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EFFECT OF PLASMODIUM VIVAX MALARIA ON LIVER FUNCTION

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Abstract:

Objective: The present study was conducted on malaria patients with plasmodium vivax infection to see the effect on liver functions and correlation between liver enzymes (SGOT & SGPT) and bilirubin

Material & Methods: The study population contained 114 subjects divided into two groups, 64 malaria patients and 50 healthy control subjects of varying age groups and both sex. All biochemical parameters Total bilirubin, Direct bilirubin, Indirect bilirubin, SGOT (aspartate transaminase), SGPT (alanine transaminase) & were analyzed by semiautoanalyser. Statistical analysis was done by , science (SPSS 21) Software

Results: In our study we have found that (Mean ± SD) of Total serum bilirubin in malaria patients were 1.41±1.56 & controls were 0.28±.038, Direct bilirubin in malarial patients were 0.48±0.43 & control were 0.13±0.031, Indirect bilirubin in malarial patients was 0.93±1.29. We observed that (Mean ±SD) of SGOT in malaria patients was 46.91±31.38 & in control were 22±5.22, the level of SGPT in malarial subjects were 35.61±19.41 & control subjects were 16±3.12. We observed statistically significant increase in levels of enzymes SGOT, SGPT and bilirubin in malarial patients ($p<0.001$) as compared to controls. Both the amino transferases (AST & ALT) did not show statistically significant positive correlation with bilirubin ($p>0.05$).

Conclusion: Our study indicates that liver enzymes SGOT & SGPT significantly increases in malaria patients with plasmodium vivax infection as compared to control subjects therefore these enzymes may be useful in diagnosis of malaria subjects.

Keyword: Plasmodium vivax, Malaria, Liver function

Introduction:

Malaria is a febrile illness caused by protozoa of the genus plasmodium, transmitted to human by the bite of infected female anopheles mosquito. There are mainly four species of Plasmodium Vivax, P. Falciparum, P. Ovale and P. Malaria. A fifth species P. Knowlesi, a zoonotic malaria parasite, is an important cause of malaria in parts of Southeast Asia, but not reported in India.[1] Malaria is responsible for infecting 300-500 million and 1-3 million deaths annually.[2] 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.[3]

In India, the epiodemiology of malaria is complex because of geo-economical diversity, multiethnicity and wide distribution of nine anopheline vectors transmitting three Plasmodial species: P. falciparum, P. vivax and P. malariae. Anopheles culcifacies is widely distributed and is the principal vector of rural malaria. The proportion of P. vivax and P. falciparum

varies in different parts of India. Mostly indo-gangatic plains and northern hilly states, north-western India and southern Tamil Nadu state have < 10% p. falciparum and rests are p. vivax infections. In the forested area inhabited by the rthnic tribes, the situation is reversed with p. falciparum proportion 30-90% whereas in the remaining areas it is between 10-30%.[4, 5]

P. falciparum infection in India is a major cause of severe and complicated malaria, but with the implementation of molecular diagnosis, it has become evident that P. vivax mono infection could also result in multiple organ dysfunction and severe life-threatening disease, like P. falciparum infection.[6] large studies from Indonesia, Papua new guinea, Thailand and India now show a strong association between P. vivax infection and severe disease and death. So there is a recent changing trend of benign behavior of P. vivax to malignant behavior.

Malarial transmission to the human host is established by sporizoites infection to the liver. The malarial sporozoite once injected into the blood by the bite of female anopheles mosquitoes is attached to the hepatocytes through the receptor for thrombospondin and properdin. Here these sporozoites become mature to form tissue schizonts or become dormant hypnozoites. Tissue schizoints amplify the infection by producing large number of merozoites.[7] Merozoite infects and ruptures the liver cells in an attempt to escape back into the circulation and continues the infection. The infection of liver cells by the sporozoites form of the malarial parasite can cause organ congestion, sinusoidal blockage and cellular inflammation. These changes in hepatocytes can lead to the leakage of parenchymal (transaminases) enzymes of the liver to the circulation. Hence increase in liver enzymes AST & ALT observed in malaria infected patients also demonstrated that the serum activities of these liver enzymes increased with the increase in malarial parasite density and confirmed that the hepatic stage of the parasite's life cycle in human host is accompanied by significant perturbation in the hepatocyte's parenchyma and membrane leading to leakage of liver enzymes into the general circulation.[8,9] Jaundice is also one of the common manifestations of severe malaria in adults causing high mortality rate and incidence of jaundice vary from 10-45% in different regions.[4]

P. vivax infection is common in children and pregnant woman.[10] Pregnant women are also especially vulnerable. Susceptible groups are children and adults who have lost or never acquired immunity. Morbidity and mortality due to malaria have remained unabated primarily as a result of the unavailability of suitable vaccines and the spread and intensification of drug resistant Plasmodium parasites. In severe vivax malaria, the various complications were thrombocytopenia (89%), renal (33%), hepatic (19%), cerebral (08%), metabolic acidosis (04%), and pulmonary (01%).[11] Thus it is rational to assess the current status of malaria related complications in order to estimate the burden among biologically risked groups, children and endemic areas.

Materials and methods

The subjects included in the study were 64 clinically diagnosed patients suffering from P. vivax malaria of both sex and varying age groups, attending the out-patients department (OPD), emergency ward and from indoor patients, from K.D. Medical College Hospital & Research Center, Mathura (U.P.) Fifty healthy controls were selected for the study from volunteers such as paramedical staff, healthy relatives / attendants of patients. The patients comprised 38 males and 26 females. The control group comprised of 28 males and 22 females.

Patients selection criteria: Patients with the following conditions; pregnancy, renal diseases, liver diseases including cirrhosis, hepatitis, obstructive jaundice, alcoholism, cancer, metabolic bone diseases, gastrointestinal tract infection, protein energy malnutrition, diabetes, heart failure, infectious mononucleosis and magnesium / vitamin D deficiencies, were excluded from the study. This is because these conditions are associated with significant changes in serum alanine and aspartate transaminases activities. Similarly, patients on self-medication with any antimalarial drug prior to presentation were also excluded from the study. Blood samples were collected by clean veinpuncture and centrifuged. Sera was collected and analysed for serum bilirubin and enzyme activity of SGOT & SGPT using kit method by erba chem semiautoanalyzer.

Statistical analysis

Statistical analysis was done, using the statistical package for social science (SPSS 21) for Windows Software. Differences in the parameters between the groups were analyzed by means of the t test. Variables were presented

as mean ± standard deviation (S.D.). The accepted level of significance for all statistical analyses used in the study was $P \leq 0.05$.

Results

Level of serum bilirubin and liver enzymes (SGOT, SGPT) were increased in the patient with malaria infection as campared to the controls and the increase was statistically highly significant ($p<0.001$). (Table-1)

Table-1: Comparison of serum bilirubin and liver enzymes among controls and malaria patients

Variables	Controls	Malaria Patients	P value
Total Bilirubin (mg/dl)	0.28±.038	1.41±1.56	0.0001
Direct bilirubin (mg/dl)	0.13±0.031	.48±0.43	.0001
Indirect bulirubin (mg/dl)	0.15±0.012	.93±1.29	.0001
SGOT (IU/L)	22.31±5.22	46.09±31.37	.0001
SGPT (IU/L)	16.84±3.12	35.62±19.440	.0001

Significant increase in serum bilirubin & liver enzymes was obtained in malaria female patients as compare to the control (Table-2)

Table-2: Comparison of serum total bilirubin and liver enzymes among female controls and female malaria patients

Parameters	Controls	Test	P value
Total Bilirubin (mg/dl)	0.27±0.04	1.09±1.26	0.011
Direct bilirubin (mg/dl)	0.13±0.03	0.44±0.54	0.020
Indirect bulirubin (mg/dl)	0.16±.01	0.64±0.82	0.020
SGOT (IU/L)	21.01±5.2	48.07±32.69	.0002
SGPT (IU/L)	16.07±3.2	33.67±18.82	0.001

Significant increase in bilirubin and hepatic enzymes levels was obtained in malaria male patients as compared to the controls (Table-3)

Table-3: Comparison of serum total bilirubin and liver enzymes among male controls and male malaria patients

Parameters	Controls	Test	P value
Total Bilirubin (mg/dl)	0.30±0.03	1.67±1.75	0.001
Direct bilirubin (mg/dl)	0.14±0.02	0.53±0.34	0.0001
Indirect bulirubin (mg/dl)	0.17±0.01	1.18±1.56	0.005
SGOT (IU/L)	22.56±5.3	44.44±30.88	0.002
SGPT (IU/L)	17.56±3.04	37.21±20.15	0.0001

Significant difference was not obtained in liver function parameters

Table-4: Comparison of serum total bilirubin and liver enzymes among male and female malaria patients

Parameters	male	female	P value
Total Bilirubin (mg/dl)	1.56±1.72	1.09±1.26	0.354
Direct bilirubin (mg/dl)	0.46±0.21	0.46±0.52	0.941
Indirect bulirubin (mg/dl)	1.12±1.61	0.65±0.82	0.267
SGOT (IU/L)	48.38±32.67	48.07±32.69	0.974
SGPT (IU/L)	37.53±19.66	33.66±18.82	0.502

Statistically significant positive correlation could not be established with liver enzymes and serum total bilirubin. (Table-5)

Table-5: Pearson correlation coefficient among bilirubin and liver Enzymes

Enzymes	Total Bilirubin	P Value
SGOT	0.015	0.463
SGPT	0.094	0.553

Discussion

Investigations into the effects of Plasmodium parasites on the levels of serum enzymes have gained recognition as an important area of research in the pathogenesis of malaria. Malaria involves the liver where infective sporozoites invade and multiply in the hepatocytes and in the erythrocyte stage the merozoites cause the destruction of infected red blood cells.[12] Malyneux et al suggested that jaundice, which may be deep, is usually accompanied by only moderate elevation of hepatic enzymes and results more from

hemolysis than from hepatic damage.[13] The role of liver injury or hepatocellular damage in the malarial patients has been proposed by many workers especially in the Indian subcontinent. Raised serum bilirubin, hepatomegaly along with increase in liver enzymes are important denominator of liver injury in these patients.[14]

P. vivax was widely believed to be incapable of causing cytoadherence and microvascular sequestration as seen in P. falciparum infection and therefore unable to cause organ dysfunction. Recent observations have shown evidence of sequestration of parasite in lung vasculature during evaluation of lung injury in p. vivax malaria. Cerebral dysfunction of P. vivax malaria may occur through generation of nitric oxide.[15] cytokines and leukotriennes may be responsible for severe anemia and hemostatic complications. A few study clearly demonstrated that clinical severity of vivax malaria infection is strongly associated with potent activation of proinflammatory response and cytokines imbalance. Plasma tumor necrosis factor (TNF) which is related to P. vivax paroxysm was higher according to infection severity.[16] Interferongamma (IFN) is also implicated in both resistance to malaria and disease immune pathology.

In our study, level of serum total bilirubin ranged from 0.31-7.33 mg/dl. Mean serum total bilirubin was significantly higher as compared to controls ($p<0.001$). Out of 64 malarial patients, 19.04% had increased serum total bilirubin level. Of these 75% patients had mild jaundice (2-5 mg/dl), 25% had moderate jaundice (5-10 mg/dl) and 0% had severe jaundice (>10mg/dl). Our finding was in accordance with Kocher *et al* who showed that 70.6% of children suffering from malaria (p. vivax) had mild jaundice where moderate and severe jaundice was present in 23.5% and 5.9% of the children respectively.[17] Patwari *et al* observed jaundice in only 8.7% on p. vivax malarial cases.[18]

We observed statistically significant increase in levels of enzymes SGOT & SGPT in malarial patients ($p<0.001$) as compared to controls. These enzyme activities were also significantly higher in test males and test females as compared to their respective controls ($p<0.01$). But we could not find the significant difference in the mean enzyme activities in both male and female malarial patients ($p>0.05$). Our finding was supported by that of Jigam AA et al. According to them transaminases and ALP activities were significantly higher in patient groups but when com ($p<0.05$).[19] Mohmad Ali et al showed increased activities of SGOT, LDH, ALP and CPK in patients with P. vivax malaria where in cases of P. falciparum malaria, enzymes ALP, SGOT and CPK activities decreased and LDH activity increased significantly1. The increase in serum levels of hepatic enzymes; transaminases are the markers of liver damage. SGPT is a specific enzyme of liver. In this study we found that serum SGOT & SGPT levels were increased in 31% & 19% of the malarial patients. The mean level of AST was higher than that of ALT. It was similar to the findings of Kocher et al[17]. Study of Noppadon et al showed that AST levels were increased in 26% of P vivax infection, 31% of P. malariae infection and 40% of P. ovale infection. Similarly, increased ALT levels was observed in 21% P vivax, 30% P. malariae and 40% of P. ovale infections.ALP was increased in 20%, 22% and 20% of P. vivax, malariae and ovale infections respectively.[20]

Both the aminotransferases (AST & ALT) did not show statistically significant positive correlation with bilirubin ($p>0.05$) it signifies that rise in bilirunbin from other sources like erythrocytes. Whereas other studies like Kauser MW et al, in their study obtained significant positive correlation of serum transaminases and ALP with serum bilirubin (2). Kocher et al also showed an excellent positive correlation of SGOT with bilirubin n ($p<0.01$).[17]

Conclusion

Malaria is a disease whose pathogenesis is not clearly defined as it is species-specific and of geographical variability. Thus the assessment of bilirubin and liver enzymes (like SGPT & SGOT) in malaria patients could represent additional and useful parameters in determining the clinical and prognostic aspects of the disease.

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