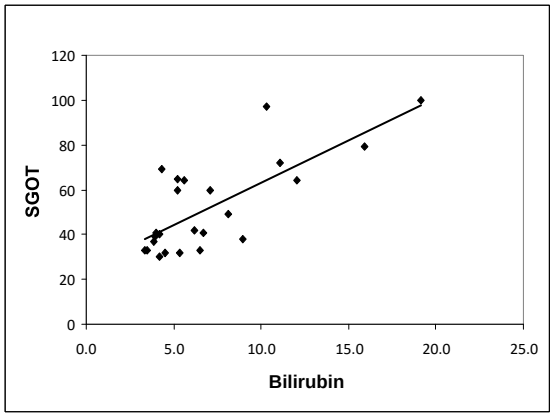

Figure 2: Correlation Coefficient of bilirubin and SGOT in Group II

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 hepatocytes, and at the red blood cell stage, merozoites cause the destruction of infected red blood cells. Molyneux et al. Deep jaundice is often accompanied by a moderate increase in liver enzymes and is caused by haemolysis rather than liver damage.

The study was conducted to assess acute liver damage caused by malaria falciparum. Plasmodium vivax infected cases were also included in the comparative analysis. History has shown that subjects are more severe than chronic malaria.

In acute malaria, both enlarged liver and spleen are caused by reticulo-endothelial cell hyperplasia. In this study, the liver was enlarged in 28 (38.9%) patients in the range 0.5 cm to 4.0 cm, and the spleen could be affected in 27 (37.5%) patients in the range 0.5 cm to 3 , 0 cm. Clinically pale reflects low hemoglobin. Low hemoglobin in malaria can be the result of acute hemolysis or destruction of infected and uninfected red blood cells, dystropoiesis and nutritional deficiencies. Table 2 shows anemic (<10 g / dl) hemoglobin, group I and group II levels, 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 correspond to 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. In this study, 64.3% of the cases where bilirubin-related hemoglobin levels showed hyperbilirubinemia showed a significant negative correlation with a type of unconjugated 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 indicators 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 ($p < 0.001$). These results

overlap with the Premaratna results. Similarly, while SGPT and SGOT showed a good negative correlation coefficient r = -0.63 and r = -0.53, respectively (p <0.01), compared to hemoglobin, the SGPT group was associated with excellent positive correlation coefficient. (r = 0.88 and r = 0.82). In II and group III (P <0.01). An increase in serum alkaline phosphatase indicates that 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. When comparing patients from group I and group II infected with plasma falciparum, the results of the difference in the mean value of this enzyme are very important. This finding is related to the results of Garba and Ubom.

CONCLUSION:

The results of our study show a relationship between valuable information and biochemical liver disorders in patients with malaria Falciparum. This test was performed on a small sample, and because it contains basic information about these problems, we recommend performing the same type of test on large samples and performing liver function tests with early detection of infection. Plasmodium falciparum must be diagnosed to prevent malaria complications and reduce mortality.

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