Evaluation of Liver Function Test and Renal Function Test in Pre-eclampsia: A Case Control Study

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Original Research Article

ABSTRACT

Pre-eclampsia is a multisystem disorder, which occurs only in pregnant women during the second and third trimesters of pregnancy and is associated with raised blood pressure and proteinuria. Liver function Test (LFT) abnormalities occur in 3% of the pregnancies and probably the lesion that causes elevated serum liver enzymes. With severe renal involvement, glomerular filtration may be impaired and the plasma creatinine concentration begins to rise. This study was conducted to compare the liver function tests and renal function tests in pre eclampsia with normal pregnancy. This study was carried out on 60 pregnant women after 20 weeks of gestation admitted in Obstetrics & Gynaecology units of Shri Shankaracharya Institute of Medical Sciences, Bhilai, Chhattisgarh. The subjects were divided into two groups. Group A comprised of 30 cases of pre-eclampsia having blood pressure ≥ 140/90mm Hg, proteinuria in 24 hours ≥ 300 mg and edema. Group B had 30 normal pregnant women after 20 weeks of gestation. The data including parity, period of gestation, blood pressure and presenting complaints of all subjects were recorded. The mean value of serum bilirubin in cases was 3.45 and in controls it was 0.50. The mean value of enzymes ALT in cases was 92.7 while in the controls it was 22.37. Mean serum AST in the cases was 85.43 and in the controls it was 21.96. Total protein in cases was 7.77 and controls it was 7.26. Albumin level in cases was 4.62 and controls were 4.17. The mean value of urea in cases was 43.76 and control it was 24.5. The mean value of Creatnine in cases was 1.51 and in control it was 0.80. The mean value of Uric Acid in cases was 5.41 and in control it was 4.45. Increased concentrations of serum bilirubin, total protein, albumin and liver enzymes ALT, AST,urea, creatinine and uric acid were found in pre-eclampsia cases.

KEY WORDS: hypertension, liver function test (LFT), pre-eclampsia, renal function tests (RFT)

INTRODUCTION:

Hypertension is the most common medical disorders in pregnancy[1]. Abnormal liver function test (LFT) occurs in 20% to 30% of pregnancies complicated by Pre-eclampsia and are associated with poor maternal and fetal outcomes[2,3]. Pre-eclampsia and eclampsia are pregnancy induced hypertensive disease[4].

Pregnancy Induce Hypertension (PIH) is raised blood pressure without proteinuria during the second half of pregnancy. Pre- eclampsia is a multisystem disorder, unique to pregnancy that is usually associated with raised blood pressure and proteinuria after 20 weeks of gestation. Eclampsia is one or more convulsions in association with syndrome of pre-eclampsia[5,6]. In pre-eclampsia the systolic BP is ≥ 140 mm Hg and diastolic BP ≥ 90mm Hg in a woman with previously normal blood pressure and with proteinuria ≥ 0.3gm in a 24 hour urine collection[5]. The main cause of pre-eclampsia is vasoconstriction and thickening of vascular media which decreases vascular capacity and increases peripheral resistance. The factors that appear to have role include placenta, maternal immune response, maternal vascular disease, genetic predisposition and maternal low calcium level. The cellular cause of pre-eclampsia lies within the placenta and resolution of pre-eclampsia starts with removal of placenta at delivery. In pre-eclampsia the ratio of prostacy-cline–thromboxane production rate is decreased favoring the vasoconstrictive thromboxane. During preeclamptic pregnancy, the placenta is under oxidative stress with increased production of lipid peroxides and decreased production of antioxidants.

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Maternal circulating oxidized lipids may be the cause of endothelial cell activation[7].

Liver function Test (LFT) abnormalities occur in 3% of the pregnancies and pre-eclampsia is the most frequent cause. In the last trimester liver disease associated with abnormal liver function tests, nausea and/or vomiting and abdominal pain is due to severe pre-eclampsia, HELLP syndrome or acute fatty liver of pregnancy with or without sub-capsular hepatic hematomas, amongst which there is an ovelap[8].

Liver dysfunction during pre-eclampsia has serious consequences. In pre- eclampsia accompanied by HELLP syndrome, an elevation in liver function test result is noted. Alanine aminotransferase (ALT) and Aspartate aminofransferase (AST) may also be elevated and hyper-bilirubinemia may occur, especially in the presence of haemolysis. Periportal hemorrhagic necrosis in the periphery of the liver lobule is probably the lesion that causes elevated serum liver enzyme levels. Haemorrhage under the liver capsule can be so severe that the capsule ruptures and causes life threatening intra peritoneal bleeding[8].

In normal pregnancy there is decreased blood pressure response to pressor substance but in pre-eclamptic there is marked response to vasopressin, epinephrine end angiotensin. This response of arterial system leads to generalized vasoconstriction and hypertension in preeclampsia. Generalized vasoconstriction is responsible for decreased Glomerular filtration Rate (GFR) and renal plasma flow. This causes alteration in urea, creatinine and uric acid levels[15].

The objective of this study was to compare liver function tests & renal function tests in pre-eclamptics and normal pregnant females.

MATERIAL AND METHODS:

This study was carried out on 60 pregnant women after 20 weeks of gestation admitted in Obstetrics & Gynaecology units of Shri Shankaracharya Institute of Medical Sciences, Bhilai, Chhattisgarh from July 2017 to July 2018 with convenience sampling. The subjects were divided into two groups. Group A comprised of 30 cases of pre-eclampsia having blood pressure ≥ 140/90mm Hg, proteinuria in 24 hours ≥ 300 mg and edema. Group B had 30 normal pregnant women after 20 weeks of gestation. The data including parity, period of gestation, blood pressure and presenting complaints of all subjects were recorded.

Serum bilirubin, total protein, albumin, ALT, AST, urea, creatinine & uric acid were measured by MERIL AUTO QUANT 200i analyzer.

Total and direct bilirubin was measured by Diazo method. Total protein by Biuret method (end point). Albumin by BCG dye method (end point). AST & ALT was measured by IFCC Kinetic method. Urea was measured by Urease-GLDH method. Creatinine by Jaffe's method. Uric acid by Uricase method.

Both the cases and controls were in the age group 15-45 years. Those with a major systemic disease which may elevate the patient's blood pressure or which may change the liver function tests eg. renal diseases, liver diseases, diabetes and cardiac disease were excluded. Patients using any drugs that affect liver function were not included.

Verbal and written consent was obtained from each subject. Complete obstetrical and family history was recorded on proforma designed for the study.

Four variables were measured for all cases and controls ie. Serum bilirubin level, total protein, albumin and plasma levels of liver enzymes ALT, AST were measured using auto quant Meril 200 analyzer. Mean and standard deviation were calculated. The data were calculated.

The data was analyzed using SPSS-16. The mean values were compared between cases and controls using t-test at 5% level of significance.

RESULTS :

The mean value of serum bilirubin in cases was 3.45 and in controls it was 0.50. The mean value of enzymes ALT in cases was 92.7 while in the controls it was 22.37. Mean serum AST in the cases was 85.43 and in the controls it was 21.96. Total protein in cases was 7.77 and controls it was 7.26. Albumin level in cases was 4.62 and controls were 4.17.

The mean value of urea in cases was 43.76 and control it was 24.5. The mean value of creatnine in cases was 1.51 and in control it was 0.80. The mean value of Uric Acid in cases was 5.41 and in control it was 4.45.

The LFT & RFT variables were noted on cases as well as control. All the variables are continuous in nature. It has been observed that cases and controls were matched for age and there was no significant difference found in age of cases and control. Total bilirubin levels were found to be higher in cases compared to control. The difference of total bilirubin turned out to be highly significant statistically. Direct bilirubin readings show that the

Table 1: Liver Function Test (lft)

	Control Mean(SD)	Cases Mean(SD)	t – statistic	p – value
Age	29.23(6.08)	27.53(5.15)	1.16	0.24
Total bilirubin	0.503(0.19)	3.45(0.78)	-20.02	0.00001*
Direct bilirubin	0.282(0.05)	1.58(0.34)	-20.66	0.00001*
Indirect bilirubin	0.302(0.09)	4.02(1.68)	-12.06	0.00001*
SGPT	22.37(6.97)	92.7(19.91)	-18.25	0.00001*
SGOT	21.96(5.43)	85.43(13.65)	-23.64	0.00001*
TP	7.26(0.65)	7.77(0.91)	-2.44	0.01785*
Albumin	4.17(0.4)	4.62(0.95)	-2.37	0.02251*
Globulin	2.77(0.46)	3.12(0.73)	-2.22	0.0308*

*Statistically significant

Table 2: Renal Function Tests (RFT)

	Control Mean(SD)	Cases Mean(SD)	t – statistic	p – value
Urea	24.5(6.01)	43.76(6.03)	-12.38	0.00001*
Creatinine	0.80(0.09)	1.51(0.18)	-18.62	0.00001*
Uric Acid	4.45(1.09)	5.41(0.84)	-3.8	0.00035*

*Statistically significant

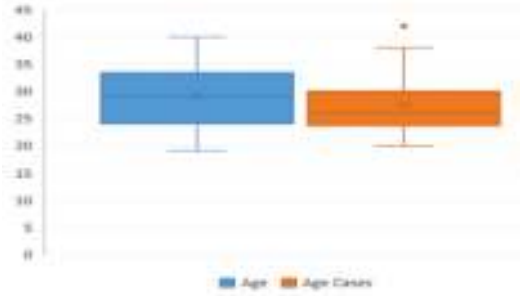

Figure 1: Box and Whisker plot for age distribution.

levels were elevated in cases and the difference between levels of direct bilirubin among cases and controls turned out to be highly significant. Indirect bilirubin was found to be significant and the readings were observed to be higher in cases. SGPT and SGOT were found to be very high in cases and the difference was statistically highly significant. TP levels were slightly elevated in cases and the difference was statistically significant. In case of albumin and globulin the observations were recorded higher in cases compared to control. Albumin and globulin were found to be highly significant. Urea and Creatinine were highly signigicant in cases when compared to controls.

Figure 2: Box & whisker plot for total bilirubin among control and cases

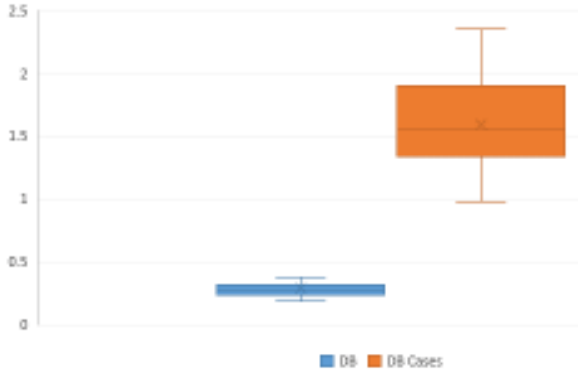

Figure 3: Box & whisker plot for direct bilirubin among control and cases.

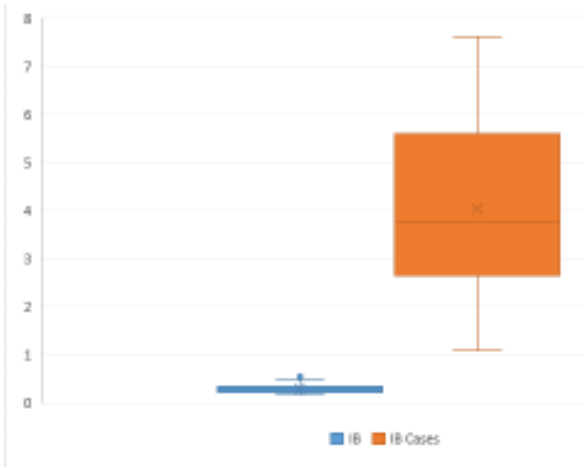

Figure 4: Box & whisker plot for indirect bilirubin among control and cases.

DISCUSSION:

Hypertensive disorders complicating pregnancies are common now a days and consists of both eclampsia and pre-eclampsia. Pre-eclampsia is a condition that develops in previously normotensive pregnant women after 20 weeks of gestation and is

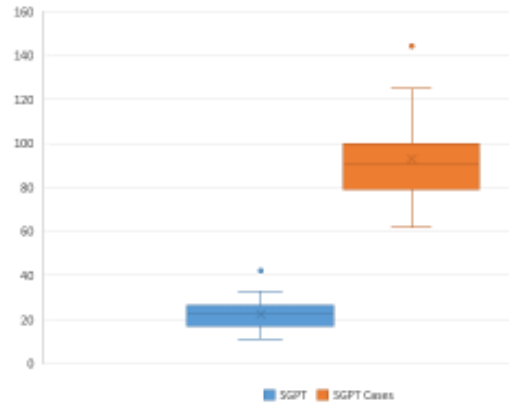

Figure 5: Box & whisker plot for SGPT among control and cases

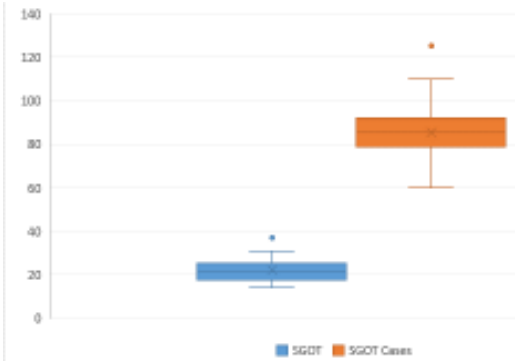

Figure 6: Box & whisker plot for SGOT among control and cases.

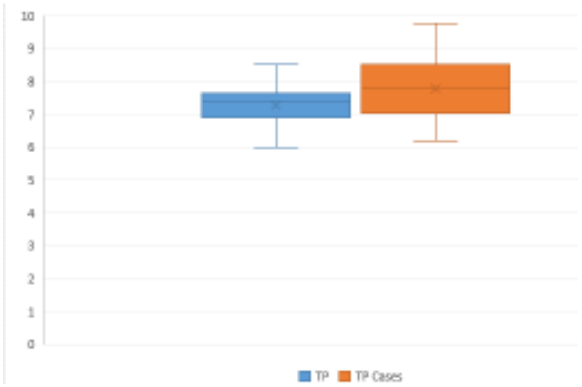

Figure 7: Box & whisker plot for TP among control and cases.

characterized by onset of hypertension and proteinuria. Pre-eclampsia can affect every maternal organ, predominantly the vascular, renal, hepatic, cerebral and coagulation system[5,9,10]. Concentration of serum bilirubin in the present study was significantly higher ($p < 0.001$) in patients of pre-eclampsia before delivery than the control group of same age and parity with normal blood pressure. Malvino et al. showed that in HELLP syndrome serum

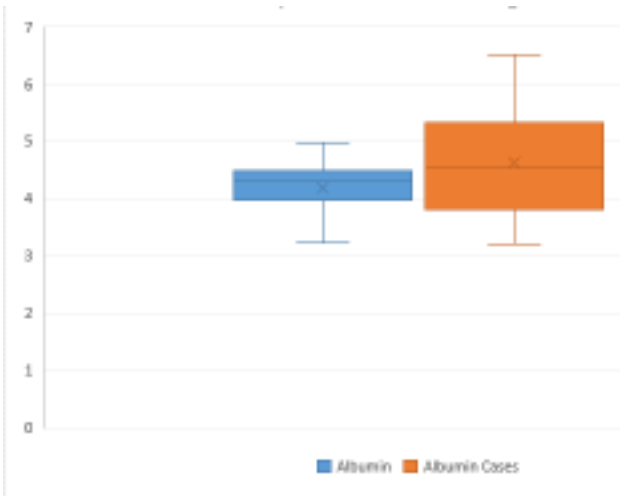

Figure 8: Box & whisker plot for albumin among control and cases.

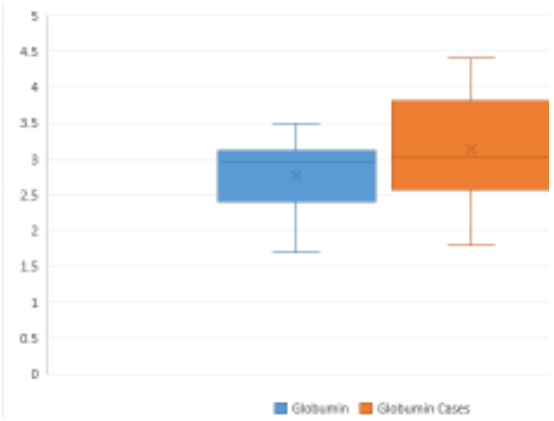

Figure 9: Box & whisker plot for Globumin among control and cases.

bilirubin concentration was elevated from its normal value to about > 1.2 mg/dl[11]. Similarly Jaleel et al. noted that there was a highly significant rise in serum bilirubin, lactate dehydrogenase and aspartate aminofransferase level in pre-eclamptic women compared to normotensive pregnant women.[12] Serum ALT of pre-eclamptic women in the present study was significantly ($p<0.001$) elevated from their normotensive pregnant counterparts. Malvino et al. observed that in pre-eclampsia the serum transaminase level was raise to >10 U/L and that of ALT to 271±297 U/L[11].

In the present study the mean serum AST level in pre-eclamptic cases was found significantly higher ($p < 0.001$) than the normotensive control group. Serum AST level in pre-eclampsia was also found more than 70 U/L by Malvino et al, which rose upto 209±178 U/L in eclampsia[11].

Rath et al also noticed elevated level of ALT and AST in severe pre-eclampsia[13].

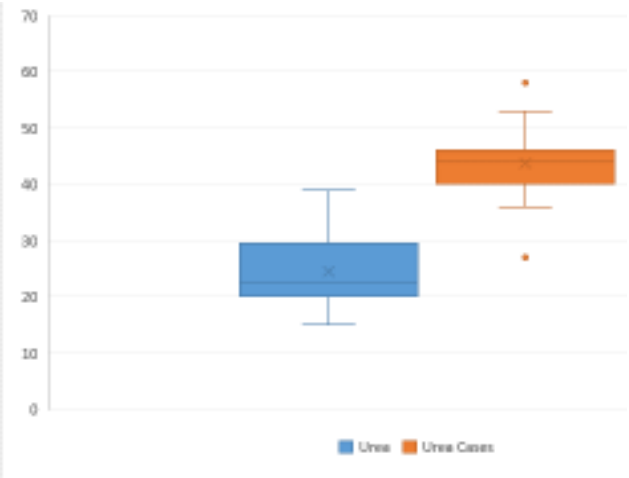

Figure 10: Box & whisker plot for Urea among control and cases.

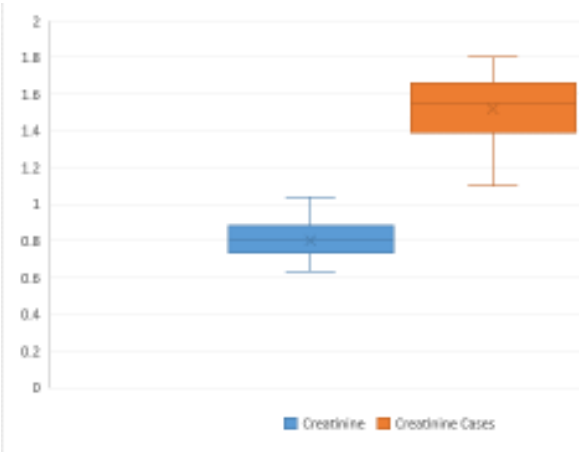

Figure 11: Box & whisker plot for Creatinine among control and cases.

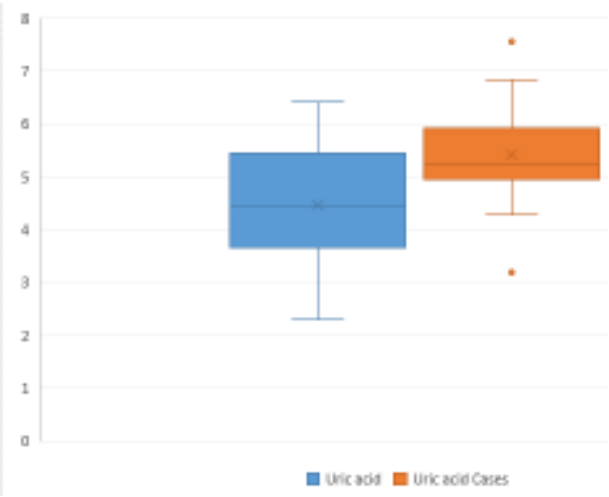

Figure 12: Box & whisker plot for Uric Acid among control and cases.

Mechanism of raised liver enzymes hypervascularisation and vaso constriction of liver leading to cell injury, alteration of membrane permeability & damage to hepatocytes. Liver dysfunction during pre-eclampsia has serious consequences. In pre- eclampsia accompanied by HELLP syndrome, an elevation in liver function test result is noted. Alanine aminotransferase (ALT) and Aspartate aminofransferase (AST) may also be elevated and hyper-bilirubinemia may occur, especially in the presence of haemolysis. Periportal hemorrhagic necrosis in the periphery of the liver lobule is probably the lesion that causes elevated serum liver enzyme levels. Haemorrhage under the liver capsule can be so severe that the capsule ruptures and causes life threatening intra peritoneal bleeding[8].

In normal pregnancy there is decreased blood pressure response to pressor substance but in pre eclamptic there is marked response to vasopressin, epinephrine end angiotensin. This response of arterial system leads to generalized vasoconstriction and hypertension in preeclampsia. Generalized vasoconstriction is responsible for decreased Glomerular filtration Rate (GFR) and renal plasma flow. This causes alteration in urea, creatinine and uric acid levels.

In our study the mean gestation age of pre-eclamptic patients was 35.4 ± 4.18 weeks. This is in agreement with Kim et al. who noted that among the abnormal liver function tests in pregnancy 39.4% occurred between 30 and 40 gestational weeks while 29% occurred between 10 and 20 weeks and common causes were hyperemesis gravidarum followed by pre-eclampsia; viral hepatitis and HELLP syndrome[14].

Renal Function Test (RFT) like urea and creatnine are significantly elevated. Serum uric acid is not increased significantly. Serum urea, creatnine is significantly elevated ($p > 0.001$) in Jlmaah et al.[16] Some investigators found that the activity of Monoamine Oxidance (MAO) is lower and serotonin is higher. Reduced GFR with reduced plasma renal blood flow causes increased serum creatinine and blood urea Hussein el al[17].

In the present study there is significant increase in urea and creatinine which has been interpreted to act as important co-factor in the pathogenesis of pre-eclampsia. Present study also suggests that serum liver enzymes, bilirubin, total protein, urea, creatnine to be of immense value in undertaking the pathogenesis and also appears to be important factor deciding pregnancy.

CONCLUSION:

In the present study, serum levels of total bilirubin , SGOT, SGPT, total protein were significantly raised in the cases compared to controls. During pre eclamptic pregnancy, the placenta is under oxidative stress with increased production of lipid peroxides along with anti oxidants. Maternal circulating oxidized lipids may be the cause of endothelial cell destruction leading to liver cell injury. These results in abnormal liver function tests. More studies are required to substantiate our hypothesis.

Liver and Renal involvement in Pre-eclampsia is very common in co relation to oxidative stress, deranged plasma renal blood flow leading to decreased GFR and increased renal parameters to combat with marker of oxidative stress.

Present study will be helpful to determine the status of the working of kidney and liver to plan the definitive and proper treatment of pre eclampsia along with management of liver and kidney parameters.

LIMITATION OF THE STUDY:

The limitation of our study is that the study subjects are less & should be done on a larger population.

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