CORRELATION OF BILIRUBIN WITH LIVER ENZYMES IN PATIENTS OF VIVAX MALARIA
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ABSTRACT: Plasmodium vivax is the most common human malarial parasite of the four species affecting humans. Liver involvement is common and may manifest as raised serum bilirubin, hepatomegaly and elevated liver enzymes. Unconjugated hyper bilirubinemia is usually seen leading to increased mortality. Alanine aminotransferase (SGPT) is a marker of liver damage. The present study was conducted on Plasmodium vivax patients to observe the correlation coefficient of bilirubin with liver enzymes (Transaminases and Alkaline Phosphatase). The present study was conducted in the Department of Biochemistry, VIMS & RC white field, Bangalore. This study was conducted on 40 confirmed Plasmodium vivax patients. Serum bilirubin and liver enzymes were measured by using auto analyzer Beckman coulter DXC600. Transaminases (AST, ALT) and Alkaline phosphatase showed a statistically significant positive correlation \( r = 0.469, r = 0.029 \) & \( r = 0.371 \) respectively with bilirubin \( (P<0.05) \). Positive correlation of liver enzymes and bilirubin shows that liver function tests should be performed along with early diagnosis of Plasmodium vivax infections in order to prevent complications and to reduce mortality.

KEYWORDS: Malaria, liver enzymes, bilirubin, Plasmodium vivax.

INTRODUCTION: Malaria is responsible for 1-3 million deaths annually and 300-500 million infections worldwide.\(^1\) At present, about 109 countries in the world are considered endemic for malaria, 45 countries within the WHO African region. Karnataka is one among the most affected states and Bangalore is one of the 15 major cities including 4 metropolitans account for nearly 80% of malaria cases covered under urban malaria control schemes.

Malaria in man is caused by four distinct species of the malaria parasite – P. vivax, P. falciparum, P. malariae and P. ovale.\(^2\) In India, 60-65% cases of malaria are due to Plasmodium vivax and 30-35% cases are due to Plasmodium falciparum.\(^3\) Malaria is one of the commonest parasitic diseases characterized by febrile paroxysm occur with definite intermittent periodicity repeating every third or fourth day depending upon the species of the parasite involved.\(^2\) Malarial transmission to the human host is established by sporozoites infection to the liver.\(^4\) The malarial sporozoites once injected in blood by the bite of female Anopheles mosquitoes are attached to hepatocytes through receptor for thrombospondin and properdin.\(^5\)

Here these sporozoites become mature to form tissue schizonts or become dormant hypnozoites. Tissue schizonts amplify the infection by producing large number of merozoites \((10,000 \text{ to } 30,000)\). Each merozoite released from the liver is capable of invading a human red blood cell and establishing the asexual cycle of replication in that red cell with the release of 24 to 32 merozoites at the conclusion of 48 to 72 hours asexual cycle.\(^6\) Malaria causes abnormalities in the liver however; opinions differ about the clinical importance of this damage.\(^7\)
MATERIALS AND METHODS: Study Centre and period: This duration based study was done from January 2012 to March 2013 in Department of Biochemistry, VIMS & RC, Bangalore.

SUBJECT SELECTION: Patients selection was done by simple random sampling from those presenting at VIMS & RC, Bangalore, with a history of fever, chills and malaise & who were subsequently confirmed to be Plasmodium vivax positive by Geimsa stained peripheral blood film. Based on the following selection criteria 40 patients were selected. Consent was sought and obtained.

EXCLUSION CRITERIA: Patients on self-medication with any anti-malarial drugs prior to presentation and patients with any type of liver disease & pregnant woman were excluded from the study.

SPECIMEN COLLECTION AND ASSAY: 5ml of venous blood sample was taken by aseptic precaution. Samples were centrifuged and serum AST, ALT, ALP & TB were measured by using auto analyzer Beckman Coulter Synchron DxC by using Beckman Coulter Kits (USA).

STATISTICAL ANALYSIS: The data obtained were analyzed & correlation co-efficient between bilirubin and liver enzymes was observed by applying regression analysis using SPSS version 10, taking P value significant when less than 0.05.

RESULTS: From Table 1: Transaminases (AST, ALT) and Alkaline phosphatase showed a statistically significant positive correlation ($r = 0.469$, $r = 0.340$ & $r = 0.371$) respectively with bilirubin ($P<0.05$). Graph 1 & Graph 2 shows the correlation coefficient of bilirubin with SGOT & SGPT respectively.

Graph 1: correlation coefficient of bilirubin with SGOT in Plasmodium vivax infected patients.
**DISCUSSIONS:** Malaria is a mosquito-borne tropical disease caused by the Plasmodium species of protozoa. It affects mainly the hepatocytes and red blood cells (RBCs) and manifests clinically as fever and splenomegaly.\(^8\)

Liver dysfunction: Mild hemolytic jaundice is common in malaria, severe jaundice is associated with P. falciparum infections, is more common among adults than among children and results from hemolysis, hepatocytic injury and cholestasis. When accompanied by other vital organ dysfunction (often renal impairment) liver dysfunction carries a poor prognosis. Hepatic dysfunction contributes to hypoglycemia, lactic acidosis and impaired drug metabolism. The hemolysis results from the invasion of the erythrocytes by malarial parasites. P. malariae is known to invade mature RBCs, whereas P. vivax and P. ovale are known to invade young RBCs. P. falciparum parasites are capable of invading RBCs of any age and hence can lead to very high levels of parasitemia; while parasitemia is limited in all other types of Plasmodium infections.\(^9\)

A transient derangement of liver function is a common feature of childhood malaria, and hepatic dysfunction takes place to a significant degree even in P.vivax.\(^{10}\) Malaria parasites avoid the
immune system when they move from the liver to the red blood cells (RBC). Malaria parasites move to liver after entering the human body and changes into a new form that can infect RBC and begin to reproduce. The parasites kill the liver cell they occupy and detach from its neighbor.\(^{(11)}\)

In vivax malaria only 33.3% had conjugated hyperbilirubinemia & 55.5% had mild jaundice with unconjugated hyperbilirubinemia. This can be explained by hemolysis rather than hepatocytic dysfunction.\(^{(12)}\) In extensive study done by Marcela Echeverri et al, from Colombia on 104 patients with vivax malaria, it was revealed that 20% of the jaundiced patients had high levels of indirect bilirubin in contrast to only 6% patients showing high direct bilirubin levels.\(^{(13)}\) The serum transaminases in vivax malaria patients were found to be 2-3 times more than the upper limit of normal.\(^{(14)}\)

**CONCLUSION:** Positive correlation of liver enzymes and bilirubin shows that liver function tests should be performed along with early diagnosis of Plasmodium vivax infections in order to prevent complications and to reduce mortality.

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Date of Submission: 01/11/2014.
Date of Peer Review: 03/11/2014.
Date of Acceptance: 06/11/2014.
Date of Publishing: 08/11/2014.