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"COMPARATIVE STUDY OF HEPATOCELLULAR DYSFUNCTIONS BETWEEN PLASMODIUM FALCIPARUM AND PLASMODIUM VIVAX IN WEST BENGAL".

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ABSTRACT

Aims: Our aim in this study was to compare the spectrum of hepatic damage between plasmodium falciparum and vivax. Materials and methods: From 228 (114 each for falciparum and vivax) diagnosed malaria patients, blood were collected for hematological, biochemical and serological tests (to exclude other causes of hepatitis). Data were collected and analyzed to compare severity between them. Results: In case of vivax affected females, serum bilirubin were raised, albumin and total protein were depressed significantly, whereas, in case of falciparum affected males, serum bilirubin, SGPT, SGOT, alkaline phosphatase were raised and total protein, albumin decreased significantly. In case of plasmodium falciparum affected patients, SGPT and alkaline phosphatase were elevated, whereas, serum albumin and prothrombin time were decreased significantly. In both groups, hemoglobin level was near normal. Conclusion: Falciparum was responsible for severe hepatocellular dysfunction. Hence, early detection of hepatic damage is necessary to prevent its future possible complications.

KEY WORDS: Hepatic dysfunctions, plasmodium falciparum, plasmodium vivax, West Bengal, www.ijpbs.net.

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INTRODUCTION

Malaria is an endemic disease of Tropical and sub-tropical areas of Asia, North, South America and Middle East. There are four subtypes of Plasmodium species responsible for malaria. These are Plasmodium falciparum (p. falciparum), vivax (p. vivax), malaria and ovale. Globally, malaria is responsible for 300-500 million cases and 1.5-2.7 million deaths per year[1]. Again, 2.48 million malaria cases in South-east Asia, only India is responsible for 75% of of these cases[2]. In West Bengal, Plasmodium falciparum and vivax are the main causative agents for this disease. Malaria transmission occurs through the bite of infected Anopheles mosquito, which injects sporozoites into the blood of human being. Sporozoites attach to the hepatocytes through the receptor for thrombospondin and properdin[3]. In the hepatocytes, sporozoites are transformed into schizonts, which in turn, produce large numbers of merozoites. Again, each merozoite invades human red blood cell (RBC), and produces 24-32 merozoites in the asexual cycle of replication[4]. Ultimately, parasitized RBC ruptures, releasing its cellular debris, or, is phagocytosed by reticuloendothelial cell of liver and spleen producing organ enlargements[5, 6]. Plasmodium falciparum invades both younger and mature RBCs as compared with other subtypes[7] and is responsible for multiorgan dysfunctions[8]. Again, coagulation system may be affected, which may be correlated with amount of hepatocellular damage[8]. Serum alkaline phosphatase (ALP) may be elevated due to hepatic stage of parasites with significant perturbation of hepatocytes membrane leading to leakage[9]. Decreased serum protein may be due to decreased synthesis in case of long standing hepatic involvement[10], or increased loss due to capillary leakage[11]. In our present study, we tried to demonstrate as well as compare the spectrum of hepatic damage done by plasmodium falciparum and vivax after exclusion of other causes of hepatitis (viral, drugs[12], alcohol causes).

MATERIALS AND METHODS

This study was performed only after getting permission from the local Ethical Committee. Total 228 patients were admitted in our hospital with fever paroxysm, loose motion, and severe headache between 2011-2013. After taking written consent from the patient's party, proper history followed by thorough physical examination was performed and collected data were stored in a structured questionnaire. For confirmation of the diagnosis, blood was collected from the pulp of the finger aseptically to make thick and thin films and was stained with Giemsa stain to detect malaria parasite under microscope. Simultaneously, blood was sent to the laboratory to get different hematological, biochemical and serological parameters. Serological parameters were carried out to exclude all hepatitis viruses, Leptospirosis. Intake of hepatotoxic drugs for at least two months was excluded from history. Hemoglobin was estimated by Cyanmethemoglobin method, hematocrit by Microhematocrit method on Microhematocrit machine, one stage prothrombin time, serum bilirubin by Jendrassik Grof method, all liver enzymes by enzyme methods, total protein by Biuret method, and albumin by Bromocresol method using kit (AB362) Randox. These biochemical parameters were compared between males and females affected by p. falciparum and vivax, as well as between all patients affected by p. falciparum and p. vivax respectively.

Statistics

Firstly, we collected the mean values with standard deviation for all the necessary biochemical and required hematological parameters in all males and females affected by p. falciparum and p. vivax. Secondly, we calculated the p value at 95% confidence interval (level of significance: $p < 0.05$) of mean values of affected males and females, as well as all the affected patients.

RESULTS

Total number of affected patients were 228, having 114 in each group. Total number of females affected was 82, amongst which, p. falciparum and p. vivax affected were 50 and 32 respectively, whereas, total males affected was 146, amongst which, p. falciparum and p. vivax affected were 64 and 82 respectively. Mean age of females and males affected by p. vivax were 41.928±13.760 years and 26±11.376 years respectively, whereas, in case of p. falciparum, mean age of females and males were 35.04±16.92 years and 32.91±9.30 respectively. In case of p. vivax affected females, bilirubin was significantly raised (1.705±2.84 mg/dl vs. 1.14±0.425 mg/dl, p=0.000) and total protein as well as albumin were significantly low (6.3±0.25 g/dl vs. 6.9±0.44 gm/dl, p=0.005 in case of total protein and 3.7±0.1 gm/dl vs. 4.3±0.9 gm/dl, p=0.000 in case of albumin) as compared to p. falciparum affected females, whereas, alanine aminotransferase (SGPT) was significantly raised (66.173±37.795 U/L vs. 48.672±24.366 U/L), as well as ALP (112.434±38.426 U/L vs. 108.245±17.25 U/L, p=0.000) in p. falciparum affected females as compared to p. vivax affected females. But in case of p. falciparum affected males, bilirubin (1.60±2.11 mg/dl vs. 1.148±0.862 mg/dl, p=0.000), SGPT (84.0±79.965 U/L vs. 48.976±36.830 U/L, p=0.000), SGOT (76.5±98.977 U/L vs. 71.906±62.296 U/L, p=0.000), ALP (123.05±49.215 U/L vs. 119.42±27.42 U/L, p=0.000) and globulin (3.4±1.2 gm/dl vs. 3.2±0.9 gm/dl, p=0,05) were significantly raised as compared to p. vivax affected males. Whereas, total protein (6.5±0.7 gm/dl vs. 6.8±0.7 gm/dl, p=0.000) and albumin (3.9±0.7 gm/dl vs. 4.25±1.5 gm/dl, p=0.000) were significantly low in p. falciparum affected males as compared to p. vivax affected males [Table 1]. Plasmodium falciparum affected patients demonstrated significantly elevated level of SGPT (62.754±75.798 U/L vs. 48.894±34.091 U/L, p=0.000), reduced level of albumin (3.51±0.518 gm/dl vs. 3.71±0.451, p=0.05) and prothrombin time (14.3±0.35 vs. 15.2±0.45 U/L, p=0.005) as compared to p. vivax affected patients [Table 2].

DISCUSSION

In our study, age of incidence in females was higher than in males in case of p. vivax malarial infection, which was similar to the study done by JS et al. where the age of incidence in males was around twenties[13]. Again, mean age of incidence in p. falciparum affected females and males in our study were similar to the study done by Abro AH et al.[14] In our study, hemoglobin was decreased in p. vivax affected patients (mean value for males =11.395±1.791 gm/dl and for females = 11.535±1.375 gm/dl) than p. falciparum affected patients (mean value for males = 12.033±1.235 gm/dl vs. and for females = 12.170±1.456 gm/dl), which was opposite to the study done by Kausar et al.[15], where, p. falciparum affected patients showed low hemoglobin. But, in the study done by Nadeem et al.[3] hemoglobin level in p. falciparum affected patients, was 13.7 gm/dl, this value was more than that was observed in our study.[3] Anemia in p. vivax affected patients may be due to multiple causes, like, destruction of both parasitized and non parasitized RBC, dyshemopoiesis or nutritional deficiencies, last being more common in females. Our study demoed 53.07% patients showed raised bilirubin, which was similar to the study done by Nadeem et al[3], but, it was raised in the study done by Mishra et al[16]. (64.3%).[16] In our study, raised bilirubin was seen in both p. Vivax and p. falciparum affected patients with no statistical difference (1.285±1.59 mg/dl in p. vivax and 1.489±1.783 mg/dl in p. falciparum), but, in the study done by Mishra et al. statistically significant hyperbilirubinemia (2.4±0.32 gm/dl),was seen in p. falciparum group than p. vivax group.[16] Males showed statistically significant raised bilirubin, SGPT in both the groups – this was not demonstrated in any study after thorough search. Since, SGPT is a specific enzyme, produced in liver; hence, SGPT and ALP are the markers of liver injury. Mean value of

SGPT in p. falciparum group was significantly higher than p. vivax group as shown in our study (62.754±75.798 U/L vs. 48.894±34.091 U/L), which was similar to the study done by Kausar M W et al.[15] (47.7±4.89 U/L in p. falciparum vs. 35.4±1.10 U/L in p. vivax group) . SGOT level was raised slightly in p. vivax group than p. falciparum group in the study done by Pir M A et al.[17], which was similar to our study, where, SGOT value was slightly raised in p. vivax group as compared to p. falciparum group. SGOT is released from muscles apart from the liver. So, excessive rigor in case of vivax group may be responsible for raised SGOT.

Jaundice in case of p. falciparum malaria is due to a number of causes, like, hemolysis of parasitized or non-parasitized RBC (innocent by stander), quinine –induced hemolysis, hepatic dysfunction, hemoglobinopathies or associated viral hepatitis. Since, in our study, hemoglobin level was normal or, little below the normal and the patient didn't received quinine or, no history of hemoglobinopathies or viral hepatitis, so it may be due to hepatic dysfunction. Again, SGPT level was high in these patients in the background of normal or little below the normal hemoglobin level, favored the cause as hepatic dysfunction. Since, hepatic dysfunction is reversible in case of p. falciparum malaria, hence, the survivors, after being cured by antimalarial therapy, show no residual biochemical derangement in the liver.[18] The level of bilirubin will come to normal within 72 hours of starting antimalarial therapy, it may be delayed if there is associated renal dysfunction.[19] In our study, serum level of bilirubin, SGPT were reduced to normal in all the patients of both groups within 72 hours of starting antimalarial therapy. In the present study, serum ALP was raised in p. falciparum group as compared to p. vivax group (117.15±21.315 U/L vs. 110.42±18.91 U/L), which was similar to the study done by Kausar M W et al.[15] This elevated ALP activity indicates hepatic stage of parasites as well as significant perturbation in the hepatocytes membrane leading to its leakage. Liver is responsible for the synthesis of albumin. In our study, serum albumin level was within reference range, but in case of p. falciparum group, its level was slightly lower, but significant (p = 0.05). Since, decreased protein synthesis is seen only in chronic long standing hepatic dysfunction, hence, in this case, low albumin level in case of falciparum group may be due to increased capillary leakage. This was shown also in the study done by Areekul et al.[11] Coagulation abnormalities may be observed in p. falciparum malaria. In our study, mean value of prothrombin time was significant in p. falciparum group (15.2±0.45 sec. vs. 14.3±0.35 sec) as compared to p. vivax group. This study were in accordance with Kausar M W et al.[15] and Hemmer et al.[20]

Biochemical parameters	Female (Vivax affected) (n=32)	Female (Falciparum affected) (n=50)	P value	Male (Vivax affected) (n=82)	Males (Falciparum affected) (n=64)	P value
	Range (mean±SD)	Range (mean±SD)		Range (mean±SD)	Range (mean±SD)	
Bilirubin mg/dl	(1.705±2.84)	(1.14±0.425)	0.0001	(1.148±0.862	(1.60±2.11)	0.0001
SGPT (U/L)	(48.672±24.366)	(66.173±37.795)	0.0055	48.976±36.830)	(84.0±79.965)	0.0001
SGOT (U/L)	(75.642±27.743)	(46.652±25.374)	0.2829	(71.906±62.296)	(76.5±98.977)	0.0001
Hemoglobin (g/dl)	(11.535±1.375)	(12.170±1.456)	0.3728	(11.395±1.791)	(12.033±1.235)	0.0012
Alkaline phosphatase (U/L)	(108.245±17.25)	(112.434±38.426)	0.0001	(119.42±27.42)	(123.05±49.215)	0.0001
Total Protein (g/dl)	(6.3±0.25)	(6.9±0.44)	0.006	(6.8±0.38)	(6.5±0.7)	0.0001
Albumin (g/dl)	(3.7±0.1)	(4.3±0.9)	0.0001	(4.25±1.5)	(3.9±0.7)	0.0001
Globulin (g/dl)	(3.1±1.1)	(3.4±1.2)	0.3069	(3.2±0.9)	(3.4±1.2)	0.0074

Table 1
Comparison of biochemical parameters between Plasmodium vivax and falciparum affected males and females

Biochemical parameters	Plasmodium vivax (mean±SD)	Plasmodium falciparum (mean±SD)	P value
Bilirubin (mg/dl)	1.285±1.59	1.489±1.783	0.1184
SGOT (U/L)	72.824±55.729	68.905±64.331	0.0643
SGPT (U/L)	48.894±34.091	62.754±75.798	0.00001
Albumin (mg/dl)	3.71±0.451	3.51±0.518	0.0412
Globulin (mg/dl)	2.833±0.504	2.769±0.494	0.4158
Alkaline phosphatase (U/L)	110.42±18.91	117.15±21.315	0.1023
Prothrombin time	15.2±0.45	14.3±0.35	0.0040
Hemoglobin (g/dl)	11.429±1.694	12.054±1.259	0.0009

Table 2
Comparison of hepatic biochemical parameters in plasmodium vivax and falciparumaffected patients:

CONCLUSION

Plasmodium falciparum and plasmodium vivax produced hepatic dysfunctions with raised SGPT, alkaline phosphatase and bilirubin with prolonged prothrombin time, but normal or near normal hemoglobin level, -- which was more evident in the former group. In spite of acute malarial hepatopathy, serum albumin level was reduced in patients with plasmodium falciparum. So, in all patients with plasmodium falciparum infection, liver function test should be performed as early as possible to detect early hepatocellular dysfunction and serially follow-up is needed to prevent the possible complications and to differentiate it from viral hepatitis.

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