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Study of Serum Hepatic Enzymes in Preeclampsia.

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Abstract:

This study was conducted to examine the possible role of Live Fucnction Test (LFT) in the prediction of severity of preeclampsia. The study graph comprised of 40 preeclamptic cases and 40 healthy normotensive pregnant controls. Serum samples of all cases were assessed for LFT , Gramma Glytamyl Transferase (GGT) and Lactate Dehydrogenase (LDH).

The results indicated that total bilirubin level and activities of enzymes, Asparate Transaminase (AST) ,Alanine Transaminase (ALT), Alkaline Phosphate (ALP), Glytamyl Transferase (GGT) and Lactate Dehydrogenase (LDH) were significantly increased in mild and severe preeclampsia whereas decreased total protein and albumin level were observed.

Keywords: Serum Hepatic Enzymes, Preeclampsia , Liver Fuction Test etc.

Introduction:

Hepatic dysfunction with preeclampsia has long been recognized. Several studies have suggested that liver involvement in preeclampsia is serious and frequently accompanied by evidence of other organs involvement, especially the kidney and brain along with hemolysis and thrombocytopenia. This is commonly referred to as HELLP syndrome (hemolysis, elevated liver enzymes and low platelets) (1, 2). In India, the incidence of preeclampsia amongst the hospital patients is about 7-10 % of all antenatal admissions (3).

Many of the clinical and laboratory signs usually associated with liver disease are present in normal pregnancy. Serum alkaline phosphotase levels increase in late pregnancy because of both a production of the placental isoenzyme and an increase in bone isoenzyme (4, 5).However values for serum aspartate transferase (AST), alanine transferase (ALT), gamma glutamyl transferase (GGT), lactate dehydrogenase (LDH) and bilirubin does not significantly altered during normal pregnancy. Any increase in these values may reflect hepatobiliary pathology (6, 7). Liver dysfunction in pregnancy can affect both maternal and fetal health. Girling JC et al (8) 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(9-12).

In India, only few studies (13-15) 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.

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.

Material And Methods:

This prospective study was conducted in the department of Biochemistry, S.R.T.R. Medical College and Hospital Ambajogai. A total of 40 preeclampsia women (22 with mild and 18 with severe Preeclampsia) and 40 healthy normotensive pregnant women (controls) were enrolled in the study. All the cases were selected in the third trimester and belongs to the age group 19-35 years cases with any medical history of hypertension, diabetes, renal disease, thyroid disease or liver disease, were excluded from the study. Controls were selected from the patients regularly attending the Antenatal clinic (ANC) and preeclampsia cases were selected from the patients admitted in the ANC ward.

Mild preeclampsia was defined as onset of hypertension after 20 weeks of gestation with diastolic blood pressure (DBP) >90 and systolic blood pressure ≤ 110 mmHg with or without proteinuria. When diastolic blood pressure (DBP) > 110 mmHg was measured on two occasions 6 hours apart with significant proteinuria (>500 mg / 24 hrs or ≥ 2+ on dipstick), preeclampsia was considered as severe.

Detailed clinical and anthropometric data was recorded. 8 ml of fasting venous blood was collected aseptically from all cases by venipuncture. The blood was allowed to clot and serum separated was used for the estimations. Serum was used for the estimations of bilirubin, total protein, and albumin, AST, ALT, ALP, GGT and LDH. Bilirubin, total protein, albumin, AST, ALT, ALP were estimated by using commercial kits of Transasia. Serum GGT was estimated using commercial kit from Teco Diagnostics by Rozaklis gamma glutamyl P-nitroaniline (GGPNA) colorimetric end point method (16). LDH was estimated using commercial kit from AGAPEE diagnostics by kinetic method (17). The estimations were carried out on semi autoanalyzer (ERBACHEM- 5 plus). The results were expressed as means ± SD and compared by applying unpaired student't' test to find out the statistical significance according to the severity of preeclampsia.

Observation & Results:

Table No. I: Demographic characteristics of Normal pregnancy and Preeclampsia cases:

Demographic data of women with preeclampsia and healthy normotensive controls are shown in Table I. A statistically significant decrease ($P<0.05$) in terms of age, gravidity and

parity was found among women with severe preeclampsia than normotensive controls. Systolic and diastolic blood pressure were significantly increased in mild (P<0.05) and severe (P<0.001) preeclamptic women, when compared with normotensive controls. Maternal weight was increased and newborn birth weight (from records) was found to be significantly low in severe preeclamptic women than normotensive controls (P<0.05).

Sr. No.	Parameters	Normal pregnancy (N=40)	Mild preeclampsia (N=22)	Severe preeclampsia (N=18)
1	Age(yrs)	25.13 ± 2.34	24.18 ± 3.71	22.16 ± 2.25
2	Gravidity	3.2 ± 2.4	3.1 ± 2.5	2.2 ± 1.4*
3	Parity	2.6 ± 0.5	1.7 ± 0.6	1.2 ± 0.4*
4	Systolic BP (mmHg)	110.0 ± 10.4	143.0 ± 12.5*	170.5 ± 10.6**
5	Diastolic BP (mmHg)	67.4 ± 4.8	92.0 ± 7.5*	112.0 ± 5.8**
6	Maternal weight (Kg)	65.6 ± 7.5	68.2 ± 5.2	72.4 ± 4.6*
7	Birth Weight (Kg)	3.2 ± 0.17	2.9 ± 0.22	2.2 ± 0.18*

Values are given as mean ± SD * p < 0.05; ** p < 0.00

TABLE-II: Laboratory data of normal Pregnancy, Mild and Severe Preeclampsia:

Sr. No.	Parameters	Normal Pregnancy (n=40)	Mild preeclampsia (n=22)	Severe Preeclampsia (n=18)
1	Urea (mg/dl)	18.65 ± 4.31	19.22 ± 2.04	24.85 ± 4.30*
2	Creatinine (mg/dl)	0.62 ± 0.14	0.75 ± 0.23	1.3 ± 0.19*
3	Uric Acid (mg/dl)	3.5 ± 0.76	5.0 ± 1.2	7.20 ± 1.4*
4	Platelets (x 10^9/l)	220 ± 30.2	205 ± 22.0	185.5 ± 28.33*
5	Proteinuria (on dipstick)	---	1 +	2 + or 3+

Values are given as mean ± SD *p < 0.05

Table II shows the laboratory data of the study groups. The levels of urea, creatinine and uric acid were found to be significantly increased in severe preeclamptic women as compared with normotensive ones (P<0.05). A statistically significant decrease (P<0.05) was found in platelet count among severe preeclamptic women when compared with those in normotensive controls. The degree of proteinuria was persistant 1+ on dipsick in mild and 2+ or 3+ in severe preeclampsia. The total bilirubin was significantly increased (P<0.05) and total protein and albumin level were decreased (P<0.05) in mild and severe preeclampsia.

Table III: Liver function Tests in Normal Pregnancy, Mild and Severe Preeclampsia

Sr. No.	Parameters	Normal Pregnancy (n=40)	Mild Pregnancy (n=22)	Severe Pregnancy (n=18)
1	Bilirubin (mg/dl)	0.79 ± 0.17	0.82 ± 0.24	1.4 ± 0.29*
2	Total protein (gm/dl)	5.91 ± 0.30	5.6 ± 0.71	5.1 ± 0.42*
3	Albumin (gm/dl)	3.67 ± 0.82	3.40 ± 1.2	2.63 ± 0.61*
4	AST (IU/L)	22.26 ± 2.55	30.00 ± 3.08	46.27 ± 3.03**
5	ALT (IU/L)	16.74 ± 2.90	29.23 ± 2.93	44.16 ± 4.28**
6	GGT (IU/L)	10.25 ± 2.01	39.48 ± 4.11	61.66 ± 12.04**
7	LDH (IU/L)	305.20 ± 42.24	535.22 ± 44.82	819.88 ± 90.7**
8	ALP (KA units)	11.28 ± 2.20	14.97 ± 1.61	22.62 ± 2.82*

Values are given as mean ± SD. *P < 0.05; ** p < 0.001

The activities of enzymes AST, ALT, GGT, LDH and ALP were significantly increased in mild (P<0.05) and severe (P<0.001) preeclampsia when compared with those in normotensive controls (Table-III). Prevalence of abnormal level of hepatic enzymes in preeclampsia, when compared with the reference value in our laboratory was shown that 16(40%) women had abnormal levels of AST, 18(45%) women had abnormal levels of ALT, 35(87.5%) women had abnormal levels of GGT and 36(90%) women had abnormal levels of LDH and 22(55%) women had abnormal levels of ALP (Fig-1).

Fig-1: Prevalence of Abnormal Hepatic Enzymes Levels in Preeclampsia

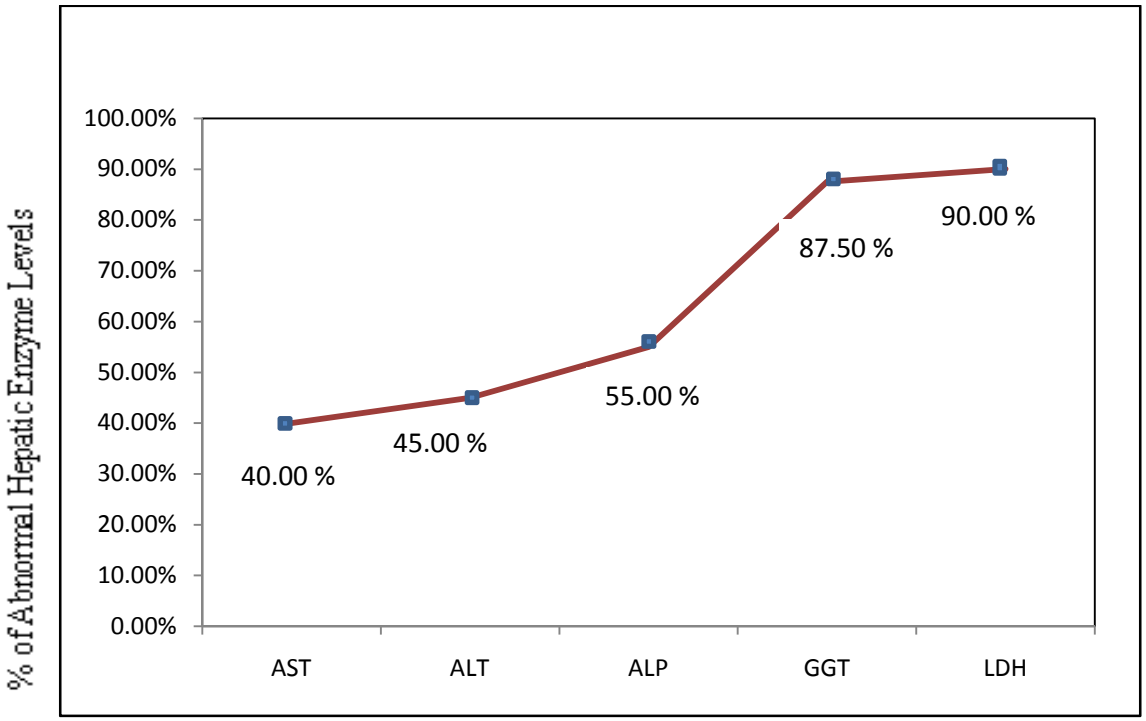

Table-IV: Symptoms According To the Abnormal Levels of GGT and LDH in Severe Preeclampsia

Sr. No.	Symptoms	GGT		LDH	
		=35-70 IU/l	>70 IU/l	=600-800 IU/l	>800 IU/l
1	Epigastric pain (n=10) 55.5%	04 (22.2%)	06 (33.33%)	02 (11.11%)	08 (44.00%)
2	Vomiting (n=10) 55.5%	03 (16.6%)	07 (38.8%)	03 (16.6%)	07 (38.8%)
3	Headache (n=12) 66.66%	07 (38.8%)	05 (27.7%)	06 (33.33%)	06 (33.33%)
4	Blurred vision (n=10) 55.5%	07 (38.8%)	03 (16.6%)	04 (22.2%)	06 (33.33%)

Table IV shows the frequency of symptoms according to the levels of GGT and LDH in severe preeclampsia cases. Among the severe preeclamptic women, headache was the most frequent symptom observed in 66.66% cases and epigastric pain, vomitting and blurred vision were each observed in 55.5 % cases. The frequency of epigastric pain was found to be higher in severe preeclamptic women with GGT >70 IU/L (33.33%) and LDH> 800 IU/L (44%). Vomitting was observed in 38.8% of severe preeclamptic cases with each GGT >70 IU/L and LDH >800 IU /L. Headache and blurred vision were observed in 27.7 % and 16.6 % of cases having GGT >70 IU/L respectively .These symptoms were observed in 33.33 % of women with LDH >800 IU/L.

Discussion:

Young age and primigravidity are the well known risk factors for developing preeclampsia (18). In the present study, the women with severe preeclampsia were significantly younger with low gravidity and parity. Maternal weight was found to be significantly increased in severe preeclampsia than mild and normal pregnant women. Mean birth weight of babies born to mothers with preeclampsia was less than the control subjects. Preeclampsia is associated with reduced placental perfusion, fetal malnutrition and fetal growth retardation (12).

In majority of preeclamptic women mild to moderately diminish glomerular filtration appears due to reduced plasma volume. Uric acid is considered as biochemical marker of preeclampsia was raised beyond the normal levels in preeclampsia suggested that elevated uric acid levels may be due to either decreased renal urate excretion or increased oxidative stress. Platelet count was significantly decreased but not reduced less than $170x10^9$ / l in severe preeclampsia which is diagnostic characteristic of HELLP syndrome. Total protein and albumin were significantly decreased where as bilirubin was significantly raised in severe preeclampsia. Hyperbilirubinemia is uncommon in preeclampsia (19).

We also observed that the levels of serum AST and ALT were significantly increased in women with preeclampsia than normal pregnancy. In mild preeclampsia increase was within normal range but in severe preeclampsia highly increased levels of AST and ALT was found. Many studies (13, 14, and 20) reported increased levels of transaminases in preeclampsia. Romero R. et al (21) reported the prevalence of liver dysfunction as determined by AST was 21% in patients with pregnancy induced hypertension. Girling J.C. (8) observed 54% of abnormal LFTs in preeclampsia by measuring AST and ALT. In the present study the prevalence of abnormal level of AST was 40% and that of ALT was 45% in severe preeclampsia. A rise in ALT is known to be more specific liver damage (22).In agreement with the studies of Makuyana D et al (9) and H.Y. Wong et al (10) our findings demonstrate a significant increase in ALP activity in preeclampsia. The activity of ALP in severe preeclampsia was higher than mild preeclampsia. Abnormal level was seen in 55% women with preeclampsia. It has been suggested that elevated serum ALP levels originate in tissues whose metabolism was either functionally disturbed (e.g. obstructed liver) or greatly stimulated (e.g. the placenta) (23).

Significantly high levels of serum GGT in preeclampsia than normal pregnancy was observed in this study. Serum GGT was higher in severe preeclampsia than mild preeclampsia. Abnormal level was found in 87.50% women with preeclampsia. Previous studies (9) reported high activity of GGT in preeclampsia and showed that increase was independent of other biochemical markers of hepatic damage. It has been reported that endothelial cell destruction within the uteroplacental circulation leads to systemic release of GGT (24). Our data support this hypothesis suggesting an association between serum GGT and preeclampsia.

H.S. Quablan et al (12) showed highly significant increase in LDH activity in severe preeclampsia women than normal pregnant women. They also reported the symptoms and complications of severe preeclampsia along with perinantal mortality were increased significantly in women with LDH > 800 IU/l compared with those who had lower levels. They conclude that LDH is a useful biomarker that reflects the severity and occurrence of complications of preeclampsia. Our findings correlate with this study. In the present study 90% women with preeclampsia had abnormal activity of LDH.

Epigastric pain or right upper quadrant pain is often a symptom of severe preeclampsia and may be caused by subcapsular hematoma, abnormal liver function in HELLP syndrome or it may be indicative of imminent eclampsia. In most cases, this symptom is associated with headache, blurred vision or vomiting(19). In our study, epigastric pain and vomiting were seen in 55.5% case of severe preeclampsia and these symptoms were significantly higher in preeclamptic women with levels of LDH ≥ 800 IU/l, GGT ≥ 70IU/l and abnormal ALP, AST and ALT activity. In 66.66% and 55.5% preeclamptic women had headache and blurred vision. All these patients with these symptoms had abnormal levels of studied enzymes. It has been reported that the abdominal pain in severe preeclampsia was associated with elevation of AST (21) and LDH > 800 IU/l (12)

and suggested that it is indicative of hepatocelluar damage.

Conclusion:

On the basis of our results we conclude that serum GGT and LDH measurements may provide a sensitive indicator of hepatic damage and could have some advantage over routine investigations of liver function, especially in early recognition or severity of preeclampsia. Hepatic enzymes measurement i.e. GGT and LDH with AST and ALT may be clinically beneficial for monitoring the liver function in the management of preeclampsia which has hepatic involvement.

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