Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2014; 2(5A):1569-1572 **ISSN 2347-954X (Print)**
©Scholars Academic and Scientific Publisher
(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com **DOI:** 10.36347/sjams.2014.v02i05.012

Research Article

Study of Liver Enzymes Especially Lactate Dehydrogenase to Predict Foetal Outcome in Pregnancy Induced Hypertension

Swati Bera[1], Soma Gupta[2]*, Santa Saha (Roy)[3], Sanjay Kunti[4], Soumi Biswas[5], Debdatta Ghosh[6]
[1]Associate Professor, Department of Biochemistry, RG Kar Medical College, Kolkata
[2]Professor & Head, Department of Biochemistry, College of Medicine & Sagore Dutta Hospital, Kolkata
[3]Associate Professor, Department of Biochemistry, Medical College, Kolkata
[4]Assistant Professor, Department of Biochemistry, College of Medicine & Sagore Dutta Hospital, Kolkata
[5]Post Graduate Trainee, Department of Biochemistry, RG Kar Medical College, Kolkata
[6]Professor, Department of Gynaecology & Obstetrics, RG Kar Medical College, Kolkata

***Corresponding author**
Soma Gupta
Email: guptasomarusa@yahoo.com

Abstract: The activity of liver enzymes, namely ALT, AST and LDH was evaluated in 68 cases of Pregnancy induced hypertension along with 56 normal primiparous subjects. The activity of all 3 enzymes were found to be elevated significantly in subjects with Pregnancy induced hypertension with respect to control subjects. Fetal birth weight was found to be significantly decreased in former condition and correlated significantly with the change in liver enzyme activity. The correlation was most in case of LDH activity (Pearson Correlation Coefficient = -0.74, p <.0001). Conditions like APGAR score below 7 at 1 and 5 minute after birth, fetal asphyxia, Intrauterine death were considered as bad fetal outcome. The accuracy of maternal liver enzyme to predict the bad foetal outcome was done by Receiver operating characteristic (ROC) curve. In this case also, LDH activity gave better result (Area under curve: 0.89) than other 2 enzymes (Area under curve 0.80 & 0.74 for ALT & AST respectively). The cut off value for LDH to predict bad fetal outcome was found to be 550 IU/L.
Keywords: Pregnancy induced hypertension, bad foetal outcome, Lactate Dehydrogenase

INTRODUCTION

Pregnancy induced hypertension (PIH) is a global problem with a 5-15% incidence rate in India and complicating 10-17 % of all pregnancies [1, 2]. The complications of PIH are responsible for significant maternal and perinatal morbidity and are the third leading cause of pregnancy related deaths, superseded only by hemorrhage and embolism [3]. Preeclampsia is associated with raised blood pressure (BP) after 20 weeks of gestation (Systolic BP ≥ 140mm of Hg. and Diastolic BP ≥ 90 mm of Hg.), with history of previous normal BP and with proteinuria ≥ 0.3 gm in 24 hours urine collection. Hemolysis, elevated liver enzymes and low platelet count (HELLP syndrome) has been recognized as a complication of pregnancy induced hypertension for decades [4].

Lactate dehydrogenase (LDH), an intracellular enzyme is often measured to evaluate the presence of cellular damage and according to Qublan et al serum LDH is an useful marker in PIH as well as an useful predictor of foetal outcome [5]. The negative correlation between LDH and birth weight of the baby was well documented by He *et al*. [6].

With this background, this study was designed to evaluate the changes of enzymes activity, such as Alanine aminotransferase (ALT), Aspartate aminotransferase (AST) and Lactate dehydrogenase (LDH) in PIH and their correlation with foetal birth weight. Moreover, an attempt was made to evaluate that whether the alteration of enzyme activity, if any, can predict fetal outcome or not.

MATERIAL & METHODS

Study Population

The study was conducted in the Biochemistry Department of R.G.Kar Medical College and the history and blood sample of the patients were obtained from Gynaecology & Obstetrics Department from January 2011- February 2013. There were 68 primipara mothers aged between 19-30 years diagnosed to be suffering from PIH and admitted for observation and treatment in R.G.Kar Medical College& Hospital. The primipara mothers who were suffering from chronic hypertension, diabetes mellitus, twin pregnancy, liver disorder, myopathy or any other medical illness were excluded from the study.

Control Group

A total of 56 age matched primipara mothers who were normotensive and admitted for normal delivery were included in the study to serve as controls.

After taking the history and noting the BP, blood samples were collected in fasting condition. About 4 ml. blood was collected in a clotted vial and the serum obtained from it was used for estimation of Alanine amino transferase (ALT), Aspartate amino transferase (AST) and Lactate dehydrogenase (LDH). ALT, AST and LDH activity in serum were estimated by modified IFCC method using the kit obtained from Crest Biosystem. [7-9]

Fetal birth weight was recorded as a routine procedure just after delivery. APGAR score was noted at one and five minutes after birth. If it remained below 7, it was considered as bad fetal outcome. IUD and Stillbirth were also recorded and considered as bad fetal outcome.

Statistical Analysis

All the data were tabulated and analysed using the software "Analyse – it" for Microsoft Excel version 2.30. The difference in mean values of maternal liver enzyme and foetal birth weight was done by t test. The correlation of maternal liver enzyme and foetal birth weight was done by calculating Pearson Correlation Coefficient. The other foetal outcomes like low APGAR score, asphyxia, IUD etc were considered as bad outcome. The accuracy of maternal liver enzyme to predict the bad foetal outcome was done by Receiver operating characteristic (ROC) curves.

RESULTS

A total of 124 subjects were included in this study, of which 68 were PIH cases and 56 were age matched controls. The changes in maternal liver enzymes, namely Alanine Transaminase (ALT), Aspartate Transaminase (AST) and Lactate Dehydrogenase (LDH) and foetal birth weight in PIH cases with respect to controls are shown in Table 1. All the enzymes were found to be significantly elevated in PIH cases, whereas foetal birth weight was found to be significantly decreased.

Among 68 PIH subjects, only 49 cases could be traced upto delivery. So, whether any correlation exists between the changes in maternal liver enzyme with foetal birth weight was determined by Pearson Correlation Coefficient (Table 2) in 49 subjects only. All three enzymes (ALT, AST, LDH) were found to have significant negative correlation ($p < 0.05$) with foetal birth weight. However, LDH was found to be most strongly correlated (- 0.74).

So far other bad fetal outcomes were concerned, in 2 cases there were still birth and intrauterine death was observed in 4 cases. Low APGAR score or asphyxia was found in 21 cases. Normal baby was born to rest 22 mothers. The role of liver enzymes to predict bad fetal outcome was analysed by Receiver operating characteristic (ROC) curve. Here also LDH appeared as better than other two enzymes, as area under ROC curve is most (0.89) with LDH. Figure 1 shows the ROC plot of LDH in predicting foetal outcome in PIH. The least value of LDH which gave bad foetal outcome is 547 IU/L. Rounding off the value, we considered that 550 IU/L of LDH can be considered as cut off value. The sensitivity, specificity and positive predictive value in that case are depicted in table 3.

Table 1: Changes in maternal liver enzyme and foetal birth weight in cases with PIH

Parameter			Cases (n = 68)	Controls (n = 56)	2 tailed p
Maternal Liver enzyme	ALT (IU/L)	mean	109.1	36.2	<0.0001
		SE	7.36	1.37	
		SD	60.7	10.2	
	AST (IU/L)	mean	58.2	32.6	<0.0001
		SE	2.29	1.21	
		SD	18.9	9.1	
	LDH (IU/L)	mean	746.6	132.6	<0.0001
		SE	26.18	4.67	
		SD	215.8	35.0	
Foetal birth weight (kg)		mean	2.30	2.59	<0.0001
		SE	0.030	0.037	
		SD	0.24	0.28	

Table 2: Correlation of Maternal liver enzymes and Foetal outcome in PIH

Maternal liver enzymes	Foetal birth weight (n = 49)		Foetus with bad outcome (n = 49)
	Pearson Correlation Coefficient	2 tailed p	Area under Receiver operating characteristic (ROC) curve
ALT	-0.41	0.0006	0.80*
AST	-0.42	0.0004	0.74*
LDH	-0.74	<0.0001	0.89 **

*= Fair, ** = Good

Table 3: Role of LDH as a marker to predict bad fetal outcome

Cut off value of LDH	Sensitivity	Specificity	Positive predictive value
≥ 550 IU/L	95.5%	44.4%	58%

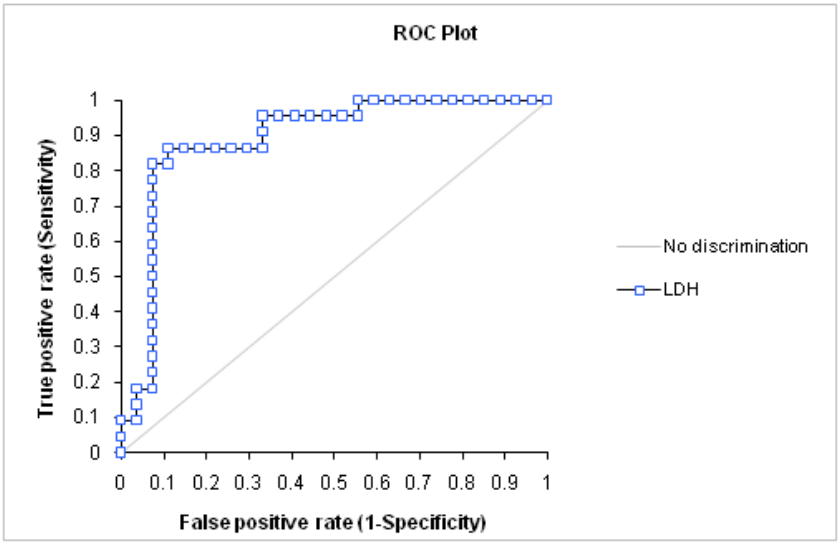

Fig. 1: ROC plot to determine cut off value of LDH

DISCUSSION

Though the exact pathology of PIH is still unknown, vascular endothelial dysfunction has been suggested as central cause of preeclampsia [10]. This dysfunction leads to increased sensitivity of the vasculature to vasoactive compounds which leads to reduction of perfusion and loss of fluid from intravascular compartment [11]. The hemodynamic alteration, activation of coagulation cascade with microthrombi formation results in perinatal as well as maternal complication [12].

These findings corroborates with the study by Qublan *et al*. [5]. They observed that perinatal mortality increased significantly with LDH > 800 IU/L. Small for gestational age (SGA) babies in mothers suffering from PIH are thought to be initiated with improper remodeling of the uterine spiral arteries due to inadequate trophoblast invasion in early pregnancy leading to reduced placental and fetal perfusion and subsequent inefficient function of maternal vascular endothelium [13]. A study conducted by Prakash *et al*. showed that incidence of intrauterine growth retardation (IUGR) was 6.6% and 66.66% of the fetuses had low birth weight [14]. Increased risk of adverse fetal outcome in patients with elevated liver enzymes was also observed in a study conducted by Sibai *et al*. [15].

CONCLUSION

Pregnancy induced hypertension is associated with increased activity of ALT, AST and LDH. The fetal birth weight was found to be negatively correlated with all these three enzyme activity. LDH is a good parameter to predict severity of PIH and bad fetal outcome.

REFERENCES

1. Raddi SA, Nayak BS, Prakash R, Puri R, Metgud MC; Stress, coping strategies and lived experience of women with pregnancy induced hypertension 2009; 1(1) : 65-68.
2. Gilstrap LC, Ramin SM; Diagnosis and management of preeclampsia and eclampsia: In clinical management guidelines for obstetrician –gynaecologist. ACOG Practice Bulletin, 2002; 33(1): 1-9.
3. Mackey AP, Berg CJ, Atrash HK; Pregnancy related mortality from preeclampsia and eclampsia. Am J Obstet Gynecol., 2001; 97(4): 533-538.
4. LoJo Mission JF, Caughey AS; Hypertensive disease of pregnancy and maternal mortality. Curr Opin Obstet Gynecol., 2013; 25(2): 124-132.
5. Qublan HS, Amanin V, Bataineh O, Shraideh ZA, Tahat Y, Awamieh I *et al*.; Lactic dehydrogenase as a biochemical marker of adverse pregnancy outcome in severe prteclampsia. Medi Sci Monit., 2005; 11(8): CR 393-397.
6. He S, Bremme K, Kallnar A, Blomback M; Increased concentrations of lactate dehydrogenase in pregnancy with preeclampsia : a predictor for the for the birth of small-for- gestational-age infants 1995. Gynecol Obstet Invest., 1995; 39(4) : 234-238.
7. IFCC methods for the measurement of catalytic concentration of enzymes. J Clin Biochem., 1986; 24: 497.

8. IFCC methods for the measurement of catalytic concentration of enzymes. J Clin Biochem., 1986; 24: 481.
9. Recommendations for the measurement of LDH in human serum at 30^0C. Ann Biol Chem., 1982; 40: 87.
10. Solomon GC, Selly EW; Preeclampsia-Searching for the cause. N Eng J Med., 2004; 350: 641-642.
11. Bell M; Historical overview of preeclampsia-eclampsia .J Obstet Gynecol Neonatal Nurs., 2010; 39(5): 510-518.
12. Page NM; The endocrinology of preeclampsia. Clin Endocrinol., 2002; 57: 413-423.
13. Robert JM, Gammil HS; Preclampsia-recent insight. Hypertension, 2005; 46(6): 1243-1249.
14. Prakash J, Pandey LK, Singh AK, Kar B; Hypertension in pregnancy: Hospital based study. JAPI, 2006; 54: 273-278.
15. Sibai, Baha M; Diagnosis, controversies and management of hemolysis, elevated liver enzymes, and low Platelet count. Obstetrics & Gynecology, 2004; 5(1): 981-991.