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LIVER FUNCTION BIOMARKERS IN HEPATITIS B AND MALARIA CO-INFECTION AMID PATIENTS WITH FEBRILE ILLNESS

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Abstract:

Background: *Malaria and hepatitis B virus (HBV) co-infections pose a serious threat to public health throughout tropical and sub-Saharan Africa. The present study was conducted to analyze the status of liver enzymes and serum protein in patients with co-infection with HBV and malaria.*

Methods: *Standard microscopy and Rapid Diagnostic Test (RDT) were used separately to screen for mono and co-infections in 200 outpatients with fever. Their serum protein and liver enzymes were tested.*

Place and Duration: *The study is a descriptive cross-sectional study held in the Medicine department of Saidu Teaching Hospital, Saidu Sharif Swat for one-year duration from March 2019 to March 2020.*

Results: *Of all the subjects, 25.5% were positive for malaria. Women had a higher rate of malaria infection (18%) than men (7.5%). The 15–24 age group had the highest incidence of malaria (11%). Thirteen (6.5%) patients were HBV positive. Males had a higher infection rate (4.5%) than females (2.0%). Males had a higher incidence of coinfection, 4.5%, and the 25-34 age groups had the highest rate of coinfection, 1.5%. The analyzed biochemical parameters in all categories of the examined show a significant difference in their mean values compared to the other groups ($p < 0.05$). However, there was no significant difference in ALP in all groups. There was also a statistical difference in ALB values between the co-infection and malaria groups ($P = 0.037$) and between the malaria group and the control group ($P = 0.022$). There is also a statistical difference in the mean total bilirubin value between the P groups below 0.05 and the mean DB value between HBV and the control group ($P = 0.022$).*

Conclusion: *The study showed that co-infection with malaria and HBV infection had no significant effect on the level of serum protein and the activity of liver enzymes in the serum.*

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INTRODUCTION

Malaria infection remains the most common protozoa infection affecting humanity worldwide. Several attempts to reduce transmission speeds have been widely used, but while there is a downward trend in some parts of endemic areas, all efforts are still futile. Sub-Saharan Africa has a high incidence and accounts for a significant proportion of visits to permanent units in most hospitals in Nigeria and other parts of the world where it is endemic[1-2]. It is estimated that 3.3 billion people are affected in 106 countries, with 350 to 500 million cases of malaria infection in African countries, with 2 million and 3 million deaths per year[3]. More than 2 billion people worldwide are infected with 300-350 million people as asymptomatic carriers of the antigen virus, so they are susceptible to a form of chronic infection that causes hepatocellular carcinoma and cirrhosis. It is obtained by exposure to blood and blood products, other body fluids and the use of sharp objects. Malaria and hepatitis B are found in endemic regions around the world. Both infections pose a serious threat to the survival of the population in the area. Both have periods of high activity in liver cells, and the involvement of blood cells can lead to a weakening of the individual's immunity, thereby increasing the chances of developing other infections. The effect of malaria and hepatitis B on liver cells leads to changes in liver enzymes and serum protein caused by liver damage. Liver cells are clearly infected by plasmodic parasites for obvious reasons with certain stages of the life cycle in hepatotropic HBV and hepatocytes[4-5]. Liver enzymes (transaminase amino acid, area amino acids), alkaline phosphate and serum proteins are diagnostic proportions that determine cell membrane integrity and synthetic abilities in liver dysfunction[6-7]. The activity of liver enzymes increases in the serum, when there are factors responsible for damage to the cell membrane. However, in a serious medical environment, there may be a decrease in serum protein levels. This leads to a decrease in the synthetic abilities of the liver. Invasion of liver cells by malaria parasites can lead to organ obstruction; Blocked sine wave with associated cell inflammation can lead to a decrease in the synthetic ability of the liver as a result of a leakage of liver transaminase and low serum protein levels[8-9]. Acute or chronic HBV infection is associated with a mild, moderate or high increase in ammonoids and may be accompanied by a deterioration in synthetic liver function[10]. In this study, malaria and HBV are designed to assess the integrity of the liver in a co-infection environment.

MATERIALS AND METHODS:

The study is a descriptive cross-sectional study held in Medicine department of Saidu Teaching Hospital**,** Saidu Sharif Swat for one-year duration from March 2019 to March 2020. The study was conducted among patients presenting with febrile diseases. The study was conducted on 200 patients with febrile illnesses. Two hundred informed men and women between the ages of 15 and 64 were recruited for the study and gave their consent. Patients with an established clinical condition other than malaria and / or HBV infection, such as obstructive jaundice, cirrhosis, kidney disease, hypertension, diabetes mellitus, sickle cell anemia, pregnancy, cancer, and patients already undergoing or recent chemotherapy two weeks of treatment for previously diagnosed diseases were also excluded. Five milliliters of blood were collected by intravenous line from the patients using a vercontainer needle. Two milliliters of these were placed in EDTA bottles for parasitological and hematological analysis. The remaining 3 ml was withdrawn into a universal bottle and centrifuged at 3000 rpm for 5 minutes to obtain serum for serological detection of HBsAg. Malaria parasites were examined by gold standard microscopy using the Giemsa staining technique on thick and thin smears to determine the species and level of parasites. Parasite levels are expressed as the number of parasites / µl blood. HBsAg was detected in serum samples using a commercial Micropoint ELISA technique according to the manufacturer's instructions. The spectrometric method as described by Reitman was used to determine aspartate and alanine aminotransferases. Serum protein was determined by the Biuret method, and albumin by the bromocresol green method. Alkaline phosphatase was estimated using the Kingamstrong method. The obtained results were analyzed using the SPSS software (version 20) for both descriptive and inferential analysis. The results are expressed as mean and standard deviation. One-way analysis of variance (ANOVA) was used to determine the level of significance between the parameters.

RESULTS:

There were 200 subjects (Table 1), of which 90 (45.0%) were men and 110 (65.0%) women. Fifty-one (25.5%) of these 200 subjects tested positive for the malaria parasite. It includes 15 (7.5%) men and 36 (18.0%) women. Although the statistical analysis showed no significant difference (P> 0.05) in the rates of infection between males and females, it was observed that the female population had a higher infection rate.

Table 1: Distribution of the respondents based on gender and age group

Age (years)	GENDER		
	Male	Female	Total
15-24	28(14)	39(19.5)	67(28.5)
25-34	38(19)	37(18.5)	75(37.5)
35-44	20(10)	17(8.5)	37(18.5)
45-54	01(0.5)	11 (5.5)	12(6.0)
55-64	03(1.5)	06(3.0)	09(4.5)
Total	90(45)	110(55)	200(100)

Among the malaria-positive male population (Table 2), those with a higher infection rate are in the 25-34 age group, with 7 (3.5%) affected and then 6 (3.0%) observed in the 15-24 age group. Moreover, it was observed that malaria-bearing females in the 15-24 age group had the highest infection rate of 18 (9.0%), followed by the 25-34 and 45-54 age groups each 6 (3.0%) of the total studied population. Women aged 35-44 have an infection rate of 4 (2.0%).

Table 2: Distribution of the respondents based on malaria, HBsAg positivity and co-infection according to sex and age

Age(yrs)	Male	Female	Total	Male Female Total	Male Female Total
15-24	6 (3.0)	18 (9.0)	24 (11.0)	2(1.0) 2(1.0) 4(2.0)	1(0.5) 1(0.5) 2(1.0)
25-34	7 (3.5)	6 (3.0)	13 (6.5)	3(1.5) 1(0.5) 4(2.0)	3(1.5) 2(1.0) 5(2.5)
35-44	2 (1.0)	4 (2.0)	06 (3.0)	3(1.5) 1(0.5) 4(2.0)	2(1.0) 0(0.0) 2(1.0)
45-54	0 (0.0)	6 (3.0)	06 (3.0)	0 (0.0) 0(0.0) 0(0.0)	0(0.0) 0(0.0) 0(0.0)
55-64	0 (0.0)	2(1.0)	02 (1.0)	1(0.5) 0(0.0) 1(0.5)	0(0.0) 0(0.0) 0(0.0)
Total	15 (7.5)	36(18.0)	51(25.5)	9(4.5) 4(2.0) 13(6.5)	6(3.0) 3(1.5) 9(4.5)

The least positive for malaria was observed in the age groups 35-44 and 55-64, in each of them 2 people (1.0%) in both sexes, respectively. Thirteen out of 200 (13/200) subjects were positive for HBsAg as shown in Table 2. A higher infection was observed in men with 9 (4.5%) infection rates than in women with 4 (2.0%). Higher rates of infection were observed in the 25-34 and 35-44 age groups, with 3 (1.5%) among the male population. It is followed by 2 (1.0%) in the 15-24 age group, both in the population of men and women. The lowest infection rate 1 (0.5%) was recorded in the 55-64 age group in the male population and in the 25-34 and 35-44 age group among women. Nine patients (4.5%) had co-infection with malaria and hepatitis B (Table 2). Again, the male population has a higher co-infection rate of 6 (3.0%) than their female colleagues 3 (1.5%). A higher co-infection rate of 3 (1.5%) was observed in men in the 25-34 age group. It was followed by 2 (1.0%) for both women and men in the 35-44 and 25-34 age groups, respectively. The lowest co-infection rate was observed in the age group 15-24 years 1 (0.5%) for both the male and female population. The density of malaria parasites is presented in Table 3. It shows that the co-infection group was characterized by a low average parasite density than the groups. with malaria infection only. The results of the biochemical parameters are shown in Table 4 below. It shows high serum AST in people with HBV infection (14.6 ± 12.2) than in those with malaria alone (11.5 ± 6.4) and in those with co-infection (11.7 ± 5.7) compared to the control group (10.7 ± 5.3). However, a statistically significant difference is observed between the value in the HBV group and the control value P = 0.036. In addition, people with HBV infection have a high level of ALT in the serum (11.5 ± 8.7) compared to the co-infection group (7.6 ± 6.1), malaria (7.2 ± 6.0) and the control group (6.5 ± 5.2). There is a statistically significant difference between the HBV group and those with malaria alone P = 0.017, and between those with HBV and the control group P = 0.003, but there is no significant difference for the coinfection groups P> 0.05. A high level of ALP occurs in the group of patients with malaria (152.5 ± 79.8) and co-infected (154.3 ± 43.7)

compared to the level obtained in patients infected with HBV only (146.2 ± 80.6) and the control group (120.5 ± 75.8), but not the difference between the groups P> 0.05. Serum total protein remains relatively normal in malaria (5.9 ± 1.6), co-infected (5.9 ± 1.9), and controls (5.9 ± 1.5) and shows a slight decrease in the malaria group. HBV infection (5.5 ± 1.3) with no significant difference P> 0.05.

Table 3: Malaria parasite density in relation to infection

Infection	Mean parasite density/µl
Malaria (n=51)	1,200±2,270
Co-infection (n=9)	518.3±263.2

Higher serum albumin content was found in the co-infection group (4.0 ± 1.6) and the control group (4.4 ± 1.1) compared to the HBV group (3.7 ± 1.0), and people with malaria alone (3.6 ± 0.9). a statistically significant difference between people with co-infection and the group of patients with malaria P = 0.037 and between the control group and patients only with malaria P = 0.022. Total bilirubin was found to be relatively high among malaria alone (2.1 ± 1.6) compared to the HBV (1.1 ± 1.6), co-infected (0.7 ± 0.3) and control (0.7 ± 0.6), with a statistically significant difference between the P groups less than 0.05. It was found that the concentration of direct bilirubin was higher in people with HBV alone (0.6 ± 1.3) than in those with malaria alone and a control group (0.3 ± 0.2) and co-infection (0.3 ± 0.1). However, there is a significant difference between people with HBV alone and the control group P = 0.022.

Table 4. Mean and Standard Deviation of biochemical parameters in all test's groups and control

Parameters	*Malaria +ve (n=51)*	*HBs Ag +ve (n=13)*	*Co-infection (n=9)*	*Control (n=127)*
AST(iu/l)	11.5±6.4	14.6±12.2a	11.7±5.7	10.7±5.3b
ALT(iu/l)	7.2±6.0a	11.5±8.7b,c	7.6±6.1	6.5±5.2d
ALP(iu/l)	152.5±79.8	146.2±80.6	154.3±43.7	120.5±75.8
TP(g/dl)	5.9±1.6	5.5±1.3	5.9±1.9	5.9±1.5
ALB(g/dl)	3.6±0.9[b,c]	3.7±1.0	4.0±1.6a	4.4±1.1d
TB(g/dl)	2.1±0.2[a,e,g]	1.1±1.6[b,f]	0.7±0.3c	0.7±0.5[d,h]
DB(g/dl)	0.4±0.3	0.6±1.3a	0.3±0.1	0.3±0.2b

DISCUSSION:

Hepatic function biomarkers are important indicators that help to assess the severity of the disease. Several studies reveal changes in the level of liver enzymes and serum proteins due to plasmodium infection and HBV infection[9-10]. In this study, changes in alt, AST, ALP, total serum protein, albumin and bilirubin were compared in patients with malaria, HBV and fever, which is a common infection and control group. For serum AST and ALT effects alone in the HBV infection group alone, according to malaria group, screening and control. This condition can be associated with chronic HBV infection in this category of patients with complications of hepatocyte necrosis, which cause damage to the membrane and thus increase serum activity of specific liver enzymes. Some researchers have reported an increase in serum activity in liver dysfunction due to infection with Plasmodium parasites. In this study, significant changes in AST and ALT activity in malaria infections were observed as controlled (p.05)[11]. Serum AST and ALT activity was observed in the equal infection group, but the mean value in the group was significantly lower than the values observed only in HBV positive. This image shows together, reported by binary Andrade, when it can show modulation of severity in a disease with malaria or HBV infection[12]. Although it is not specific to the liver, the activity of serum of the alps also increases slightly. This is in line with other findings. This study also looked at the total concentration of serum protein and albumin, a synthetic liver product. This shows that the development of diseases together slows down many synthetic liver functions. The total serum protein was found to be the same in the infected group and malaria, but slightly higher than in the HBV infected group[13]. This means that in this study group, the formation of both infections in the same person may increase the severity of the other and then the net effect on synthetic liver cell function. This finding contrasts with other studies that found that the total number of serum proteins decreased among co-infected patients compared only to patients with malaria infection. Bilirubin metabolism may not matter much of the liver[14]. Therefore, implicitly, any condition of the disease affecting the integrity of the liver can lead to complications of liver bilirubin and auxiliary complications. Malaria and HBV infection can destroy red blood cells and cause damage to hepatocytes, thereby causing bilirubin accumulation and mistreatment by the liver in the circulatory system[15]. However, in this study, high serum bilirubin levels may be reported among malaria patients compared to other test groups, which is consistent with the results of Ikepeazu

malaria infection. People with coin projection and control group exhibit the same level of bilirubin for both total and direct bilirubin.

CONCLUSION:

The study showed that malaria and HBV infection had no profound effect on serum protein levels and serum liver enzymes. This indicates the preservation of liver function in common infectious environments, and the presence of both pathogens in the same person is a factor reducing the severity of infection with the malaria parasite or HBV.

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