

## ORIGINAL ARTICLE

## LIVER FUNCTION TESTS IN PREECLAMPSIA

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**Background:** Preeclampsia is a multisystem disorder that can induce damage to cardiovascular system, kidneys, brain and liver. Pregnancy-induced hypertension (PIH) is responsible for significant maternal and perinatal morbidity. This study was conducted to compare the liver function tests in preeclampsia with normal pregnancy. **Methods:** This study was carried out on 100 pregnant women after 20 weeks of gestation admitted in Obs/Gyn units of Ayub Teaching Hospital, Abbottabad. The subjects were divided into two groups. Group A consisted of 50 cases of preeclampsia having blood pressure  $\geq 140/90$  mmHg, proteinuria in 24 hours  $\geq 300$  mg and oedema; Group B had 50 normal pregnant women after 20 weeks of gestation. The data including BMI, parity, period of gestation, blood pressure and presenting complaints of all subjects were recorded. Serum bilirubin and plasma levels of liver enzymes ALT, AST and ALK were measured. **Results:** The mean BMI of the cases was  $29.04 \pm 3.97$  and that of controls was  $26.54 \pm 3.11$ . The mean value of serum bilirubin in cases was  $10.78 \pm 3.74$   $\mu\text{mol/L}$  and in controls it was  $7.92 \pm 2.42$   $\mu\text{mol/L}$  ( $p < 0.001$ ). The mean values of enzyme ALT in cases was  $55.81 \pm 31.93$  U/L while in the controls it was  $15.22 \pm 3.30$  U/L ( $p < 0.001$ ). Mean serum AST in the cases was  $41.34 \pm 10.76$  U/L and in the controls it was  $24 \pm 2.54$  U/L ( $p < 0.001$ ). Mean ALK level of cases before delivery was  $454.16 \pm 243.69$  U/L, and in controls it was  $181.34 \pm 66.76$  U/L ( $p < 0.001$ ). **Conclusion:** Raised levels of serum bilirubin and liver enzymes ALT, AST and ALK were found in preeclampsia cases.

**Keyword:** Preeclampsia, Liver Function Tests, Pregnancy, Hypertension, Morbidity, Women

## INTRODUCTION

Hypertension is the most common medical disorder in pregnancy.<sup>1</sup> Hypertensive disorders of pregnancy are responsible for significant maternal and perinatal morbidity and are the third leading cause of pregnancy related deaths, superseded only by haemorrhage and embolism.<sup>2</sup> Pregnancy Induce Hypertension (PIH) is raised blood pressure without proteinuria during the second half of pregnancy. Preeclampsia 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 preeclampsia.<sup>3,4</sup> In preeclampsia the systolic BP is  $\geq 140$  mmHg and diastolic BP  $\geq 90$  mmHg in a woman with previously normal blood pressure and with proteinuria  $\geq 0.3$  gm in a 24-hour urine collection. Severe preeclampsia is associated with one or more of elevated blood pressure  $\geq 160$  mmHg systolic, or  $\geq 110$  mmHg diastolic, on two occasions at least 6 hours apart, on bed rest; with proteinuria  $\geq 5$  g in a 24-hour urine collection; along with other functional symptoms such as headache, hyper-reflexia, oliguria, epigastric or right upper quadrant pain, impaired liver function, and thrombocytopenia (HELLP syndrome).<sup>3,5</sup> The main cause of preeclampsia is vasoconstriction and thickening of vascular media which decreases vascular capacity and increases peripheral resistance.<sup>6</sup> The precise aetiology of preeclampsia is not still clearly known.<sup>5</sup> It affects almost every organ. 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 preeclampsia lies within the placenta and resolution of preeclampsia starts with removal of placenta at delivery.<sup>7</sup> The increase in peripheral vascular resistance is likely to be a cause of hypertension in these women. Women with preeclampsia have persistent vasoconstriction due to an increased vascular responsiveness to physiologic vasoconstrictive agents like angiotensin-II or an increase in vascular tone or reactivity.<sup>6,8</sup> In preeclampsia the ratio of prostacycline-thromboxane production rate is decreased favouring the vasoconstrictive thromboxane. Both these substances also play a role in the event of thrombocytopenia.<sup>9</sup> During preeclamptic pregnancy, the placenta is under oxidative stress with increased production of lipid peroxides and decreased production of antioxidants.<sup>10,11</sup> Maternal circulating oxidised lipids may be the cause of endothelial cell activation.<sup>12</sup>

Liver Function Test (LFT) abnormalities occur in 3% of the pregnancies, and preeclampsia is the most frequent cause.<sup>12</sup> The liver diseases peculiar to pregnancy have a characteristic time of onset. In the last trimester liver disease associated with abnormal liver function tests, nausea and/or vomiting and abdominal pain is due to severe preeclampsia, HELLP syndrome or acute fatty liver of pregnancy with or without sub-capsular hepatic haematomas, amongst which there is an overlap.<sup>13</sup> Patients with HELLP syndrome are subsets of those with severe

preeclampsia who are at increased risk of multiple system dysfunction.<sup>14</sup> Liver dysfunction during preeclampsia has serious consequences. In preeclampsia accompanied by HELLP syndrome, an elevation in liver function test results is noted. Alanine aminotransferase and aspartate aminotransferase levels 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.<sup>15</sup>

The objective of this study was to compare liver function tests in preeclampsia and normal pregnancy.

### MATERIAL AND METHODS

This study was conducted in Obstetrics and Gynaecology Units of Ayub Teaching Hospital, Abbottabad from 1<sup>st</sup> March to 31<sup>st</sup> August 2008 with convenience sampling. This study was carried out on 100 pregnant women (50 preeclamptic and 50 controls) after 20 weeks of gestation belonging to Hazara Division. The subjects were divided into two groups. Group A had 50 cases of preeclampsia having BP  $\geq 140/90$  mmHg, proteinuria  $\geq 300$  mg in 24 hours, and oedema. Group B included 50 pregnant women with normal BP after 20 weeks of gestation.

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, e.g., renal disease, 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 a proforma designed for the study.

Four variables were measured for all cases and controls, i.e., serum bilirubin level and plasma levels of liver enzymes ALT, AST and ALK. Mean and Standard Deviation were calculated. The data were analysed using SPSS-10. The mean values were compared between cases and controls using *t*-test at 5% level of significance.

### RESULTS

All cases presented with hypertension, proteinuria and oedema, 11 (22%) in unconscious condition, 30 (60%) with headache, and 12 (24%) with pain epigastrium. The mean BMI of the cases was  $29.04 \pm 3.974$  and of the controls was  $26.54 \pm 3.105$ . The difference in the mean values of the two groups was highly significant ( $p < 0.001$ ) (Table-1).

Mean systolic blood pressure of the cases was  $166.60 \pm 24.042$  mmHg and of the controls was  $116.80 \pm 9.022$  mmHg ( $p < 0.001$ ). The mean diastolic blood pressure of the cases was  $106.50 \pm 13.180$  mmHg and of the controls was  $73.44 \pm 7.288$  mmHg ( $p < 0.001$ ) (Table-2).

The mean value of serum bilirubin in cases was  $10.78 \pm 3.743$   $\mu\text{mol/L}$ , and in controls it was  $7.92 \pm 2.423$   $\mu\text{mol/L}$  ( $p < 0.001$ ). The mean values of enzyme ALT in cases was  $55.81 \pm 31.925$  U/L while in the controls it was  $15.22 \pm 3.304$  U/L ( $p < 0.001$ ). The mean values of serum AST in the cases was  $41.34 \pm 10.764$  U/L and in the controls it was  $8.24 \pm 2.544$  U/L ( $p < 0.001$ ). ALK levels of cases before delivery were  $454.16 \pm 243.694$  U/L and in the controls were  $181.34 \pm 66.764$  U/L. The levels of ALK were significantly higher in hypertensive cases than in normotensive controls ( $p < 0.001$ ) (Table-3).

**Table-1: Mean Body Mass Index of cases and controls**

|                          | Subjects | Number | Mean $\pm$ SD     | <i>p</i> |
|--------------------------|----------|--------|-------------------|----------|
| BMI (Kg/m <sup>2</sup> ) | Cases    | 50     | 29.04 $\pm$ 3.974 | <0.001   |
|                          | Controls | 50     | 26.54 $\pm$ 3.105 |          |

**Table-2: Mean Blood Pressure of cases and controls**

|                     | Subjects | Mean $\pm$ SD       | <i>p</i> |
|---------------------|----------|---------------------|----------|
| Systolic BP (mmHg)  | Cases    | 166.60 $\pm$ 24.042 | <0.001   |
|                     | Controls | 116.80 $\pm$ 9.022  |          |
| Diastolic BP (mmHg) | Cases    | 106.50 $\pm$ 13.180 | <0.001   |
|                     | Controls | 73.44 $\pm$ 7.288   |          |

**Table-3: Mean Liver Profile of cases and controls**

|                                       | Subjects | Mean $\pm$ SD        | <i>p</i> |
|---------------------------------------|----------|----------------------|----------|
| Serum bilirubin ( $\mu\text{mol/L}$ ) | Cases    | 10.78 $\pm$ 3.743    | <0.001   |
|                                       | Controls | 7.92 $\pm$ 2.423     |          |
| ALT (U/L)                             | Cases    | 55.81 $\pm$ 31.925   | <0.001   |
|                                       | Controls | 15.22 $\pm$ 3.304    |          |
| AST (U/L)                             | Cases    | 41.34 $\pm$ 10.764   | <0.001   |
|                                       | Controls | 8.24 $\pm$ 2.544     |          |
| ALK (U/L)                             | Cases    | 454.16 $\pm$ 243.694 | <0.001   |
|                                       | Controls | 181.34 $\pm$ 66.764  |          |

### DISCUSSION

Preeclampsia is a condition that develops in previously normotensive pregnant women after 20 weeks of gestation, and is characterised by onset of hypertension and proteinuria. If left untreated, preeclampsia can progress to a convulsive state known as eclampsia.<sup>3-5</sup> This multisystem, pregnancy specific condition illustrates that preeclampsia can affect every maternal organ, predominantly the vascular, renal, hepatic, cerebral and coagulation systems.<sup>3,5,16</sup> Hypertensive disorder affects 5–10% of all pregnancies.<sup>16</sup> High BMI before pregnancy has been seen to increase a woman's risk of developing preeclampsia.<sup>5,17</sup> In our study the preeclamptic patients had a significantly higher ( $p < 0.001$ ) BMI than their normotensive counterparts. Hauger *et al* and other researchers in their studies also concluded that raised BMI is associated with an increase in the incidence of development of preeclampsia.<sup>18,19</sup> Serum bilirubin level in the present study was found significantly higher ( $p < 0.001$ ) in patients of preeclampsia before delivery than the control group of same age and

parity with normal blood pressure. This is in accord with a study by Malvino *et al* that showed that in HELLP syndrome serum bilirubin level was elevated from its normal value to about >1.2 mg/dl.<sup>20</sup> Similarly Jaleel *et al* noted that there was a highly significant rise in serum bilirubin, lactate dehydrogenase and aspartate aminotransferase level in preeclamptic women compared to normotensive pregnant women.<sup>21</sup> Serum ALT of preeclamptic women in this study was significantly ( $p<0.001$ ) elevated from their normotensive pregnant counterparts. Several research workers also had found an elevated level of ALT in their study populations which is in line with the findings of the present study.<sup>22</sup> Malvino *et al* observed that in preeclampsia the serum transaminase level was raised to >10 U/L and that of ALT to  $271\pm 297$  U/L.<sup>20</sup> In the present study the mean serum AST level in preeclamptic cases was found significantly higher ( $p<0.001$ ) than the normotensive control group. Serum AST level in preeclampsia was also found more than 70 U/L by Malvino *et al* which rose up to  $209\pm 178$  U/L in eclampsia.<sup>20</sup> An elevated level of AST in preeclampsia was also cited by some other workers.<sup>23,24</sup> Rath *et al* also noticed elevated level of ALT and AST in severe preeclampsia.<sup>25</sup> In our study the mean gestation age of preeclamptic patients was  $35.4\pm 4.18$  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 preeclampsia, viral hepatitis and HELLP syndrome.<sup>26</sup>

## CONCLUSION

Raised levels of serum bilirubin and liver enzymes ALT, AST and ALK were seen in preeclampsia cases.

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