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Research Article

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# The Effect of Malaria on Biochemical Liver Function Parameters in Sudanese Pregnant Women

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## Abstract

**Objective:** The study was conducted to investigate the effect of malaria, on different biochemical liver parameters in Sudanese pregnant women.

**Methods:** This was a case control, hospital-based study, which was carried out at Medani Maternity Teaching Hospital, Gezira State, and in an area of seasonal mesoendemic malaria transmission. A total of 150 pregnant women, with peripheral blood film evidence of falciparum malaria, were taken as cases and 50 healthy malaria free pregnant women, were selected as controls. Albumin and globulin levels and liver enzymes were estimated colorimetrically, for both patients and controls.

**Results:** Age of the patients ranged from 22-41 years (mean: 31.0 ± 4.33). The mean gestational age of the patients, at booking was 24.6 ± 7.2 weeks (range: 5-36) and their mean haemoglobin level was 8.7± 2.06. Patients with malaria, had higher level of AST, ALT, total bilirubin and indirect bilirubin, while the level of hemoglobin, total protein, albumin and globulin was significantly dropped. Most of the biochemical parameters were affected by the gestational age. A significant positive correlation using Pearson's correlation coefficient, was found between liver enzymes, age, hemoglobin, bilirubin level ($p<0.005$); a negative insignificant correlation with albumin and total protein $p>0.005$.

**Conclusion:** Our study showed that the mean level of most of the biochemical liver function test parameters, were below the normal reference ranges, and a highly significant difference was observed between pregnant women with malaria, and their controls, in the level of AST, ALT, total protein, albumin and globulin, but not in the level of total bilirubin, direct bilirubin and indirect bilirubin.

## Introduction

In Africa, 30 million women living in malaria-endemic areas, become pregnant each year. For these women, malaria was a threat, both to them and to their babies, with up to 2,00, 000 newborn deaths each year, as a result of malaria in pregnancy. Pregnant women were particularly vulnerable to malaria. This is because pregnancy reduces woman's immunity, making her more susceptible to malarial infection, increasing the risk of illness, causing severe anemia and death. For the unborn child, maternal malaria increases the risk of miscarriage, stillbirth, premature delivery and low birth weight, increasing the risk of perinatal mortality [1]. During pregnancy, the liver synthetic and metabolic functions are affected, by the increased serum estrogen and progesterone levels. Pregnancy is associated with many normal physiological changes, which can mimic chronic liver diseases: spider angioma, palmar erythema, elevated alkaline phosphatase due to placental production, increased plasma volume and hypoalbunemia [2].

Pregnancy is a time of great maternal physiological and metabolic changes. These affect the biochemical and hematological parameters used in the assessment of liver disease, and it is important to appreciate the different reference ranges in pregnancy, to facilitate recognition of liver disorders in pregnancy. *Plasmodium falciparum* infestation of red blood cells, can result in hemolysis and subsequent anemia, the condition was aggravated during pregnancy with physiological increase in plasma volume and hemodilution [3].

Due to the increased physiological and metabolic stress of pregnancy, liver disorders that have previously been subclinical, may become symptomatic, for eg: Primary biliary cirrhosis [4]. Several liver diseases occur only during pregnancy, and are considered to be associated with the pregnancy state. The liver disorders unique to pregnancy, have characteristic clinical features and timing of onset; hyperemesis gravidarum occurs in the first trimester, preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes and low platelets count) and acute fatty liver of pregnancy, usually in the third trimester. The third trimester disorders of pregnancy, may progress to severe liver dysfunction [3]. Liver enzymes are increased in malaria parasitemia, to a level dependent on the degree of parasitemia [5]. Ducarme et al. stated that, malaria may be complicated by development of thrombocytopenia, elevated liver enzymes and/or haemolysis, which may be difficult to distinguish from HELLP syndrome in a pregnant patient [6]. There is a positive correlation between liver enzymes activities and the degree of parasitemia. Compared to the control, there is a significant difference in the mean activities of liver enzymes and malarial patients [5]. The aim of our study was to investigate the effect of malaria, on different biochemical liver function parameters in Sudanese pregnant women. Effect of malaria on liver function biomarkers during pregnancy was scarcely documented. This study is expected to provide guidelines to heath care providers, in this area of research.

## Material and Methods

This was a case control, hospital-based study, carried out during the period of September 2004- January 2006 at Medani Maternity Teaching Hospital, Gezira state, which is an area of seasonal mesoendemic malaria transmission. A total of 150 patients with gestational malaria were recruited in this study, and 50 healthy pregnant women were selected as a control group, which was matched with regard to age, gravidity and gestational age. A full medical & obstetric history was obtained, and physical examination was performed. A sample of 5 ml venous blood was drawn from each patient, centrifuged at 4000 rpm for 10 minutes & kept frozen at -70°C. Kits and chemical reagents

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were purchased from Spin React, SA. Ctra. Santa Coloma, 7E- 17176 SANT ESTEVE DE BAS (GI), SPAIN. Using calorimeter, albumin & globulin were estimated, using Bromocresol green method [7], total protein by using Biuret method [8], and biluribin by DMSO method [9]. Alanine aminotransferase (ALT) and Aspartate aminotransferase (AST) were estimated spectrophotometrically, using NADH Kinetic UV.IFCC rec. Liquid method [10] Malarial infection and strain were confirmed by (thin and thick) blood film respectively, using Giemsa stain [11]. Parasitemia was calculated using the patients' white blood cells [12]. Haemoglobin was estimated colorimetrically [13]. Anemia was classified as mild anemia (Hb: 9.0-10.9 gm/dl); moderate anemia (Hb: 7.0-8.9 gm/dl); and severe anemia (Hb: <7 gm/dl), respectively [14].

Normally distributed continuous variables were compared using analysis of variance, and Spearman correlation was used for non-normally distributed continuous variables, which were compared by means of the Pearson 2-tailed correlation test. Significance levels of $P<0.05$ were reported. Statistical programs used were SPSS for Windows, version 16.0. Ethical clearance for the study, was obtained from the ethical committee of the Faculty of Medicine, University of Gezira. Informed consent was obtained from cases and controls.

## Results

Our study included 150 pregnant women with gestational malaria and other 50 healthy pregnant women. Age of the patients ranged from 22-41 years (mean: 31.05 ± 4.33). Of those with gestational malaria, 126 (84%) had anemia (hemoglobin [Hb]: <11 gm/dl); 48.6% had mild anemia, 21.3% had moderate anemia and 14% had severe anemia, while only 4 (8%) of the control had anemia (Hb: 9.0-10.9 gm/dl). Alanine Aminotransferase (ALT) levels ranged from 6-26 IU/L (mean 17.6 ± 5.4), while the Aspartate Aminotransferase (AST) levels ranged from 5-26 IU/L (mean 17.8 ± 4.5). The mean level of AST and ALT was raised, in the cases compared to the controls. Total protein, albumin and globulin were found to be lower, in the cases compared to the controls. While the total biluribin and the indirect biluribin were slightly raised, the direct biluribin was slightly lower in the cases compared to the controls (Table 1).

It was found that most of the biochemical parameters were affected by the gestational age. There was a significant difference in the levels of ALT, AST, total protein, albumin, and insignificant difference in total bilirubin, between the first two trimesters of the cases and controls. While there was a significant difference in the levels of total protein, albumin, and an insignificant difference in the levels of ALT, AST and total bilirubin, between the third trimesters of the cases and controls (Table 2). A significant ($p<0.005$) positive correlation using Pearson's correlation coefficient, was found between the liver enzymes, age, hemoglobin level and bilirubin. Changes in blood albumin and total protein were not significant $p>0.005$ (Table 3).

## Discussion

The severity of gestational malaria depends on the initial immunity of the pregnant woman. The impact of malaria on pregnancy and conversely, the impact of pregnancy on malaria, are two factors which must be put into consideration during gestational malaria [15]. Proteins are known to be very important in immune response; serum albumin level in pregnancy-related hypertension is a significant determinant of disease severity, and may be considered as a useful marker for predicting time to delivery, severe proteinuria, and pregnancy outcomes [16]. Both total protein and albumin were reduced in the cases compared to the controls, with a high significant difference as shown in table 1 ($p<0.05$) (95% CI) [17,18]. The decrease in plasma total protein concentrations found in pregnant women with malaria, may be due to the reduction in protein synthesis. This results from the malarial parasite-induced destruction of the cells that are responsible for protein synthesis during malaria with pregnancy. This finding agrees with an earlier report, that showed chronic infections and autoimmune diseases may lead to reduced protein synthesis [17]. Gestational age is the best guide to differential diagnosis of pregnancy-related liver diseases [19]. Serum albumin levels decrease during the first trimester, and this decrease becomes more accentuated as the pregnancy advances [20]. The decrease in serum concentration is explained by the hemodilution phenomenon. Indeed, the intravascular mass of albumin has been found to be normal in pregnancy, and the rates of synthesis or catabolism are unaltered in normal pregnancy, compared to controls [21]. The levels of AST and ALT were significantly raised in gestational malaria, but still within the normal range. Elevated transaminase levels, upto 3-4 times of the upper normal limit during the first two trimesters, could be safely observed with careful history taking and hepatitis viral antigen tests [22]. However, abnormal results in the third trimester were associated with a shorter duration of pregnancy, and should be managed carefully [23].

The positive correlation found between gestational malaria and liver enzymes, suggest that the latter increased in malarial parasitemia to a level dependent on the degree of parasitemia, and also suggest that the liver is involved in the pathophysiology of malaria [22]. Our findings confirmed a non-significant rise of the bilirubin (total, direct and indirect) as haemolysis significantly contributes to the rising

**Table 1**: Socio-demographic data and liver function biomarkers of the study group and control.

| Variables | Pregnant with Malaria mean ±SD & Range (N=150) | Healthy Pregnant mean ±SD & Range (N=50) | P-value |
|---|---|---|---|
| Age(Years) | 31.0 ± 4.3 (22-41) | 29.9 ± 4.6 (19-42) | 0 .112 |
| Gestational Age (weeks) | 24 .6 ± 7. 2 (5-36) | 21 .8 ± 5.7 (13-35) | 0 .006 |
| Parity | 1 ± 1.3 | 0 .7 ± 1. 05 | 0 .101 |
| Hemoglobin g/dl | 8.7 ± 2.06 (4.0-12) | 11.6 ± 1.33 (9-14) | 0.001 |
| Total Protein g/dl | 5.8 ± 0.74 (4.0 -8.50) | 7.1 ± 0.37 (6.6 – 8.0) | 0.000 |
| Albumin g/dl | 3.1 ± 0.46 (2.1- 4.2) | 3.7 ± 0.24 (3.5-4.5) | 0.000 |
| Globulin g/dl | 2.7 ± 0.54 (1.1- 4.0) | 3.3 ± 0.48 (2.0-4.50) | 0.000 |
| ALT (IU/l) | 17.6 ±5.4 (6.0-26) | 13.2 ±2.4 (9-19) | 0.000 |
| AST (IU/l) | 17.8 ± 4.5 (5.0 -26) | 13.0 ± 2.2 (10-19) | 0.000 |
| T. Biluribin mg/dl | 1.0 ± 0.6 (0.3-3.50) | 0.93 ± 0.12 (0.84-1.0) | 0.275 |
| Direct Biluribin mg/dl | 0.21 ± 0.05 (0.09 -0.6) | 0.23 ± 0.01 (0.2- 0.25) | 0.117 |
| Indirect Biluribin mg/dl | 0.8 ± 0.62 (0.2 -3.3) | 0.7 ± .04 (0.6-0.7) | 0.260 |

**Table 2:** Clinical differences between the first two and third trimesters in pregnant women with malaria and controls.

| Variables | First and Second trimesters of cases (N=82) mean ±SD | First and Second trimesters of control (N=40) mean ±SD | Sig. (2-tailed) | Third trimester of cases (N=68) mean ±SD | Third trimester of control (N=10) mean ±SD | Sig. (2-tailed) |
|---|---|---|---|---|---|---|
| ALT (IU/l) | 17.782 ±5.102 | 12.925 ±2.46 | 0.001 | 17.54 ±5.84 | 14.40 ±1.46 | 0.097 |
| AST (IU/l) | 17.145 ± 4.471 | 12.62 ± 2.071 | 0.001 | 18.72 ± 4.51 | 14.60 ± 2.46 | 0.006 |
| Total Protein g/dl | 5.848 ±0.29 | 7.158 ±0.391 | 0.000 | 5.95 ±0.69 | 6.94 ±0.26 | 0.000 |
| Albumin g/dl | 3.163 ± 0.503 | 3.773 ± 0.342 | 0.000 | 3.05 ± 0.41 | 3.78 ± 0.32 | 0.001 |
| T. Biluribin mg/dl | 1.066± 0.761 | 0.939± 0.05 | 0.294 | 1.01± 0.52 | 0.94± 0.037 | 0.656 |

ALT = alanine amino transferase
AST = aspartate amino transferase

*Table 3: Correlation between various biomedical measures including liver function test in pregnant women with malaria.*

| Variables | AST | | ALT | | T.Protein | | Albumin | | CK | | Hb | | Age | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | r | P | R | P | r | P | r | P | r | P | r | P | r | P |
| T.Bilirubin | -0.12 | 0.14 | -0.36 | <0.001 | -0.05 | 0.52 | -0.05 | 0.520 | -0.06 | 0.4 | -0.18 | 0.025 | -0.22 | 0.005 |
| AST | | | 0.23 | 0.004 | -0.081 | 0.32 | -0.07 | 0.33 | 0.08 | 0.2 | 0.25 | 0.001 | 0.07 | 0.39 |
| ALT | | | | | 0.019 | 0.81 | 0.022 | 0.79 | 0.2 | 0.01 | 0.16 | 0.04 | 0.27 | 0.001 |
| T.Protien | | | | | | | 0.6 | <0.001 | -0.001 | 0.9 | -0.02 | 0.77 | -0.07 | 0.34 |
| Albumin | | | | | | | | | 0.07 | 0.3 | 0.03 | 0.67 | 0.002 | 0.98 |

bilirubin level in severe malarial infection. The parasite, especially *P. falciparum,* infects a large number of cells, which are then destroyed in the spleen, resulting in hemolytic anemia. This is characterized by elevated serum bilirubin (dominant unconjugated fraction), without any significant elevation of the liver enzymes [24]. Derangement of liver function in non-pregnant women with malaria occurs only during malarial hepatopathy [22]. This can be seen as a complication of severe *falciparum* malarial infection. In those patients, serum conjugated bilirubin was elevated in contrast to unconjugated bilirubin, which is raised in pregnant counterparts with malaria due to hemolysis. Liver enzymes may be elevated 2-3 times the normal values, in patients with hepatopathy [25].

## Conclusion

The study revealed the normal levels of bilirubin ( total, direct and indirect) among the cases, while a highly significant difference was reported in the levels of AST, ALT, total protein, albumin and globulin between the cases and controls.

### References

1. WHO (2003) Lives at risk: malaria in pregnancy.
2. Kondrackiene J, Kupcinskas L (2008) Liver diseases unique to pregnancy. Medicina (Kaunas) 44: 337- 345.
3. Anand AC, Puri P (2005) Jaundice in Malaria. J Gastroenterol Hepatol 20: 1322-1332.
4. Mackillop L, Williams Son C (2010) Liver diseases in pregnancy. Postgrad Med J 1013: 160-164.
5. Ignatius CM, Emeka EN, Blessing NE (2008) Effect of malaria parasitemia on liver enzymes tests. International Journal of Trop Med 3: 49-52.
6. Ducarme G, Thuillier C, Wernet A, Bellier C, Luton D (2010) Malaria in pregnant woman masquarding as HELPP syndrome. Am J Perinat 27: 171-172.
7. Gendler S, Kaplan A, Pesce AJ (1984) Clin Chemistry. The CV Mosby Co, ST Louis Toronto Princeton 1268-1273.
8. Burtis CA, Edward R, Tietz NW (1999) Tietz Text Book of Clinical Chemistry. (3rd edition) W.B. Saunders, USA 564.
9. Urea KA, Pesce KA (1984) Analysis and correlation. A J Clinical Chemistry theory 437-418.
10. Schumann G, Bonora R, Ceriotti F, Clerc-Renaud P, Ferrero CA, Férard G, et al. (2002) IFCC primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37°C. Part 6. Reference procedure for the measurement of catalytic concentration of g-glutamyltransferase. Clin Chem Lab Med 40: 635-642.
11. Nkrumah B, Agyekum A, Acquah SEK, May J, Tannich E, et al. (2010) Comparison of the Novel Partec Rapid Malaria Test to the Conventional Giemsa Stain and the Gold Standard Real-Time PCR. J Clin Microbiol 48: 2925–2928.
12. Adam I, Khamis AH, Elbashir MI (2005) Prevalence and risk factors for anaemia in pregnant women of eastern Sudan. Trans R Soc Trop Med Hyg 99: 739-743.
13. Lewis SM, Bain BJ, Bates I, Laffan M (2006) Dacie and Lewis practical haematology. (10thedn) London, Churchill Livingstone.
14. Simpson JA, Aarons L, Collins WE, Jeffery G, White NJ (2002) Population dynamics of the *Plasmodium falciparum* parasite within the adult human host during the expansion phase of the infection. Parasitology 124: 247-263.
15. World Health Organization (1997) World Malaria Situation in 1994. Wkly Epidemiol Rec 72: 285-290.
16. Seong WJ, Chong GO, Hong DG, Lee TH, Lee YS, et al. (2010) Clinical significance of serum albumin level in pregnancy-related hypertension. J Obstet Gynecol Res 36: 1165-1173.
17. Bygbjerb LC, Flashs H (2001) Effects of chloroquine on human lymphocyte proliferation. Tran Soc Tro Med Hyg 80: 231-235.
18. Fisayo AM (2007) Plasma Proteins and proteinuria in gestational malaria. Indian J Clin Biochem 22: 93-95.
19. Kondrackienė J, Kupčinskas L (2008) Liver diseases unique to pregnancy Medicina (Kaunas) 44:337-345.
20. Bacq Y, Zarka O, Bréchot JF, Mariotte N, Vol S, et al. (1996) Liver function tests in normal pregnancy a prospective study of 103 pregnant women and 103 matched controls. Hepatology 23: 1030–1034.
21. Honger PE (1968) Albumin metabolism in normal pregnancy. Scand J Clin Lab Invest 21: 3-9.
22. Bhalla A, Suri V, Singh V (2006) Malarial hepatopathy. J Postgrad Med 52: 315-320.

23. Kim JH, Kwon C, Ko EH, Kim DY, Kim HY, et al. (2007) Abnormal Liver Function Tests in Pregnancy: A Single Institution Experience. Korean J Gastroenterol 50: 36-41.

24. Ignatius C M, Emeka EN, Blessing NE (2008) Effect of Malaria Parasitaemia on Liver Enzyme Tests. International Journal of Tropical Medicine 3: 49-52.

25. Devarbhavi H, Alvares JF, Kumar KS (2005) Severe falciparum malaria simulating fulminant hepatic failure. Mayo Clin Proc 80: 355-358.

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