ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 12, Issue, 11, pp.14970-14974, November, 2020

DOI: https://doi.org/10.24941/ijcr.40276.11.2020

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

EVALUATION OF HEPATIC BIOMARKERS AMONG SUDANESE PREGNANT WOMEN WITH PREECLAMPSIA IN KHARTOUM STATE

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ARTICLE INFO

Article History:
Received 20th August, 2020
Received in revised form
17th September, 2020
Accepted 25th October, 2020
Published online 30th November, 2020

Key Words:
Preeclampsia;
HELLP; ALT;
AST; Bilirubin,
Normotensive Pregnant,
Sudanese.

ABSTRACT

Back ground: Liver damage associated with preeclampsia may array from mild hepatocellular necrosis with serum enzyme aminotransferase and lactate dehydrogenase abnormalities to the ominous hemolysis and elevated liver enzyme. **Aim:** the aim of this study was to assess the serum liver function test (LFT) in preeclampsia women in Khartoum State **Materials and Methods:** This cross-sectional case control study conducted in Jabel Awalia Hospital Khartoum state, in the period from March to June 2020. Hundred subjects were involved, fifty were preeclamptic women as cases and fifty normal pregnant women as control group. A venous blood was collected from each participant, obtaining the serum; Serum level of liver biomarkers (ALT, AST, and ALP), total bilirubin and direct bilirubin were measured by calorimeter method in fully Automated Biochemistry Analyzer (Mindary Bs380). Data were analyzed using the SPSS version 20 t-test was used for comparison of means between two groups and Pearson's correlation test was used to test the association between study parameters and variables, P-value < 0.05 is considered significant. **Results:** pregnant women with preeclampsia had significantly increase in means of serum AST, ALT, total bilirubin and direct bilirubin . (P value= 0.033, 0.019 0.002, 0.000) respectively .There was a significant decrease in the serum albumin level in case compared to control group (P. value =0.039), while there were insignificant different of serum ALP, total protein between two groups (P value= 0.811, 0.44). There were significant positive correlation .between AST and (ALT, ALP and total and direct bilirubin) (p vaule <0.05) while there were significant negative correlation between albumin, total protein and AST. Also found significant positive correlation between ALT and other hepatic markers (ALP, albumin , total and direct bilirubin) (p vaule <0.05). **Conclusion:** The outcomes of this study show that hepatic biomarkers in pregnant women with preeclampsia was higher than normal pregnant women, therefore, we can predict more likely to develop HELLP syndrome in pregnant women with preeclampsia.

Citation: ***Amal Abdoh Mohammed Saeed and Nuha Eljaili Abubaker.*** **2020.** "Evaluation of Hepatic Biomarkers among Sudanese Pregnant Women with Preeclampsia in Khartoum State", *International Journal of Current Research*, 12, (11), 14970-14974.

INTRODUCTION

Preeclampsia is a pregnancy-related disorder and considered as one of the major reasons of infants and mothers death in developed nations (Leung *et al.*, 2001). Some of the risk factors for the development of preeclampsia are diabetes mellitus, hypertension, obesity and anti-phospholipid antibody syndrome (Powe, 2011). Each year, 585,000 women die due to complications related to pregnancy that is 95% of them in developing countries and among them, 30% of cases are due to problems of hypertension during pregnancy and particularly preeclampsia (Conde-Agudelo, 2000).

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Preeclampsia has been described as a systemic syndrome of pregnancy, which is characterized by a new onset high blood pressure (systolic ≥140mm Hgordiastolic ≥90mmHg) and proteinuria of ≥ 0.3 grams per 24 hours that occurs after 20 weeks of gestation in a woman that was previously normotensive (Robertsand, 2004) Many of the clinical and laboratory signs usually associated with liver disease are present in normal pregnancy. Serum alkaline phosphatase levels increase in late pregnancy because of both a production of the placental isoenzyme and an increase in bone isoenzyme (Adeniyi, 1984; Valenzuela, 1987). However values for serum aspartate transferase (AST), alanine transferase (ALT), gamma glutamyltransferase (GGT), lactate dehydrogenase (LDH) and bilirubin does not significantly altered during normal pregnancy. Any increase in these values may reflect hepatobiliary pathology (Elliot, 1971; Steven, 1981).

Liver dysfunction in pregnancy can affect both maternal and fetal health. Girling *et al*., (1997) reported the higher prevalence of elevated liver function tests (LFT) in preeclamptic group (54%) than gestational hypertension. In other study the activity of enzyme ALT did not show any difference in preeclamptic and normal pregnant women but activities of AST, ALP and GGT were significantly elevated in preeclampsia. LDH is useful biomarker reflects the severity of occurrence of complications of preeclampsia has been reported (Makuyana, 2002; Kashanian, 2011). In general, only few studies like (Qublan, 2005; Naval Kishore, 1969) have been studied LFT in preeclampsia and observed significantly raised values of AST, ALT, and LDH in preeclampsia. Deterioration of hepatic function is a crucial determinant in the clinical management of the hypertensive pregnancies. In this disorder, although not too much information in this field (Loganathan, 2005). In addition, a study was conducted in Iran, winter and urinary tract infection were considered as risk factors for preeclampsia (Riely, 1999). It has been reported that slight changes occur in biomarkers of the liver during pregnancy, indeed in this period, the level of AST, ALT, GGT, serum bilirubin, and bile acids usually remain within the normal range, therefore any change in their level may indicate a problem (Haram, 2009). Hence to assess the liver function and severity of diseases, we plan to study the LFT in preeclamptic women and compared with normal pregnant women.

MATERIALS AND METHODOLOGY

Study design: This was a cross-sectional case control study.

Study area and Period: The Study conducted in Khartoum state, Sudan from period between March to June 2020.

Study Population: A total of 100 Sudanese pregnant women were recruited (from Jabel Awalia Hospital in Khartoum) and divided into two group including 50 pregnant women with preeclampsia as cases and 50 normotensive pregnant women as control were enrolled in this study. Age was matched between the groups (range between 20 to 38 years).

Inclusion criteria: pregnant women with preeclampsia as cases and normotensive pregnant women as control were included in this study.

Exclusion criteria: Pregnant women with other medical conditions such as viral hepatitis, diabetes mellitus renal failure, autoimmune diseases, anaemia, tuberculosis, chronic hypertension, and myelo-proliferative disorders were excluded from this study.

Ethical Consideration: The study was approved by the Scientific and ethical committee of the Clinical Chemistry Department of Faculty of Medical Laboratories Sciences AlNeelain University. Then an Informed consent was obtained from participants of the study. Demographic data was collected through questionnaire.

Sampling: Under aseptic and antiseptic precaution, blood specimens was collected. The blood were collected in a hepranized tube at room temperature and centrifuged for 10 minutes at 3500rpm. All the precautions were taken in accordance with the Clinical and Laboratory Standards Institute criteria.

Methods: enzyme activity of liver biomarkers (ALT, AST, and ALP), total bilirubin and direct bilirubin were measured by calorimeter method in fully Automated Biochemistry Analyzer (Mindary Bs380).

Quality Control: The internal control sera of two different levels were used to calibrate the instruments and to assure the accuracy of results.

Data Analysis: Data was analyzed by using SPSS computer program, the mean and standard deviation were obtained and the independent t. test was used for comparison of means, and Pearson's correlation test was used to test the correlation between study parameters and age and weight. P-value of ≤ 0.05 was considered significant.

RESULTS

In the current study; the age of participants ranges between 20 to 38 years. In comparison with the controls, pregnant women with preeclampsia had significantly increase in means of serum AST,ALT ,total bilirubin and direct bilirubin . (P value= 0.033, 0.019 0.002, 0.000 respectively) There was a significant decrease in the serum albumin level in case compared to control group (P. value =0.039), while there were insignificant different of serum ALP, total protein between two groups (P value= 0.811, 0.44) as in table (1).

Table 1. Mean comparison of AST, ALT, ALP, total bilirubin , direct bilirubin, total protein and albumin in case versus control group

Parameters	Case (Mean±SD)	Control (Mean±SD)	P-value
AST (IU/ml)	26.40±8.26	24.58±6.82	0.033
ALT (IU/ml)	26.68±7.98	23.20±6.49	0.019
ALP (IU/ml)	114.8±38.66	113.2±25.79	0.811
T.Protein (g/dI)	6.91±0.34	6.96±0.31	0.445
Albumin (g/dI)	4.47±0.75	4.78±0.72	0.039
T.B (mg/dI)	0.89±0.70	0.49±0.13	0.000
D.B (mg/dI)	0.33±0.24	0.21±0.09	0.002

The current data shows that there were significant positive correlation .between AST and (ALT, ALP and total and direct bilirubin) (p vaule <0.05) while there were significant negative correlation between albumin, total protein and AST presented as in Figures 1, 2, 3, 4, 5 and 6 respectively.

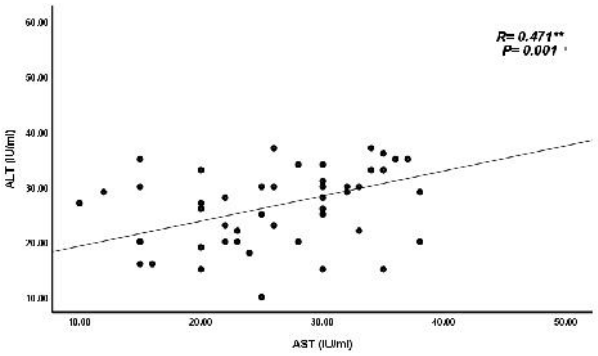

Figure 1. Correlation between serum AST and ALT

Also found significant positive correlation between ALT and other hepatic markers (ALP, albumin, total and direct bilirubin) (p vaule <0.05), while there was significant negative correlation between ALT and total protein presented in Figure 7, 8, 9, 10 and 11.

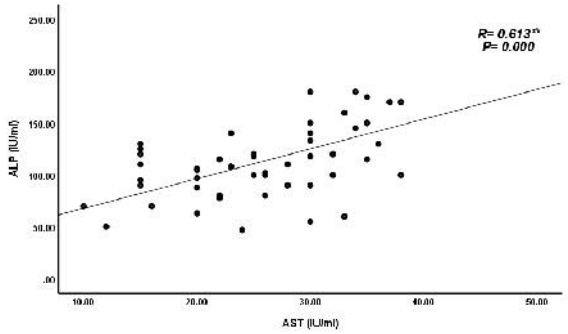

Figure 2. Correlation between serum AST and ALP

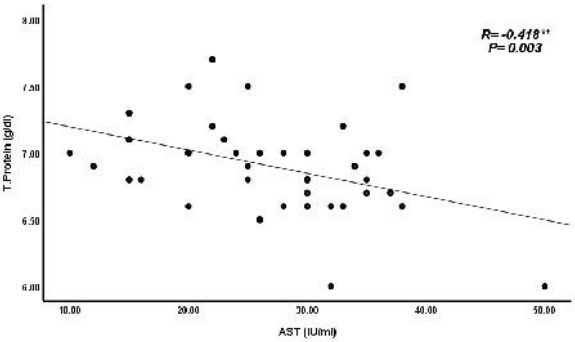

Figure 3. Correlation between serum ASTand total protein

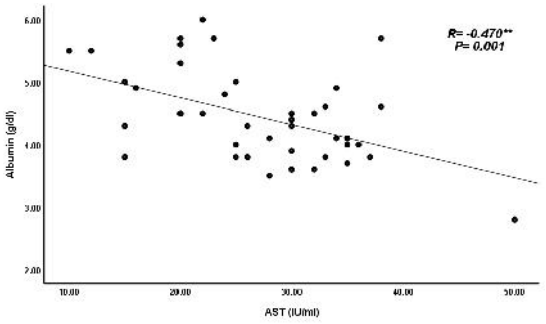

Figure 4. Correlation between serum AST and albumin

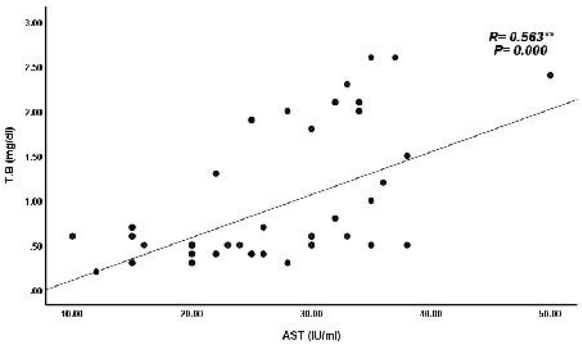

Figure 5. Correlation between serum AST and T.B

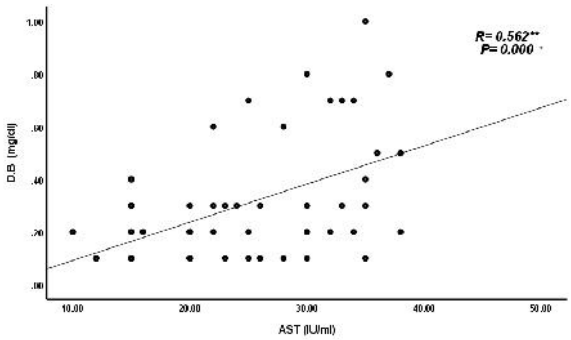

Figure 6. Correlation between serum AST and D.B

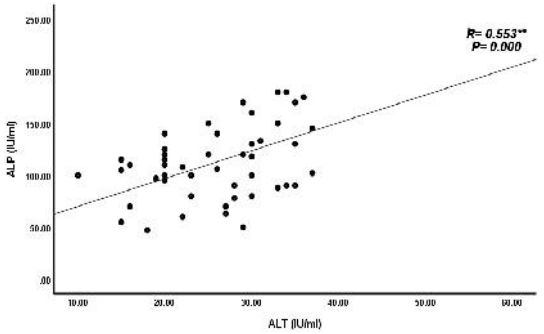

Figure 7. Correlation between serum ALT and ALP

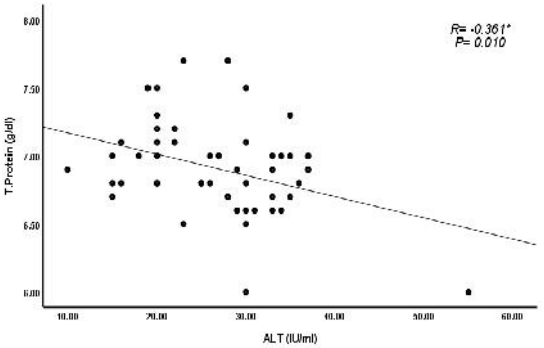

Figure 8. Correlation between serum ALT and total protein

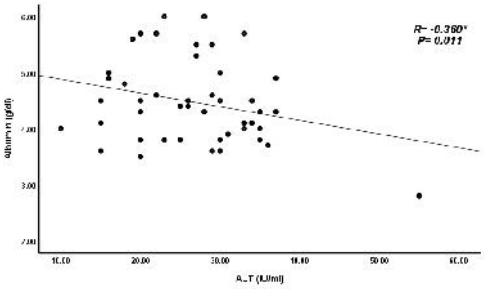

Figure 9. Correlation between serum ALT and albumin

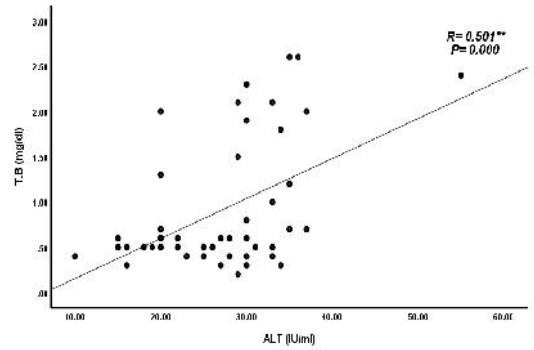

Figure 10. Correlation between serum ALT and T.B

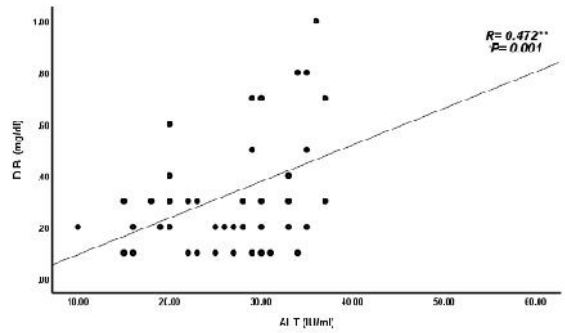

Figure 11. Correlation between serum ALT and D.B

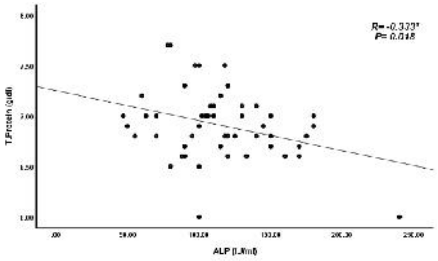

Figure 12. Correlation between serum ALP and total protein

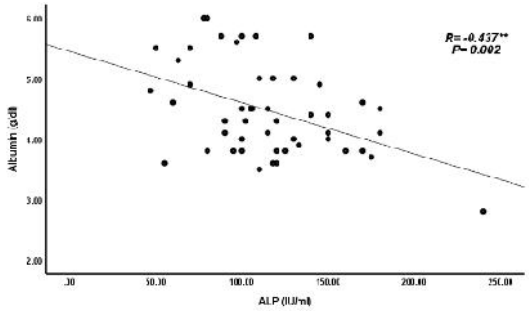

Figure 13. Correlation between serum ALP and albumin

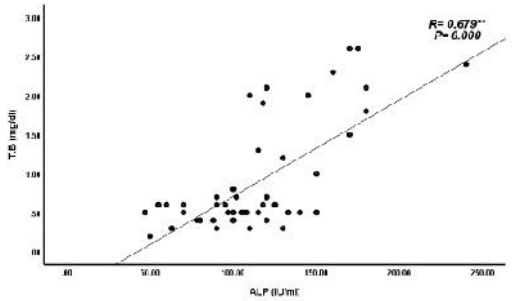

Figure 14. Correlation between serum ALP and total T.B

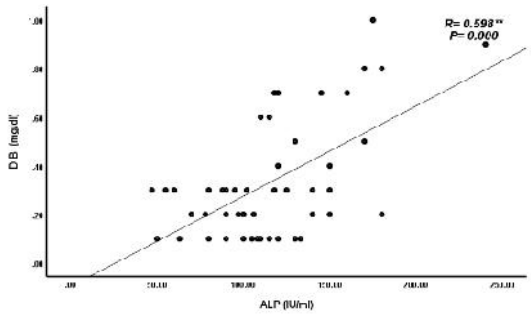

Figure 15. Correlation between serum ALP and D.B

The results also reported significant positive correlation between ALP and (albumin, total and direct bilirubin) (p vaule<0.05), while there was significant negative correlation between ALP and total protein presented in Figure 12, 13, 14 and 15.

DISCUSSION

Liver function tests are irregular in 20% to 30% of pregnancies that are related with preeclampsia, and are related to reduced motherhood and embryonic result (Romero *et al.*, 1989). Proteinuria, hypertension, and edema are three features of Preeclampsia that appear during last trimester of 5%-10% of pregnancies. The impairment of liver function is infrequent in this disease, nevertheless intense preeclampsia is related to perinatal illness and death.

Liver involvement of preeclampsia requires no specific therapy, although the involvement is an indicator to prevent more serious disorders such as eclampsia, hepatic rupture, or necrosis (Hay, 2008). This study was carried out in Khartoum-Sudan to assess liver function tests in pregnant women in both normotensive and preeclamptic group. The result of this study showed significant increased in means of serum AST, ALT , total bilirubin and direct bilirubin in pregnant women with preeclampsia compared to normotensive pregnant women . (P value= 0.033, 0.019 0.002, 0.000 respectively). This result in agreement with studies conducted by Weinstein (Weinstein, 1982) and Shukla (Shukla, 1978). Also this result similar to another result , which finding confirmed that , there were significant increased in means of serum AST, ALT, total bilirubin and direct bilirubin in pregnant women with preeclampsia compared to normotensive pregnant women (Hazari, 2014; Dacaj, 2016). It is thought that elevated transaminases among preeclamptic women are possibly due to hypoxic effect of preeclampsia on their livers, since hypoxia results in necrosis with a result ant degeneration of hepatocytes (Dacaj, 2016).

Moreover, the mean of albumin as observed in this study was significantly decreased in pregnant women with preeclampsia compared to normotensive pregnant women ($p<0.05$). This study similar to another study carried out by Moran *et al* who observed significant decreased in albumin level ($p<0.05$) among preeclamptic group when compared with normotensive control group and he justify that , as observed in her study there was urinary loss of protein with spot urine protein which was significantly higher ($p<0.05$) among preeclamptic test group when compared with the normotensive control. It has been shown that proteinuria as seen in preeclampsia may be due to consequence of a loss of both size and charge selectivity of the glomerulus (Moran *et al.*, 2003). Result of this study found that, that there were significant positive correlation .between AST and (ALT, ALP and total and direct bilirubin) (p vaule <0.05) while there were significant negative correlation between albumin, total protein and AST among preeclampsia group. This result similar to another result carried out by Kamath *et al* (2001). Also result of this study found significant positive correlation between ALT and other hepatic markers (ALP, albumin, total and direct bilirubin) (p vaule <0.05), while there was significant negative correlation between ALT and total protein among preeclampsia group.This result in agreement which another result carried out by Limdi *et al.* (2003). The results also reported significant positive correlation between ALP and (albumin, total and direct bilirubin), while there was significant negative correlation between ALP and total protein. This result parallel to another result Thapa *et al.* (2007).

Conclusion

This study concluded that:

Serum AST, ALT, total bilirubin and direct bilirubin had increased in pregnant women with preeclampsia due to hypoxic effect of preeclampsia on their livers.

Acknowledgement

We thank all the study participants, all members of staff at the faculty of medical laboratory sciences-Alneelain University for their help and support, and colleagues at Laboratory and Research Unit

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