e-ISSN: 2582-5208
International Research Journal of Modernization in Engineering Technology and Science
Volume:03/Issue:06/June-2021 Impact Factor- 5.354 www.irjmets.com

ASSOCIATION BETWEEN LFT TEST AND PREECLAMPSIA

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ABSTRACT

Aims: To bring out the pin point correlation between the level of liver function test (LFT) levels in preeclamptic women and healthy pregnant women & to compare the levels of liver function tests with blood pressure

Study Design: This is a case-referent study

Place and Duration of Study: Run in Department of Biochemistry in association with the Department of Obstetrics and Gynecology, ST. Paul's Healthways, Bokaro, Jharkhand for a period of 1year from January 2019 to December 2019

Material and methods: Samples of 30 preeclamptics and 30 healthy pregnant women above 18 years of age admitted in the obstetrics Antenatal ward of ST Paul's Healthways, Bokaro, Jharkhand was taken samples were analyzed for serum Liver function test. The data were analyzed using analytical tools through SPSS 21.0, p-value <0.05 was considered significant

Results: The mean levels of serum bilirubin were higher at 0.98±0.40mg% in cases as compared to controls which was 0.42±0.23mg% with p-value <0.001. The mean value of AST for cases was higher at level of 56.21±35.76IU as compared to the controls at 27.18±16.34IU with p<0.001. Mean value of ALT was higher at 47.56±26.19IU in cases as compared to 22.64±11.85IU in controls with p-value of <0.001. For ALP the mean levels were also higher at level of 304.46±110.50IU in cases and 170.91±67.37IU in controls with p-value of <0.001. The mean level of GGT in cases was 35.36±34.79IU which was higher than controls at level of 20.96±34.79IU and p<0.001. The mean level of total protein was lower in cases with 5.15±0.19 as compared to controls at level of 6.57±0.55, at p-value <0.001.

Conclusion: Based on the results obtained in this study in ST. Paul's Healthways, Bokaro, it was concluded that LFT particularly AST, ALT and ALP levels can be used as potential markers for Diagnosing preeclampsia.

I. INTRODUCTION

Preeclampsia is a pregnancy specific, multisystem and multifactorial syndrome that affects both mother and in fetus by vascular dysfunction and intrauterine growth restriction respectively.[1] It is diagnosed as blood pressure (BP) of ≥ 140 mmHg systolic or ≥90mm Hg diastolic on two occasion at least 4 hours apart after 20 weeks gestation in previously normotensive women and proteinuria ≥300mg in 24hours urine collection or ≥+1 by dipstick method.[2] Several complications have been reported with this disease and it remains a major cause of maternal and fetal morbidity and mortality worldwide.[3] The incidence of preeclampsia is about 5-7% of all pregnancies.[4] According to the World Health Organization (WHO) the incidence of preeclampsia is seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%).[5] In India it is around 10% and in United States of America it is 2.5%.[6]

The exact etiology of preeclampsia is still clearly not known. The most widely accepted being the defective implantation characterized by incomplete invasion of the spiral arteriolar wall by extra villous trophoblasts resulting in small caliber vessels with high resistance to flow.[7] The factors that appear to have role include placenta, maternal immune response, maternal vascular disease, genetic predisposition, and maternal low calcium level.[8] The cellular cause of preeclampsia lies within the placenta and resolution of preeclampsia starts with removal of placenta at delivery.[9] During pregnancy, every organ system undergoes changes in response to increased demands of rapidly growing fetus and placenta. There are intense anatomical and physiological changes in almost all body systems, most importantly hematological, cardiovascular, respiratory, gastrointestinal and hepatobiliary system. These changes are evident in the form of altered biochemical markers.[10]

Liver Function Test (LFT) abnormalities occur in 3% of the pregnancies, and preeclampsia is the most frequent cause.[11] 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 hematomas, amongst which there is an overlap.[12] Liver damage accompanying preeclampsia may range from mild hepatocellular necrosis with serum enzyme abnormalities (aminotransferase and lactate dehydrogenase) to the life threatening hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, with markedly elevated enzyme levels and even subcapsular bleeding or hepatic rupture. The HELLP syndrome represents serious disease and is associated with significant maternal morbidity.[13.14]

This study was planned with the objective to evaluate the liver function tests (LFT) in preeclamptic women and normotensive pregnant women.

II. MATERIALS AND METHODS

Study design: Case-control study

Study setting: Conducted in the Department of Biochemistry in collaboration with Department of Obstetrics and Gynecology, ST Paul's Health ways, Bokaro, Jharkhand.

Study duration: The study was carried out for a period of 12 months from January 2019 to Dec2019 **Study population:** 30 preeclamptic and 30 healthy pregnant women admitted in Antenatal Ward, ST Paul's **Inclusion Criteria:** Patients considered as cases were preeclamptic women aged 18 years and above, admitted in Antenatal ward and willing to participate in the study and patients considered as controls were normotensive pregnant women with no proteinuria admitted in Antenatal ward

Exclusion Criteria: Chronic hypertension, diabetes mellitus, multiple pregnancies, renal disease, smokers, neoplastic diseases

Measurement of liver function tests levels:

1. Total Bilirubin: Done by fully Automated Analyzer Hitachi-704
2. Estimation of AST: Done by fully Automated Analyzer Hitachi-704
3. Estimation of ALT: Done by fully Automated Analyzer Hitachi-704
4. Estimation of Total protein: Done by fully Automated analyzer Hitachi-704

Statistical analysis: was done using SPSS version 21. p-value <0.05 was considered significant

III. RESULTS

Table 1: Mean Blood Pressure of cases and control

	Subjects	Number	Means	p-value
Systolic BP (mmHg)	Cases	30	167.33±25.45	<0.001
	Control	30	113.33±7.58	
Diastolic (mmHg)	Cases	30	103.33±12.41	<0.001
	Control	30	75.00±5.08	

**p < 0.05 is considered to be statistically significant*

As depicted in table no 1, the mean systolic blood pressure of the cases was 167.33±25.45 mmHg which was higher compared to the controls which was 113.33±7.58 mmHg and the difference was statistically significant with p-value <0.001. The mean diastolic blood pressure of the cases was 103.33±12.41 mmHg which was also higher than in controls 75.00±5.08 mmHg and the difference was also significant with p-value of <0.001.

Table 2: Mean Liver Profile of cases and controls

	Subjects	Number	Mean ± SD	p-value
Serum Bilirubin(mg%)	Case	30	0.98±0.40	<0.001
	Control	30	0.42±0.23	

Aspartate aminotransferase (AST) (IU)	Case	30	56.21±35.76	<0.001
	Control	30	27.18±16.34	
Alanine transaminase (ALT) (IU)	Case	30	47.56±26.19	<0.001
	Control	30	22.64±11.85	
Alkaline Phosphatase (ALP) (IU)	Case	30	304.46±110.50	<0.001
	Control	30	170.91±67.37	
Gamma- glutamyl transferase (GGT) (IU)	Case	30	35.36±34.79	<0.001
	Control	30	20.96±34.79	
Total Protein (gm%)	Case	30	5.15±0.19	<0.001
	Control	30	6.57±0.55	

Table no 2 shows the mean levels of serum bilirubin was 1.08±0.40mg% in the cases as compared to controls which was 0.77±0.23mg% and the difference was statistically significant with p-value <0.001. The mean value of AST for cases was 56.21±35.76IU as compared to the controls with 27.18±16.34IU and the difference was statistically significant with p<0.001. Mean value of ALT was 47.56±26.19IU in cases and 22.64±11.85IU in controls and the difference was statistically significant with p-value of <0.001. For ALP the mean levels were 304.46±110.50IU in cases and 170.91±67.37IU in controls with statistically significant p- value of <0.001. The mean level of GGT in cases was 35.36±34.79IU and 20.96±34.79IU in controls and the difference was statistically significant with p<0.001. The mean level of total protein is lower in cases with 5.15±0.19 as compared to controls at 6.57±0.55, the difference which was statistically significant at p-value < 0.001.

Table 3: Correlation between SBP and DBP with the liver function tests

		TBIL	AST	ALT	ALP	GGT
SBP	**R**	0.424**	0.410**	0.430**	0.588**	0.125
	p-value	0.001	0.001	0.001	0.000	0.342
DBP	**R**	0.431**	0.444**	0.443**	0.586**	0.175
	p-value	0.001	0.000	0.000	0.000	0.173

r = (Pearson correlation coefficient)

***correlation is significant at the 0.01 level (2-tailed)*

Table no 3 shows that there is positive correlation between systolic blood pressure (SBP) and diastolic blood pressure (DBP) with serum total bilirubin with r=0.424**, p=0.001 for SBP and r=0.410**, p=0.001 for DBP which shows statistically significant p-value. It also shows positive correlation between SBP and DBP with AST (aspartate aminotransferase) with r= 0.410**, p=0.001 for SBP and r=0.444**, p=0.000 for DBP

This table also shows positive correlation of ALT (alanine transaminase) with SBP with r=0.430**, p=0.001 and DBP with r=0.443** and p=0.000. There was positive correlation between ALP (alkaline phosphatase) with SBP with r=0.588**, p=0.000 and DBP with r=0.586**, p=0.000. There is no significant correlation between GGT (gamma glutamyl transferase) with SBP showing r=0.125 with p-value of 0.34 and also with DBP with r=0.175 and p=0.17 which was not statistically significant.

IV. DISCUSSION

Preeclampsia (PE) is a dangerous and potentially life-threatening disease for the mother and fetus and it remains a disease of theories.[15] Recent work suggests a two-stage process - Stage 1: abnormal placentation leading to placental hypoperfusion progressing in some patients to Stage 2: endothelial dysfunction leading to multi-systemic involvement characteristic of preeclampsia. Strong evidence supports the involvement of deficient trophoblast survival, inadequate endovascular invasion, endothelial cell dysfunction, and a systemic

maternal inflammatory response.[16,17] Failure of trophoblast invasion inhibits decidualization leading to poor placental blood supply in maternal vessels which further generates placental ischemia and apoptosis.[18] Preeclampsia can cause diseases of the liver. These diseases may not be initiated by pregnancy, but interfere strongly with pregnancy. Exact diagnosis is therefore of high clinical relevance.[19]

In this study, it is evident from table 1 that the systolic blood pressure (SBP) and diastolic blood pressure (DBP) was higher in cases as compared to controls. These findings were in accordance with studies done by Munnaza B et al[9] and Al-Jameil et al.[20] As seen from table 2, it was found that there was an increased

level of plasma levels of serum total bilirubin, serum Aspartate aminotransferase (AST), Alanine transaminase (ALT), Alkaline phosphatase (ALP), Gamma - glutamyl transferase (GGT) in preeclamptic patients compared to normotensive pregnancy controls. Increased plasma levels of AST, ALP, ALT, GGT, and total bilirubin in preeclamptic women was also found by Malvino et al,[21] Munazza et al,[9] Weinstein et al,[22] and Jaleel et al.[23] The lesion due to periportal hemorrhagic necrosis in the periphery of the liver lobule was postulated to cause the elevation in the levels of liver enzymes in serum.[24] The primary fluctuations in liver function evaluation may be due to red cell destruction and ultimately leading to liver injury.[25] Cellular injury in the liver causes release of AST and ALT. ALT is a more specific indication of liver disease, whereas AST elevations may be secondary to damage of other organs (heart, kidney, brain, intestine and placenta). Alkaline phosphatase is associated with cellular membranes, and its elevated levels are caused by injury to the liver, bone, kidneys, intestines, placenta, or leukocytes. In the liver, the enzyme is located in the bile canaliculi and biliary obstruction induces increased synthesis of alkaline phosphatase and spillage into the circulation.[20] This study also showed decreased plasma total protein levels in preeclampsia compared to normotensive pregnancy controls, Gojnic et al[26] in their study found decreased total protein level in severe preeclampsia, which correlated with disease severity. These findings would suggest a reduction in the synthetic function of the liver in severe preeclampsia.

Any liver disorder can occur co-incidentally in pregnancy. Pregnancy can also occur in a patient with pre-existenting chronic liver disorder or portal hypertension. Liver dysfunction in pregnancy can also be secondary to pregnancy called the pregnancy-related liver disorders.[27] The five pregnancy-related liver disorders are acute fatty liver of pregnancy (AFLP), HELLP syndrome (hemolysis, elevated liver enzymes and low platelets), pre-eclamptic liver dysfunction, intrahepatic cholestasis of pregnancy (ICP) and hyperemesis gravidarum occurring in different gestational time periods.[28] Liver dysfunction indicates poor prognosis and is noted in up to 50% of patients with pre-eclampsia.[29]A minority of patients with pre-eclampsia have HELLP syndrome.[30] Not all patients with HELLP have pre-eclampsia, but preeclampsia increases the risk for HELLP syndrome.[31] In preeclampsia, while the cause is unknown, several factors play a role in the pathogenesis, including abnormal vascular response to placentation, increased systematic vascular resistance, enhanced platelet aggregation, activation of the coagulation system, trophoblast invasion of the spiral arteries, abnormal trophoblast differentiation, and endothelial dysfunction.[32,33]

Abnormal liver function tests occur in 20% to 30% of pregnancies complicated by pre-eclampsia and are associated with poor maternal and fetal outcomes.[34] Pre-eclampsia can manifest with few maternal symptoms and signs or as isolated intrauterine growth restriction (IUGR). If unrecognized, preeclampsia can progress to the syndrome of hemolysis, elevated liver enzyme levels and low platelet count (HELLP) and eclampsia. HELLP syndrome is noted in 5- 10% of patients with preeclamptic symptoms. Mortality is 7-35% and perinatal mortality of the child may be up to 40%.[35] Pre-eclampsia and HELLP syndrome are far more dangerous to the fetus than to the mother with rates of IUGR and premature delivery and fetal and neonatal death rates of 6 to 37%, deaths are likely the result of placental insufficiency and hypoxia.[36]

V. CONCLUSION

Based on the results obtained in this study in Bokaro, Jharkhand, it is concluded that liver function tests particularly AST, ALT and ALP levels can be used as potential biomarkers for predicting preeclampsia. The abnormal increase in the levels of liver enzymes in high-risk group compared with normal pregnant women suggests that liver dysfunction along with hypertension in early stages of pregnancy can lead to preeclampsia. Pregnancy-related liver disorders are rare but they are important causes of maternal-fetal morbidity and mortality. The improvement of the standard diagnostic approach is very important for this problem and development of future treatment strategies. Early recognition, timely referral and aggressive management can lead to better maternal and fetal outcome in these patients.

VI. REFERENCES

[1] Turner JA. Diagnosis and management of preeclampsia: An update. International Journal of Women's Health. 2010; 2:327- 337.

[2] Davey DA, MacGillivray I. The classification and definition of the hypertensive disorders of pregnancy. Am J Obstet Gynecol.

[3] 1988;158(4):892-898.

[4] Mackay AP, Berg CJ, Atrash HK. Pregnancy related mortality from preeclampsia and eclampsia. Am J Obstet Gynecol 2001;97(4):533–8.

[5] Report of national high blood pressure education program working group on high blood pressure in pregnancy. Am J Obstet Gynecol. 2000; 183(1): S1-S22.

[6] Dolea C, Abouzahr C. Global Burden of hypertensive disorders of pregnancy in the year 2000. 2003;11(1):1-7.

[7] National high blood pressure education program working group. High blood pressure in pregnancy. Am J Obstet Gynaecol.

[8] 1990; 163:1691-712.

[9] Cunningham, FG, Gant NF, Leveno KJ, Gilstrap III LC, Hauth JC and Wenstrom KD (eds): Williams Obstetrics and Gynecology 23rd ed. USA: McGraw Hill Companies. 2014;728.

[10] Cnossen JS, van der Post JA, Mol BW, Khan KS, Meads CA, ter Riet G. Prediction of pre-eclampsia: a protocol for systematic reviews of test accuracy. BMC Pregnancy Childbirth 2006; 6:29.

[11] Munazza B, Nuzrat R, Ayesha Naureen, Shahbaz AK, Fozia F et al. Liver function tests in preeclampsia. J Ayub Med Coll Abottabad 2011;23(4):3-4.

[12] Puneet M, Gupta V, Chawla D, Aarushi C. Is severity of liver enzymes derangement related to severity of hypertension in patients with preeclampsia?J Gynecol 2016;1(4):1-5.

[13] Angel Gracia AL. Effect of pregnancy on pre-existing liver disease Physiological changes during pregnancy. Ann Hepatol 2000;5(3):184–6.

[14] Burroughs AK. Pregnancy and liver disease. Forum (Genova) 1998;8(1):42–58.

[15] Lang RM, Pridjian G, Feldman T, Neumann A, Lindheimer M, Borow KM. Left ventricular mechanics in preeclampsia. Am Heart J.1991; 121:1768-75.

[16] Cunningham FG, Pritchard JA, Hankins GDV, Anderson PL, Lucas MK, Armstrong KF. Peripartum heart failure: idiopathic cardiomyopathy or compounding cardiovascular events? Obstet Gynecol. 1986; 67:157-63.

[17] Schlembach D. Pre-eclampsia—still a disease of theories. Fukushima J Med Sci. 2003; 49:69–115. [16].Roberts JM, Gammill HS. Preeclampsia: recent insights. Hypertension. 2005;46.

[18] Roberts JM, Hubel CA. The two-stage model of preeclampsia: variations on the theme. Placenta. 2009;30(suppl A):S32–S37.

[19] Fisher SJ, Roberts JM. Defects in placentation and placental perfusion. In: Linheimer M, Roberts JM, Cunningham FG, editors.

[20] Chesley's Hypertension Disorders in Prenancy. 2nd ed. Stanford, CT: Appleton & Lange; 1999:377-394. Cholongitas E, Burrough AK. Liver diseases specific to pregnancy. Ann Gastroenterol. 2008;21(3):164–72.

[21] Al-Jameil N, Tabassum H, Al-Mayouf H, Al-Otay L, Khan FA. Liver Function Tests as Probable Markers of Preeclampsia - A Prospective Study Conducted in Riyadh. J Clin Anal Med 2015;6(4): 461-4.

[22] Malvino E, Munoz M, Ceccottic C, Janello G, Mc Loughlin D, Pawlak A, et al. Maternal morbidity and perinatal mortality in HE LLP Syndrome (Multicentric studies in intensive care units in Buenos Aires area). Medicina (B Aires) 2005;65(1):17–23.

[23] Weinstein L (1982) Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. Am J Obstet Gynecol 142: 159-167.

[24] Jaleel A, Baseer A, Aamir S. Biochemical parameters for detection of hemolysis in pregnancy induced

hypertensive women. J Coll Physicians Surg Pak 1999;9(1):41–2.

[25] Baxter JK, Weinstein L, HELLP syndrome: the state of the art. Obstet Gynaecol Surv. 2004;59(12):838-45.

[26] McMahon L, O'Coigligh S, Redman C (1993) Hepatic enzymes and the HELLP syndrome: a long-standing error? Br J Obstet Gynaecol 100: 693-695.

[27] Gojnic M, Petkovic S, Papic M, Mostic T, Jeremic K, Vilendecic Z, et al. Plasma albumin level as an indicator of severity of preeclampsia. Clin Exp Obstet Gynecol 2004; 31:209-10

[28] Goel A, Jamwal KD, Ramachandran A, Balasubramanian KA, Eapen CE. Prenancy related liver disorders. Journal of Clinical and Experimental Hepatology 2014;4(2):151-162.

[29] Hay JE. Liver disease in pregnancy. Hepatology. 2008;47: 1067–1076.

[30] Kozic JR, Benton SJ, Hutcheon JA, Payne BA, Magee LA, von Dadelszen P. Abnormal liver function tests as predictors of adverse maternal outcomes in women with preeclampsia. J Obstet Gynaecol Can. 2011; 33:995–1004.

[31] Thangaratinam S, Koopmans CM, Iyengar S, et al. Accuracy of liver function tests for predicting adverse maternal and fetal outcomes in women with preeclampsia: a systematic review. Acta Obstet Gynecol Scand. 2011; 90:574–585.

[32] Abraham KA, Connolly G, Farrell J, Walshe JJ. The HELLP syndrome, a prospective study. Ren Fail. 2001; 23:705–713. [32]. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. Lancet 2005; 365:785–99.

[33] Hanna J, Goldman-Wohl D, Hamani Y, et al. Decidual NK cells regulate key developmental processes at the human fetal-maternal interface. Nat Med 2006;12: 1065–74

[34] Verghaeghe J, Anthony J, Davey Da. Platelet count and liver function tests in proteinuric and chronic hypertension inpregnancy. S. Afr Med J 1990 ; 79:590-594.

[35] Raval DS, Co S, Reid MA, Pildes R. Maternal and neonatal outcome of pregnancies complicated with maternal HELLP syndrome.

[36] J Perinatol 1997; 17:266-9.

[37] Reubinoff BE, Schenker G: HELLP syndrome-a syndrome of hemolysis, elevated liver enzymes and low platelet count- complicating preeclampsia-eclampsia. Int Gynecol Obstet 1991;36:95.