Assessment of Liver Function Tests on Malaria Patients

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Abstract: _Background: Malaria is one of the most common widespread infectious diseases in the tropical developing countries. It affects nearly 300-500 million cases every year with mortality rate of 1.2-2.7 million deaths per year. The aim of this study to evaluate the effect of plasmodium falciparum on liver function tests on malaria patients. Methodology: Cross sectional study was conducted in Sudan- Khartoum state from December 2016 to April 2017. A total of 150 adult Sudanese subjects varying in age (more than 18 years) and gender divided into two groups, 120 malaria patients and 30 healthy control subjects(C). The malaria group divided into four subgroups according to parasitemia which are M1, M2, M3, and M4 each subgroup contain 30 patients. Thick and thin blood film were done and all biochemical parameters: Total protein, Albumin, Globulins, Total bilirubin, Direct bilirubin, Indirect bilirubin, AST (aspartate transaminase), ALT (alanine transaminase) & ALP (alkaline phosphatase) were analyzed by cobas integra 400 plus analyzer. Statistical analysis was done by, science SPSS Software version (16). Results: In this study we found that mean±SD values of ALT iu/l in C (16 ±5.7), M1 (25± 11.6), M2 (31± 11.1), M3 (35 ±13.7), and M4 (45± 6.8). AST iu/l in C (20 ±4.2), M1 (32± 11.2), M2 (35± 8.5), M3 (41 ±11.2), M4 (54± 9.8). ALP iu/l in C (78 ±13.5), M1 (92± 14.7), M2 (86± 15.2), M3 (93 ±22.0), M4 (100± 14.0). T.Bilirubin mg/dl in C (0.54 ±0.15), M1(0.99± 0.32), M2(1.2± 0.37), M3(1.7 ±0.75), M4(2.1± 0.53). D.Bilirubin mg/dl in C (0.22 ±0.10), M1(0.32± 0.13), M2(0.46± 0.21), M3(0.80 ±0.48), M4(0.77± 0.19). Ind.Bilirubin mg/dl in C (0.31 ±0.10), M1 (0.67± 0.26), M2 (0.82± 0.29), M3 (0.96 ±0.33), M4 (1.3± 0.39). T.protein g/dl in C (7.4 ±0.38), M1 (7.2± 0.44), M2 (7.1± 0.29), M3 (6.9 ±0.34), M4 (6.6± 0.44). Albumin g/dl in C (4.2 ±0.38), M1 (3.8± 0.31), M2 (3.4± 0.50), M3 (3.4 ±0.46), M4 (3.4± 0.38). Globulins g/dl in C (3.1 ±0.32), M1 (3.3± 0.48), M2 (3.6± 0.53), M3 (3.5 ±0.47), M4 (3.2± 0.34). We found that there was significant increase in AST, ALT, ALP, Total, Direct, Indirect Bilirubin in all malaria patients compare to controls with p-value ≤ 0.05 and there was significant decrease in total protein and albumin in patients comparing to controls with p-value ≤ 0.05 except in T. Protein group M1 there is no significant difference when comparing to control group with p-value .075. Conclusion: Malaria affects liver function so early diagnosis and treatment will reduce the complications._

Keywords: Liver function test, Malaria, Plasmodium, Falciparum

1. Introduction

Malaria is the most significant parasitic disease of human accounting for 300-500 million clinical cases annually with a mortality rate of 1.2-2.7 million deaths per year. [1] Malaria caused by _Plasmodium falciparum,Plasmodium vivax, Plasmodium ovale, Plasmodium malariae, and rarely Plasmodium knowlesi_ in human. plasmodium falciparum is most common .[2] The liver plays a key role in the life cycle of the malaria parasite and in some cases it is seriously affected. The liver is affected in two stages in the life cycle of the malaria parasite: firstly the pre-erythrocytic cycle then the erythrocytic phase . [3]. The infection of liver cells by the sporozoites can cause organ congestion, sinusoidal blockage and cellular inflammation. These change in hepatocytes can lead to leakage of transaminases and alkaline phosphatase enzymes of liver to the circulation [4]. Clinical presentation of falciparum malaria may vary in individuals depending upon the level of parasitemia and immune status of the patient. [1]

A common feature Of falciparum malaria is mainly unconjugated hyperbilirubinemia, and it is attributed to hemolysis of both parasitized and non-parasitized RBCs and partly due to liver damage[2]

2. Materials and Methods

Cross sectional study was conducted in Sudan- Khartoum state from December 2016 to April 2017. One hundred fifty samples included in this study, thirty were normal samples as control C, one hundred twenty samples as malaria falciparum positive divided into four groups according to the parasitemia, the first group is low density (+) M1, the second group is mild density (++) M2, third group moderate density (+++) M3 and the last one is high or hyperparasitemia (++++) M4. All patients were asked to sign an informed consent prior to inclusion in this study.

Collection of Sample
A volume of 5 ml of blood was collected from each patient and control under aseptic conditions in EDTA vacutainer tube (2.5 ml) for the diagnosis of malaria and plain tube (2.5 ml) for liver function test (LFT), serum was separated after clot and centrifugation and kept at -20º C until analyzed. A thick and thin smear was prepared and stained with Giemsa stain and examined under × 100 oil emersion lenses. P. falciparum parasitaemia (density) was determined and calculated as: Low (+) 1–10 parasites per 100 fields. Mild (++) 11–100 parasites per100 fields. Moderate (+++) 1–10 parasites in one field. High density parasitaemia (++++) more than 10 parasites in one field [5].

Liver function test include AST, ALT, ALP, Total, Direct and Indirect Bilirubin, Total protein, Albumin and Globulins was determined using cobas integra 400 plus analyzer. Data were analyzed using SPSS version 16 and significance level was defined as (P-value ≤0.05).

3. Results

A total of 120 patients and 30 control subjects varying in age and gender analyzed to LFT and the results are:

ALT level show significant difference between patient groups with mean value of M1 (25± 11.6), M2 (31± 11.1), M3 (35 ±13.7) and M4 (45 ±8.6) when comparing with control group (16 ±5.7) with P- value .000 to all groups.

AST level show significant difference between patient groups with mean value of M1 (32± 11.2), M2 (35± 8.5), M3 (41 ±11.2) and M4 (54 ±9.8) when comparing with control group (20 ±4.2) with P- value .000 to all groups.

ALP level show significant difference between patient groups with mean value of M1 (92± 14.7), M2 (86± 15.2), M3 (93 ±22) and M4 (100 ±14) when comparing with control group (78 ±13.5) with p- value .000, .030, .002, .000 respectively.

Total bilirubin show significant difference between patient groups with mean value of M1 (.99± .32), M2 (1.2± .37), M3 (1.7 ±.75) and M4 (2.1 ±.53) when comparing with control group (.54 ±.15) with P- value .000 to all groups.

Direct bilirubin show significant difference between patient groups with mean value of M1 (.32± .13), M2 (.46± .21), M3 (.80 ±.48) and M4 (.77 ±.19) when comparing with control group (.22 ±.10) with P- value ≤0.05 to all groups.

Indirect bilirubin show significant difference between patient groups with mean value of M1 (.67±.26), M2 (.82± .29), M3 (.96±.33) and M4 (1.3 ±.39) when comparing with control group (.31 ±.10) with P value .000 to all groups.

Total protein show significant difference between patient groups with mean value of M2 (7.1± .29), M3 (6.9±.34) and M4 (6.6 ±.44) when comparing with control group (7.4 ±.38) with P value .006, .000, .000 respectively, but there is no significant difference between patient group M1 (7.2± .44) when comparing with control group with p-value .075.

Albumin level show significant difference between patient groups with mean value of M1 (3.8±.31), M2 (3.4± .50), M3 (3.4 ±.46) and M4 (3.4 ±.38) when comparing with control group (4.2 ±.38) with P- value .000 to all groups.

Globulins level show significant difference between patient groups with mean value of M2 (3.6± .53), M3 (3.5 ±.47) when comparing with control group (3.1 ±.32) with P- value .000 to two groups, but there is no significant difference between patient groups M1 (3.3± .48) and M4 (3.2 ±.34) when comparing to control group with p-value .087, .728 respectively.

Also we compared the malaria group M1which is low density parasitemia with malaria group M4 Which is high density parasitemia, we found that there is significant difference in all parameters with p-value ≤0.05except globulins there is no significant difference p-value ≥0.05 see table (2).

Table 1: Correlation between all patient groups and control group:

		ALT IU/L X±SD	AST IU/L X±SD	ALPIU/L X±SD	T.Bili mg/dl X±SD	D.Bili mg/dl X±SD	IND.Bili mg/dl X±SD	T.PRO g/dl X±SD	ALB g/dl X±SD	GLOB g/dl X±SD
C+M1	M1	25±11.6	32±11.2	92±14.7	.99±.32	.32±.13	.67±.26	7.2±.44	3.8±.31	3.3±.48
	C	16±5.7	20±4.2	78±13.5	.54±.15	.22±.10	.31±.10	7.4±.38	4.2±.38	3.1±.32
	P value	.000	.000	.000	.000	.000	.000	.075	.000	.087
C+M2	M2	31±11.1	35±8.5	86±15.2	1.2±.37	.46±.21	.82±.29	7.1±.29	3.4±.50	3.6±.53
	C	16±5.7	20±4.2	78±13.5	.54±.15	.22±.10	.31±.10	7.4±.38	4.2±.38	3.1±.32
	P value	.000	.000	.030	.000	.000	.000	.006	.000	.000
C+M3	M3	35±13.7	41±11.2	93±22	1.7±.75	.80±.48	.96±.33	6.9±.34	3.4±.46	3.5±.47
	C	16±5.7	20±4.2	78±13.5	.54±.15	.22±.10	.31±.10	7.4±.38	4.2±.38	3.1±.32
	P value	.000	.000	.002	.000	.003	.000	.000	.000	.000
C+M4	M4	45±8.6	54±9.8	100±14	2.1±.53	.77±.19	1.3±.39	6.6±.44	3.4±.38	3.2±.34
	C	16±5.7	20±4.2	78±13.5	.54±.15	.22±.10	.31±.10	7.4±.38	4.2±.38	3.1±.32
	P value	.000	.000	.000	.000	.000	.000	.000	.000	.728

Table 2: Effect of malaria parasite density on liver function test:

		ALT IU/L X±SD	AST IU/L X±SD	ALP IU/L X±SD	T.Bili mg/dl X±SD	D.Bili mg/dl X±SD	IND.Bili mg/dl X±SD	T.PRO g/dl X±SD	ALB g/dl X±SD	GLOB g/dl X±SD
M1+M4	M1	25±11.6	32±11.2	92±14.7	.99±.32	.32±.13	.67±.26	7.2±.44	3.8±.31	3.3±.48
	M4	45±8.6	54±9.8	100±14	2.1±.53	.77±.19	1.3±.39	6.6±.44	3.4±.38	3.2±.34
	P value	.000	.000	.045	.000	.000	.000	.000	.000	.156

P value <0.05 significant difference, P value >0.05 insignificant difference

4. Discussion

The results of this study showed significant difference in liver enzymes due to liver involvement in malaria. There is an elevation in AST more than ALT, this is due to presence of AST enzyme in red blood cells and hemolysis released enzyme from the cells, these results are confirm with previous studies such as : Sudha jha et al[6] Biradar SM et al [7] and disagree with result such as Aminul Khan et al [8].

In this study the level of bilirubin is high in the all groups of patients compare to control group and the predominant of

bilirubin is indirect bilirubin which is increase in case of intravascular hemolysis of parasitized erythrocytes. These result agree with previous studies such as :Biradar SM et al [7] and disagree with results such as : Singh R et al [9].

Total protein results show significant difference between control group and group M2, M3, and M4 but insignificant difference in group M1 comparing to control. Although total protein in the normal range but there is negative significant relation proportional to malaria parasite density seen.

There is significant decrease in albumin level in all groups comparing to control level, this is in agreement with omer balla who found that it may be due to both the role of human albumin in the intraerythrocytic development of parasites and also release of cytokines TNF- α and IFN- γ during the pro inflammatory response against the asexual blood stages of human malaria. Omer Balla et al [10] .

The decrease in total protein although in normal range is maintained to normal by the relative increasing in globins (inflammatory condition).

5. Conclusion

The result of study showed that there is deterioration on liver function in malaria patients and the deterioration is proportional to the density of malaria. We recommended that early diagnosis and treatment of malaria infection should be performed with liver function test to prevent complications.

6. Acknowledgment

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