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Research Article

STUDY OF DERANGEMENT OF ENZYMES OF LIVER IN MALARIAL P.VIVAX AND P. FALCIPARUM SPECIES

Dr Obaid Noman

Assistant Professor, Jawaharlal Nehru Medical College, Department of Pathology, Datta Meghe Institute of Medical Sciences

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Address for Correspondence: Dr Obaid Noman, Assistant Professor, Jawaharlal Nehru Medical College, Department of Pathology, Datta Meghe Institute of Medical Sciences
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ABSTRACT:

The parasite protozoan Plasmodium is what causes malaria, a parasitic illness spread by mosquitoes. In under developed nations, malaria is a serious health issue that causes 2–3 million fatalities annually. Studies have shown that blood infected with malaria exhibits haematologic and biochemical changes, and this illness is frequently accompanied by sequelae. Anemia, thrombocytopenia, and disseminated intravascular are among the haematologic changes linked to malaria infection. When sporozoites enter hepatocytes during the liver stage, this might result in organ congest, sinusoidal obstruction, and cellular inflammation. These hepatocyte alterations may cause parenchyma and membrane damage leading enzymes to leak into the bloodstream. Considerable alterations in biochemical and haematological markers are the fundamental drivers of malaria pathogenesis. As test markers of liver function, haematological values and levels of enzymes aspartate transaminase (AST), alkaline phosphatase (ALP), alanine transaminase (ALT), and bilirubin (total and direct) were examined. The evaluation of these liver enzymes helps to assess the involvement of liver in plasmodium infection and also assess the severity and frequency of involvement along various strains of malaria.

Materials and Methods: This prospective study was conducted at the Department of Pathology and Central Clinical Laboratory, JNMC-AVBRH, Sawangi Meghe, Wardha, and DMMC-SMHRC, Nagpur over a period of 2 years. A sample size of at least 180 people was chosen. Among the 180 confirmed malaria cases 82 were of plasmodium falciparum and 98 were of Plasmodium Vivax. the Orth-diagnostics dry chemistry and Beckman Coulter-Au480 to perform tests of liver functions.

Conclusion: The analysis of the results obtained in current study led us to conclude that both malarial the Plasmodium vivax and falciparum result in derangement of liver enzymes in majority of the cases. We also found that the derangement in liver enzymes is more pronounced in frequency of occurrence as well as levels of enzyme derangements in infections with Plasmodium falciparum. Total Bilirubin was the enzyme raised most frequently raised enzyme in both the species while alkaline Phosphatase was the least frequently raised enzyme.

Keywords: Malaria, Liver Enzymes, Plasmodium, Falciparum, Vivax, Liver function tests, Bilirubin, SGOT, SGPT ALP.

INTRODUCTION

The parasite protozoan Plasmodium is what causes malaria, a parasitic illness spread by mosquitoes. Malaria is carried by female anopheles' mosquitoes among humans. When a mosquito bites a human, parasites enter blood of victims[1]. Human malaria is brought on by five different Plasmodium species: Plasmodium

vivax, Plasmodium falciparum being the most commonly encountered. In underdeveloped nations, malaria is a serious health issue that causes 2–3 million fatalities annually[2]. Malaria a tropical protozoan disease transmitted through female Anopheles mosquitoes. It is mostly brought on by different plasmodium parasite species. Malaria is brought on by 4 species of Plasmodium. P. falciparum, P. vivax, P. ovale, and P. malariae are among them. The highest number and more critical illnesses are caused by P. falciparum and P. vivax species[3]. A tissue called blood flows in a practically closed network of blood vessels. Red, white, and platelet blood cells and plasma floating in a liquid media make up its solid components. Since the plasma is contained within the vascular system, it is an extracellular fluid. Plasma shares many characteristics with intracellular fluid, including the presence of water, electrolytes, minerals, proteins, metabolites and hormones. While the blood's physicochemical characteristics are static, they could experience modest changes under typical physiologic circumstances[4,5]. However, in clinically defined patho-physiologic conditions, the relative stability of the blood system's internal environment shows extensive and deep disruption and aberrations. Malignancy, genetic defects, starvation, parasite infections, etc. are a few of these disorders[6].

Studies have shown that blood infected with malaria exhibits haematologic and biochemical changes, and this illness is frequently accompanied by sequelae. Anaemia, thrombocytopenia, and disseminated intravascular are among the haematologic changes linked to malaria infection. Changes in the physicochemical properties of blood infected with P. falciparum can depend on the prevalence of haemoglobinopathies, nutritional state, demographic variables, and level of malaria immunity[7]. Therefore, knowledgeable changes in blood parameters during malaria infection allow the practitioner to make a trustworthy diagnosis and to provide effective treatments. The parasite that causes malaria alters the host's metabolism and biochemistry. When sporozoites enter hepatocytes during the liver stage, this might result in organ congest, sinusoidal obstruction, and cellular inflammation. These hepatocyte alterations may cause parenchyma and membrane and leads the enzymes to leak into the bloodstream. Considerable alterations in biochemical and haematological markers are the fundamental drivers of malaria pathogenesis. Giemsa staining of the malaria parasite on thin and thick smears supporting malaria diagnosis. As test markers of liver function, haematological values and levels of enzymes aspartate transaminase (AST), alkaline phosphatase (ALP), alanine transaminase (ALT), and bilirubin (total and direct) were examined. The evaluation of these liver enzymes help to assess the involvement of liver in plasmodium infection and also assess the severity and frequency of involvement along various strains of malaria. According to World Health Organization (WHO) guidelines, certain haematological and biochemical characteristics should increase the possibility of severe malaria. Therefore, the current study was pursued to determine profile of liver function tests in Plasmodium falciparum and Plasmodium vivax infected malaria.

Materials and Methods-

This prospective study was conducted over a two-year period, from June 2019 to July 2021, at the Department of Pathology and Central Clinical Laboratory, JNMC-AVBRH, Sawangi Meghe, Wardha, and DMMC-SMHRC, Nagpur. Following confirmation by microscopic inspection and a malarial antigen card test, 180 samples were included in the study. This research comprised patients of all ages with a history of fever, headache, vomiting, gastrointestinal, jaundice, chills, and malaise. Women who were pregnant, those with a history of chronic drinking, people with hypertension, diabetes mellitus, cardiac illness, renal failure, or other parasite disorders were not allowed to participate in this study. Additionally, participants who were receiving anti-retroviral medication and were screening positive for HBsAg and HCV were also excluded from this research. The updated 2009 WHO method was used to determine the appropriate sample size[10]. The sample size calculation follows the

procedure and assumes the required accuracy of 5% and a 95% confidence interval with a minimum of 172 patients. Moreover, a 20% non-response rate was introduced to account for a potential loss to follow-up. Finally, a sample size of at least 180 people was chosen. Among the 180 confirmed malaria cases 82 were of plasmodium falciparum and 98 were of Plasmodium Vivax.

In the request form, the patient's name, age, sex, historical information, and clinical examination results were noted. Using sterile precautions, 5 ml of blood from each patient was drawn by performing phlebotomy by trained phlebotomists. Median cubital vein was preferred for Phlebotomy. Sample drawn was collected into an EDTA bulb and a plain bulb after obtaining their informed consent. Smears of varying thicknesses were made, stained with Leishman's stain, and focussed with a 100x oil emersion lens were thick streaks. Blood samples from the patient taken in a simple tube were allowed to coagulate for 5–10 minutes. The blood samples were then centrifuged using a Laboratory centrifuge R–4C (REMI, India), separating the serum and moving on to the testing. Under the direction of a senior biochemist, technicians used the Orth-diagnostics dry chemistry and Beckman Coulter-Au480 to perform tests of liver functions.

Results

The goal of this study was to determine how malaria affected biochemical parameters of liver function. In all, 180 malaria-positive samples (82 P. falciparum and 98 P. vivax) were included in the study. In our study, there were statistically significant differences between Plasmodium vivax and P. falciparum in terms of serum values of Total bilirubin, Indirect bilirubin, SGOT, and SGPT. P. vivax was found to have less impact than Plasmodium falciparum. Out of 180 samples that tested positive for malaria, 122 i.e., 67.77 % of the samples had abnormal liver function tests, whereas the remaining 58 samples i.e., 33.33% of the samples had normal liver function tests. Out of 122 abnormal LFT samples, 68 i.e., 55.73 were males and 54 i.e., 44.27 were females**.**

Table 1: Distribution of Plasmodium Species involved and Cases in which Liver enzymes are deranged

Plasmodium Species involved	Quantum of subjects Positive	Altered liver enzymes
Plasmodium Vivax	98 (54.44%)	60(58.8%)
Plasmodium Falciparum	82 (43.66%)	62(75.6%)
Total	180	122

Table 2: Statistical Analysis

Difference	16.8 %
95% CI	2.9651% to 29.5335%
Chi-squared	5.621
DF	1
Significance level	P = 0.0177

The confidence interval is calculated according to the recommended method given by Altman et al. (2000) based on "N-1" Chi-squared test as recommended by Campbell (2007) and Richardson (2011).

It was observed that out of 98 instances of Plasmodium vivax, 60 patients (58.80%) and out of 82 cases of Plasmodium falciparum, 62 (75.6%) cases, respectively, had abnormal liver function tests.

In our study, out of 180 malaria positive samples, 76 (42.22%) samples had abnormal values for total bilirubin, 118 (65.55%) samples had abnormal values for SGOT, 102 (56.66%) samples had abnormal values for SGPT, and 71 (39.44%) samples had abnormal values for ALP. 61 (51.69%) of the 118 aberrant total bilirubin

values were caused by Plasmodium vivax, while 57 (48.31%) were caused by Plasmodium falciparum. Out of 90 abnormal SGOT values, 47 (52.22%) instances of P. falciparum and 43 (47.88%) cases of Plasmodium vivax respectively. Out of 98 patients with aberrant SGPT results, 48 (48.98%) cases involved Plasmodium vivax, and 50 (51.02%) cases involved Plasmodium falciparum. Additionally, it was noted that of the 63 cases with abnormal ALP values, 29 (46.03%) cases included Plasmodium vivax, and 34 (55.97%) cases involved Plasmodium falciparum.

Table 2: Distribution of deranged levels of liver enzymes with reference to Plasmodium Species involved.

Deranged Liver Enzyme	Plasmodium Vivax	Plasmodium Falciparum	Total
Total Bilirubin	61 (51.69%)	57 (48.31%)	118(65.55%)
SGOT	43 (47.88%)	47 (52.22%)	90 (50%)
SGPT	48 (48.98%)	50 (51.02%)	98 (54.44%)
ALP	29 (46.03%)	34 (55.97%)	63 (35%)

In our analysis we found that Mean ± SD of Total sr. bilirubin in Plasmodium Vivax was 2.41 ± 2.36 and in Plasmodium falciparum was 4.28 ± 3.38. Mean ± SD of SGOT in Plasmodium Vivax was 48.42 ± 20.16 and in Plasmodium falciparum was 54.31 ± 22.34. Mean ± SD of SGPT in Plasmodium Vivax was 41.34 ± 18.16 and in Plasmodium falciparum was 48.26 ± 33.23. Mean ± SD of ALP in Plasmodium Vivax was 101.23 ± 38.54 and in Plasmodium falciparum was 168.32 ± 113.54.

Table 3: Mean and Standard deviation of deranged levels of liver enzymes with reference to Plasmodium Species involved.

Plasmodium Species involved	Total Bilirubin (Mean ± SD)	SGOT (Mean ± SD)	SGPT (Mean ± SD)	ALP (Mean ± SD)
Plasmodium Vivax	2.41 ± 2.36	48.42 ± 20.16	41.34 ± 18.16	101.23 ± 38.54
Plasmodium Falciparum	4.28 ± 3.38	54.31 ± 22.34	48.26 ± 33.23	168.32 ± 113.54

Discussion

Malaria is a serious public health issue that affects 300–500 million people worldwide each year and causes 1-3 million fatalities. Hepatocytes in the liver are attacked by sporozoites and grow as a result of malaria. During the erythrocytic stage, merozoites are responsible for the destruction of infected RBCs[11]. According to Molyneux et al., haemolysis is more frequently to blame for mild elevations in liver enzymes than hepatic damage, which results in jaundice. It is now well acknowledged that studies into how Plasmodium parasites affect the levels of serum enzymes are crucial to understanding the pathophysiology of malaria.[12] Jaundice, which can be severe, is often accompanied by just a little increase in hepatic enzyme levels and is mostly caused by haemolysis rather than liver injury, according to Malyneux et al[12]. Numerous researchers, particularly on the Indian subcontinent, have suggested that liver disease or hepatocellular damage may play a role in malaria patients. Hepatomegaly, elevated blood bilirubin, and a rise in liver enzymes are key indicators of liver disease in these patients[12,13].

The current Prospective study was carried out in order to investigate the changes in biochemical parameters of liver brought on by Plasmodium vivax and Plasmodium falciparum due to malarial parasite. A total of 180 confirmed cases of malaria were included in this study, of which 82 cases were caused by Plasmodium falciparum and 98 by Plasmodium vivax. In our research, we discovered a statistically significant difference between the impacts of Plasmodium vivax and Plasmodium falciparum species on tests of liver functions.

Out of a total of 180 positive individuals, 68 (55.73%) are males and 54(44.27%) are females. Our study is comparable to that of dhariyal et al, in which men were shown to be more susceptible than women[14.]

The degree to which liver function was altered differed greatly between studies. According to the current study, 76 (42.22%) of cases of hyperbilirubinemia occur within the range of patients from the aforementioned collection of studies. Lowest percentage of hyperbilirubinemia 27.88 was reported by Khuraiya et al. and Arevalo-Herrera et al[15, 16]. Highest was 46.5 percent by Arevalo-Herrera et al. Godse et al., and Khuraiya et al revealed lower percentage of subjects having derangement in SGOT and SGPT, which in Godse et al had 19.23% and In Arevalo-Herrera et al it was. 45.5%[15,16,17]. In our study 118 (65.55%) samples had abnormal values for SGOT, 102 (56.66%) samples had abnormal values for SGPT which is higher than the above studies, but similar to the studies of Singh et al having quantum of subjects with deraged SGOT and SGPT at 90 (75%) and 78 (65%) respectively. Percentage of subjects having deranged values of ALP in our study was 29 (46.03%) similar findings were seen in the studies of Singh et al having the frequency 52 (43.33%) cases[18].

In our study we found Mean ± SD of Total sr. bilirubin in Plasmodium Vivax was 2.41 ± 2.36 and in Plasmodium falciparum was 4.28 ± 3.38, similar findings were seen in the study of Singh et (4.3± 3.03 and 8.34± 4.03) and Mehta et al (1.81±1.24 and 4.63±5.19) respectively[18,19]. Mean ± SD of SGOT in Plasmodium Vivax was 48.42 ± 20.16 and in Plasmodium falciparum was 54.31 ± 22.34 Mehta et al, and Singh et al 's study both came to identical conclusions. Mean ± SD of SGPT in Plasmodium Vivax was 41.34 ± 18.16 and in Plasmodium falciparum was 48.26 ± 33.23. Mean ± SD of ALP in Plasmodium Vivax was 101.23 ± 38.54 and in Plasmodium falciparum was 168.32 ± 113.54 Similar results were found in studies Mehta et al. and Singh et al[18,19].

In our study we found statistically significant derangement of liver enzymes in both the plasmodium vivax and plasmodium falciparum species. The Derangement in all liver enzymes was more frequent and pronounced in plasmodium falciparum. These findings were in coherence with the studies of Singh et al, Mehta et al and Megabiaw et al [18,19,20].

Conclusion

The analysis of the results obtained in current study led us to conclude that both malarial the Plasmodium vivax and falciparum result in derangement of liver enzymes in majority of the cases. We also found that the derangement in liver enzymes is more pronounced in frequency of occurrence as well as levels of enzyme derangements in infections with Plasmodium falciparum. Total Bilirubin was the enzyme raised most frequently raised enzyme in both the species while Alkaline Phosphatase was the least frequently raised enzyme.

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