ORIGINAL ARTICLE

LIVER FUNCTION TESTS IN SECOND AND THIRD TRIMESTER PRIMIGRAVIDA IN NORMAL PREGNANCY AND PREECLAMPSIA

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Background: Preeclampsia is a common obstetrical problem affecting 5–10% of pregnant females. The objective of this study was to determine and compare liver function tests in primigravidas in second and third trimesters of normal pregnancy and preeclampsia. **Methods:** A cross-sectional comparative study was conducted that included 100 subjects aged 15–40 years with normal pregnancy, and preeclamptic primigravidas of second and third trimester. Their liver function tests were carried out and compared among the study groups. **Results:** The mean age of the subjects was 25.92±5.56 years, mean systolic BP was 136.3±24.623 mmHg, mean diastolic blood pressure was 87.8±15.736 mmHg. There were statistically significant differences in AST, ALT, ALP, and serum albumin among cases and controls of both 2nd and 3rd trimester (p<0.05). However, serum total bilirubin among preeclamptics of 2nd and 3rd trimesters, and also between controls and preeclamptics of 3rd trimester was significantly increased (p<0.05). Serum AST and ALT were significantly decreased among controls of 3rd trimesters compared to 2nd trimester while ALP was significantly increased in 3rd trimester controls compared to 2nd trimester controls. Serum albumin was significantly decreased in both 2nd and 3rd trimester preeclamptics compared to controls. **Conclusion:** Serum AST, ALP, and bilirubin was significantly increased in 3rd trimester preeclamptics compared to 2nd trimester preeclamptics.

Keywords: Preeclampsia, Liver function tests, primigravida

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INTRODUCTION

Preeclampsia is a common obstetrical problem affecting 5–10% of pregnant females. Most of the neonatal morbidities and mortalities, and maternal deaths are caused by preeclampsia.[1] It is accountable for 14% of annual maternal deaths worldwide.[2] It is caused by uteroplacental ischemia, genetic tendency, primary immunological disorders, environmental factors, and humoral factors. Uteroplacental ischemia has been regarded as the most important cause of preeclampsia. It is a clinical syndrome having multiple causes that activate a common pathway resulting in endothelial damage, vasoconstriction, increased blood pressure, and increased vascular permeability.[3] An increase in extracellular fluid volume during pregnancy leads to abnormal liver functions. Serum albumin, aspartate transaminase (AST), alanine aminotransferase (ALT), and total bilirubin decrease in normal pregnancy while serum alkaline phosphatase (ALP) increases because it is also produced by placenta. Liver function tests (LFTs) also alter during pregnancy due to preeclampsia, HELLP (haemolysis, elevated liver enzymes, and low platelet count) syndrome, intrahepatic cholestasis of pregnancy, and very rarely due to acute fatty liver of pregnancy.[4] Similarly hyperemesis gravidarum, preeclampsia and eclampsia, acute fatty liver of pregnancy (AFLP), cholestasis, HELLP syndrome, and isolated cases of raised liver enzymes cause severe complications in pregnancy. These complications can be decreased by proper interpretation of LFTs at an early stage and by appropriate management.[5]

Serum AST and ALT are the most frequently used markers of hepatocyte injury and normal serum AST and ALT levels are 0–35 U/L and 7–56 U/L respectively.[6,7] ALT level is normally elevated during 2nd trimester in normal uncomplicated pregnancy, hyperemesis gravidarum, preeclampsia, HELLP syndrome, and thrombocytopenia. However, it rapidly falls to more than 50% of the raised values within 3 days indicating an improvement after delivery.[8,9] Liver also synthesizes and secretes about 10 gram of albumin daily. Its level falls with progressive liver damage indicating decreased synthetic activity.[5] Serum ALP activity is mostly contributed by liver and its normal level is 41–133 U/L.[6,7] It is significantly increased in the 3rd trimester of normal pregnancy showing extra production from placental tissue.[8] Peripheral arterial disease has higher levels of ALP regardless of other established cardiovascular risk factors.[10] Serum bilirubin is the degradation product of haemoglobin. It normally ranges from 2 to 21 µmol/L.[6,7] The level greater than 17 µmol/L suggest liver pathology, while levels more than 24 µmol/L reflects abnormal liver tests.[9,11] AST and ALT levels are found decreased, normal, and increased in various studies.[12] In another study[13] albumin, bilirubin, and ALT did not show significant differences between preeclamptics and normal pregnancy, while ALP and AST were drastically increased in females with preeclampsia.

SUBJECTS AND METHODS

This cross-sectional comparative study was carried out at Lahore General Hospital from Mar 2013 to Mar 2016. It included 100 subjects, aged 18–40 years and they were further subdivided into four groups, i.e., Group I: 50 primigravidas having preeclampsia. Group Ia: 25 females with preeclampsia in second trimester of pregnancy. Group Ib: 25 females with preeclampsia in third trimester of pregnancy Group II: 50 controls are primigravidas with uncomplicated pregnancy. They were further subdivided into two groups. Group IIa: 25 normal controls in second trimester of pregnancy. Group IIb: 25 normal controls in third trimester of pregnancy. Non-probability convenience sampling was used for data collection.

Group mean differences were observed using *t*-test and $p<0.05$ was taken as significant. Blood pressure was measured twice using standard sphygmomanometer after 5–10 minutes of rest. Subjects having systolic blood pressure (SBP) >140 mmHg and diastolic blood pressure (DBP) >90 mmHg were taken as preeclamptics. Three ml of blood sample was collected in disposable syringe from each subject by venepuncture. Serum was separated and stored in serum cups at a temperature of -20 °C. Serum AST and serum ALT were measured by Kinetic method, serum ALP by photometric method, serum albumin by Bromcresol Green method, and total Bilirubin by Colorimetric method.

Data obtained was entered in Microsoft Excel sheet to generate database and then was exported to SPSS-16. Data was analyzed for description, i.e., for continuous variables like age, blood pressure, and LFTs; Mean±SD was calculated.

RESULTS

The age of selected 100 subjects ranged from 18 to 40 years, while the Mean±SD age was 25.92±5.56 years. Systolic blood pressure ranged from 100 to 210 mmHg, and mean SBP was 136.3±24.6 mmHg. The recorded DBP ranged from 70 to 130 mmHg, and mean DBP was 87.8±15.7 mmHg (Table-1).

In 2nd trimester, mean serum AST in controls and cases was 9.92±3.23 (U/L) and 41.44±15.37 (U/L) respectively. In 3rd trimester, mean serum AST in controls and cases was 7.88±1.98 (U/L) and 45.72±13.70 (U/L) respectively.

In 2nd trimester, mean serum ALT in controls and cases was 18.64±5.32 (U/L) and 63.52±39.39 (U/L) respectively. In 3rd trimester, mean serum ALT in controls and cases was 15.84±2.7 (U/L) and 67.40±27.35 (U/L) respectively.

In 2nd trimester, mean serum ALP in controls and cases was 96.36±19.56 (U/L) and 357.04±190.61 (U/L). In 3rd trimester, mean serum ALP in controls and cases was 210.64 ±70.08 (U/L) and 571.88±263.46 (U/L).

In 2nd trimester, mean serum albumin in controls was 3.23±0.33 (g/dl) and mean albumin in preeclamptics was 3.01±0.18 (g/dl). In 3rd trimester, mean serum albumin in controls was 3.25±0.20 (g/dl) while mean serum albumin in preeclamptics was 2.81±0.10 (g/dl).

In 2nd trimester, mean serum total bilirubin in controls and cases was 0.42±0.07 (mg/dl) and 0.42±0.08 (mg/dl). In 3rd trimester, mean serum total bilirubin in controls was 0.39±0.13 (mg/dl) while mean serum total bilirubin in preeclamptics was 0.67±0.20 (mg/dl).

There were statistically significant differences in AST, ALT, ALP, and serum albumin amongst cases and controls of both 2nd and 3rd trimester ($p<0.05$). However, serum total bilirubin amongst preeclamptics of 2nd and 3rd trimesters and also between controls and preeclamptics of 3rd trimester was significantly increased ($p<0.05$). Serum AST, ALT, and ALP significantly changed amongst controls of 2nd and 3rd trimesters while ALP and serum albumin were significantly different among preeclamptics of 2nd and 3rd trimesters ($p<0.05$) (Table-2).

Table-1: Age and blood pressures of the subjects

Parameter	Minimum	Maximum	Mean±SD
Age (Years)	18	40	25.92±5.56
Systolic BP (mm Hg)	100	210	136.50±24.62
Diastolic BP (mm Hg)	70	130	87.80±15.73

Table-2: Serum levels in cases and controls with significant differences

Serum Markers	Mean±SD		*p*
AST (U/L)			
Control vs Cases in 2nd trimester	9.92±3.23	41.44±15.37	0.000**
Control vs Cases in 3rd trimester	7.88±1.98	45.72±13.70	0.000**
Controls in 2nd vs 3rd trimester	9.92±3.23	7.88±1.98	0.010**
Cases in 2nd vs 3rd trimester	41.44±15.37	45.72±13.70	0.304†
ALT (U/L)			
Control vs Cases in 2nd trimester	18.64±5.32	63.52±39.39	0.000**
Control vs Cases in 3rd trimester	15.84±2.71	67.40±27.35	0.000**
Controls in 2nd vs 3rd trimester	18.64±5.32	15.84±2.71	0.023*
Cases in 2nd vs 3rd trimester	63.52±39.39	67.40±27.35	0.688†
ALP (U/L)			
Control vs Cases in 2nd trimester	96.36±19.56	357.04±190.61	0.000**
Control vs Cases in 3rd trimester	210.64±70.08	571.88±263.46	0.000**
Controls in 2nd vs 3rd trimester	96.36±19.56	210.64±70.08	0.000**
Cases in 2nd vs 3rd trimester	357.04±190.61	571.88±263.46	0.002**
Albumin (g/dl)			
Control vs Cases in 2nd trimester	3.23±0.33	3.01±0.18	0.009**
Control vs Cases in 3rd trimester	3.25±0.20	2.8±0.10	0.000**
Controls in 2nd vs 3rd trimester	3.23±0.33	3.25±0.20	0.730†
Cases in 2nd vs 3rd trimester	3.01±0.18	2.8±0.10	0.000**
Total Bilirubin (mg/dl)			
Control vs Cases in 2nd trimester	0.42±0.07	0.42±0.08	0.702†
Control vs Cases in 3rd trimester	0.39±0.13	0.67±0.20	0.000**
Controls in 2nd vs 3rd trimester	0.42±0.07	0.39±0.13	0.264†
Cases in 2nd vs 3rd trimester	0.42±0.08	0.67±0.20	0.000**

*Significant, **Highly significant, †Non-significant

DISCUSSION

Liver function tests (LFTs) are considered to be the third most important predictor of maternal and foetal complications in preeclampsia after blood pressure and proteinuria according to a Delphi survey of international experts[14]. In this study, serum AST levels were significantly increased in both 2nd and 3rd trimester preeclamptics compared to controls. This is in line with a study conducted by Munazza *et al*[15] in which a significant differences in AST levels were detected between preeclamptic women and controls in 3rd trimester. Another study[13] also found significant increase in AST levels in preeclamptics as compared to uncomplicated normal pregnancy, and serum AST levels were significantly decreased in 3rd trimester of normal pregnancy compared to 2nd trimester. This was contrary to the study conducted by Salman[16] who found progressive increase in AST levels in normal pregnancy. However, in our study serum ALT levels were increased in preeclamptics both in 2nd and 3rd trimester compared to normal pregnant women in 2nd and 3rd trimester. This increase in AST and ALT levels are due to hepatic dysfunction or abnormal liver functioning in preeclampsia. Das *et al*[17] found increased ALT levels in preeclamptics compared to normotensive pregnant counterparts in third trimester only. Makuyana *et al*[13] concluded that ALT level didn't show any marked difference between preeclamptics and normal pregnant patients. This study also shows no marked difference in ALT level between 2nd and 3rd trimester preeclamptics.

Serum alkaline phosphatase levels were increased in both 2nd and 3rd trimester of preeclamptic patients as compared to controls in 2nd and 3rd trimester in our study which could be due to placental ischemia and endothelial dysfunction. Gohel *et al*[18] also found an increased level of ALP in third trimester as compared to second trimester of uncomplicated pregnancy. Another study[19] observed progressive increase in ALP levels from 28 weeks till 39 weeks in normal pregnancy but this increased ALP level was composed of ALP from placenta, bone, and liver with greater contribution from placenta. In our study, serum albumin level was significantly reduced in 3rd trimester preeclamptics and there was also a significant difference in albumin levels in both cases and controls in 2nd and 3rd trimesters. This is in accordance with another study[19] which determined decrease in albumin levels in preeclamptics in 3rd trimester compared to controls. In our study, serum albumin levels did not show any significant difference in 2nd and 3rd trimester in normal pregnant women.

Serum bilirubin level was found significantly higher in preeclamptics of 3rd trimester than their respective controls. This is in accordance with Malvino *et al*[20] who documented that serum bilirubin level was raised to >1.2 mg/dl in HELLP syndrome and peripheral blood smear showed haemolysis. Munazza *et al*[15] also found an increase in serum bilirubin in 3rd trimester preeclamptics then controls. In this study, there was no significant difference in serum total bilirubin level between 2nd trimester preeclamptics and controls in 2nd trimester. There was also non-significant decrease in controls of 3rd trimester in comparison to second trimester controls. However, another study[18] found decrease in serum bilirubin level in 3rd trimester of normal pregnancy compared to 2nd trimester. Serum bilirubin level was significantly increased in 3rd trimester preeclamptics compared to 2nd trimester preeclamptics in the current study.

CONCLUSION

Serum AST, ALP, and bilirubin was significantly increased in 3rd trimester preeclamptics compared to 2nd trimester preeclamptics. Serum AST and ALT levels were significantly decreased in 3rd trimester of normal pregnancy compared to 2nd trimester. Serum ALP was also significantly increased in third trimester controls as compared to second trimester controls. Serum albumin was significantly decreased in both second and third trimester preeclamptics as compared to controls. LFTs should be properly monitored in pregnant women at risk. This may help in early diagnosis and intervention of preeclampsia and may also help in preventing maternal and foetal complications.

REFERENCES

1. Grill S, Rusterholz C, Zanetti-Dällenbach R, Tercanli S, Holzgreve W, Hahn S, *et al*. Potential markers of preeclampsia a review. Reprod Biol Endocrinol 2009;7:70.
2. Lim KH, Steinberg G. Preeclampsia. eMedicine 2008. Available from: http://emedicine.medscape.com/article/1476919-overview.
3. Moemen ME. Pre-eclamptic pregnancy. Egypt J Anaesth 2007;23:1–6.
4. Tran HA. Biochemical test in pregnancy. Aust Prescr 2005;28(4):136–9.
5. Jamjute P, Ahmad A, GhoshT, Banfield P. Liver function test and pregnancy. J Matern Fetal Neonat Med 2009;22:274–83.
6. Mauro P, Renze B, Wouter W. Enzymes. In: Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. (4th ed), St. Louis, Mo: Elsevier; 2006.p. 604–16.
7. Diana NC. Therapeutic drug monitoring and laboratory reference ranges. In: Tierney LM, (Ed). Current Medical Diagnosis and Treatment. (46th ed). New York: McGraw Hill; 2007.p. 1767–75.
8. Bacq Y, Zarka O, Bréchot JF, Mariotte N, Vol S, Tichet J, *et al*. Liver function tests in normal pregnancy: a prospective study of 103 pregnant women and 103 matched controls. Hepatology 1996;23:1030–4.
9. Wong HY, Tan JYL, Lim CC. Abnormal liver function test in symptomatic pregnant patient: The local experience in Singapore. Ann Acad Med Singapoor 2004;33:204–8.
10. Cheung BM, Ong KL, Wong LY. Elevated serum alkaline phosphatase and peripheral arterial disease in the United States National Health and Nutrition Examination Survey. Int J Cardiol 2009;135:156–61.
11. Thapa BR, Anuj W. Liver function tests and their interpretation. Indian J Pediatr 2007;74:663–71.

12. Loganathan G, George R, Eapen CE, Mathai M, Jasper P, Seshadri L, *et al*. Liver function tests in normal pregnancy: a study from southern India. Indian J Gastroenterol 2005;24:268–9.
13. Makuvana D, Mahomed K, Shukusho FD, Mojoko F. Liver and kidney function test in normal and preeclamptic gestation –a comparison with non-gestational reference values. Cent Afr J Med 2002;48(5–6):55–9.
14. Thangaratinam S, Ismail K, Sharp S, Coomarasamy AO, Mahony F, Khan KS, *et al*. Prioritisation of tests for the prediction of preeclampsia complications: a Delphi survey. Hypertens Pregnancy 2007;26:131–8.
15. Munazza B, Raza N, Naureen A, Khan SA, Fatima F, Ayub M, *et al*. Liver function tests in preeclampsia. J Ayub Med Coll Abbottabad 2011;23(4):3–5.
16. Salman MI. Changes in liver function tests during pregnancy. J Al-Anbar Univ Pure Sci 2009;3(1):209–12.
17. Das S, Char D, Sarkar S, Saha TK, Biswas S, Rudra B. Evaluation of liver function test in normal pregnancy and preeclampsia: A case control. IOSR J Dent Med Sci 2013;12(1):30–2.
18. Gohel MG, Joshi AG, Anand JS, Makadia JS, Kamariya CP. Evaluation of changes in liver function test in first, second and third trimester of normal pregnancy. Int J Reprod Contracep Obstet Gynecol 2013;2(4):616–20.
19. Ibraheem NJ, Obiade DS. Serum calcium level and some physiological markers during preeclampsia and normal pregnancy in Babylon province women. Mag Al-Kufa Univ Biol 2013;5(2):203–12.
20. Malvino E, Munoz M, Ceccotti C, Janello G, Mcloughlin D, Pawlak A, *et al*. Maternal morbidity and perinatal mortality in HELLP syndrome. Multicentric studies in intensive care units in Buenos Aires area. Medicina (B Aires) 2005;65(1):17–23.

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