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SERUM LACTATE DEHYDROGENASE AS A BIOCHEMIAL MARKER FOR MATERNAL AND PERINATAL OUTCOME IN PRE-ECLAMPSIA

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ABSTRACT

Background: Pre-eclampsia affects about 5-10% of all pregnancies and is a major cause of maternal, fetal and neonatal morbidity and mortality, particularly in developing countries. FOGSI and other studies show the incidence of pre eclampsia in India ranges between 11-13%. Lactate Dehydrogenase (LDH) is mainly an intracellular enzyme. LDH is present in many body tissues, especially heart, liver, kidney, skeletal muscle, brain, blood cells and lungs. Its level is increased in the scenario of increased cell injury, hemolysis and cell death. Cellular enzymes in the extracellular space although of no further metabolic function in this space, are still of benefit because they serve as indicators suggestive of disturbance of cellular integrity induced by pathological conditions and is used to detect cell damage or cell death.This can be further used as help in making decision, regarding the management strategies to improve the maternal and foetal outcome.

Objectives: To compare serum LDH levels in the normal pregnant women and in women with preeclampsia and eclampsia in ante-partum period and to correlate the severity of the disease, maternal and perinatal outcome with Lactic Dehydrogenase (LDH) levels in serum in patients of pre-eclampsia and eclampsia.

Material and Methods: A prospective comparative study was conducted in the department of Obstetrics and Gynaecology, Ispat General Hospital, Rourkela. Out of 150 women studied, 50 were normal pregnant women, 32 were of mild preeclampsia, 35 were of severe preeclampsia and 33 of eclampsia. The statistical analysis was done by Chi-square test, Fischer Exact test, analysis of variance and student "t" test (two tailed and independent).

Results: LDH levels were significantly elevated in women with preeclampsia and eclampsia (p value <0.001). LDH levels had significant direct correlation with increasing blood pressure (p value <0.001) as well as poor maternal and perinatal outcome.

Conclusion: High serum LDH levels correlate well with the severity of the disease and poor maternal and fetal outcomes in patients of preeclampsia and eclampsia and can be considered as a supportive biochemical and prognostic marker from early third trimester.

KEYWORDS :

INTRODUCTION:

Hypertensive disorders represent the most common medical complications of pregnancy affecting between 7-15% of all gestations and account for approximately a quarter of all antenatal admissions [1]. According to World Health Organization's (WHO) systemic review on maternal mortality world-wide, hypertensive disease remains a leading cause of direct maternal mortality. Hypertensive disorders are responsible for substantial morbidity in pregnant women and also carry risk for baby. It is leading single identifiable risk factor in pregnancy associated with still births.

Pre-eclampsia is a multi-system disorder of unknown etiology, unique to pregnancy, with onset after 20 weeks of gestation. It is a pregnancy specific syndrome that can affect virtually any organ system. Pre eclampsia complicates 2-8% of pregnancies and is a major cause of maternal morbidity, perinatal mortality & morbidity and premature delivery [2]. Pre-eclampsia is strongly associated with fetal growth restrictions, low birth weight, respiratory distress syndrome, spontaneous or iatrogenic preterm delivery and admission to neonatal intensive care. FOGSI and other studies show the incidence of pre eclampsia in India ranges between 11-13%.

Lactate Dehydrogenase (LDH) is mainly an intracellular enzyme. As pre-eclampsia is a multisystemic disorder, it can cause a lot of cellular damage, hemolysis and cell death which eventually leads to increase in levels of serum LDH. Hence, LDH levels can provide us indirect assessment of assess the severity of disease and help in better management of patients with pre-eclampsia leading to better fetal and maternal outcomes levels.

AIMS & OBJECTIVES:

(1) To compare the serum lactate dehydrogenase level between normal pregnant mother and pre-eclampsia.
(2) To correlate the serum level of lactate dehydrogenase with maternal outcome.
(3) To correlate the serum level of lactate dehydrogenase with fetal outcome.
(4) To analyze lactate dehydrogenate (LDH) as a biochemical marker in pre-eclampsia.

MATERIAL AND METHODS:

A prospective comparative study of two years from 2014-2016 conducted in department of Obstetrics & Gynaecology, Ispat General Hospital, Rourkela, Sundergarh, Odisha. Study was done on antenatal cases with gestational age ≥20weeks between 18yrs and 35yrs of age as per the inclusion and exclusion criteria attending the OPD or admitted under O&G department.

In the present study, 150 pregnant women were included according to inclusion and exclusion criteria selected from outpatient department and admitted in labour room/ward. All consecutive patients of pre-eclampsia and eclampsia who gave consent were taken as cases, were 100 and 50 pregnant normotensive women were taken as controls. The 100 cases were sub classified into mild preeclampsia (32 patients), severe preeclampsia (35 patients), eclampsia (33 patients) according to ACOG guidelines 2013.The groups were matched for maternal age and obstetrical index. The patients were followed it delivery and 1 weeks after that, neonates were followed till early neonatal period.

INCLUSION CRITERIA: All patients with pre-eclampsia (normotensive before 20 weeks of gestation), age between 18 - 30 years, singleton pregnancy, with no previous history of hypertension were included. All the cases were in the third trimester of pregnancy (>28wk of gestation) and divided into following groups:

Group 1—Healthy normotensive pregnant women (Controls)
Group 2—Patients of pre-eclampsia and eclampsia (Cases). Sub divided into 3 groups as stated later.

EXCLUSION CRITERIA: In this pregnant women with essential hypertension or hypertension <=20 weeks gestation, multiple pregnancy, placental abnormalities; pre-existing diabetes mellitus, gestational diabetes mellitus, renal disease, liver disorder, thyroid disorder, epilepsy , cardiovascular disease, haemolytic disease, chronic hypertension , myopathies, collagen disorders & with urinary tract infection were not studied.

SAMPLE COLLECTION: About 3 ml of venous blood was drawn under aseptic precautions from selected subjects in a plain vial for serum. Serum was separated by centrifugation and used for estimation of serum levels of LDH.

Analysis of LDH which was done in fully automated biochemistry analyser. An automated method for estimating lactate dehydrogenase (LDH) in serum is presented. Fe3+ is reduced to Fe2+ by NADH formed when lactate is oxidized to pyruvate. Fe2+ complexed with 2, 2 -bipyridyl is measured colorimetrically. Solutions of Fe2+ salt are used as standards. Nicotinamide is used to stabilize NAD+ in solution and is shown to enhance enzyme activity. The method is less expensive and reagents are stable for at least 4 weeks. Results correlate well with a kinetic spectrophotometric method.

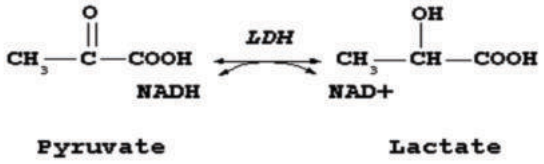


Fig.1: LDH reaction

The samples were divided according to the serum LDH levels into following groups
(a) < 600 IU/l
(b) 600–800 IU/l
(c) > 800 IU/l

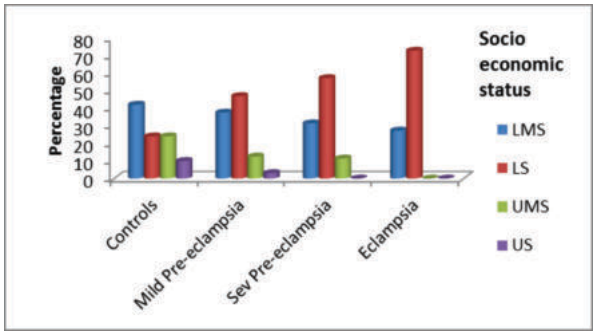
NORMAL SERUM LDH VALUES: Non pregnant women: 115 to 211 IU/L, First trimester: 78 to 433 IU/L, Second trimester: 80 to 447 IU/L, Third trimester: 82 to 524 IU/L. Serum LDH value above the reference range is taken raised.

Statistical Analysis: The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1 ,Systat 12.0 and R environment ver.2.11.1. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. Analysis of variance (ANOVA), Student t test, Chi square/ Fischer Exact test have been used to find the significance of study parameters in various groups.

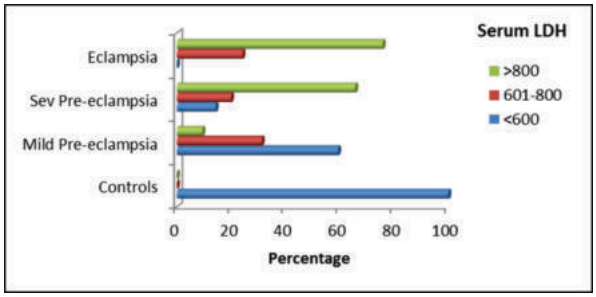
Significant figures
+ Suggestive significance (P value: 0.05< P <0.10)
* Moderately significant (P value: 0.01< P 0.05)
** Strongly significant (P value: P 0.01)

RESULTS:

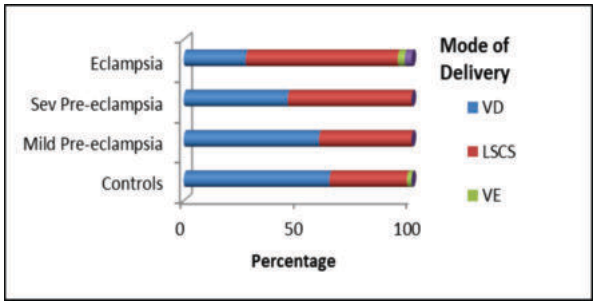
- The majority of patients in control group as well as study group belonged to the age group of 18–29 years. When statistically analysed, the age wise distribution in the subjects was almost similar to the control group.
- Out of 150 patients majority were primigravida 91(60.7%). Distribution according to gravida was similar in all groups and was not significant with p value = 0.358.
- Results from our study showed that the levels of serum LDH was significantly higher in pre-eclamptic women as compared to normal pregnant women and its value increased with increase in severity of disease. P =0.553.
- Most of the patients belonged to lower socio economic status 71(47.3%). When compared statistically p value was <0.001 which was highly significant.



- In the study 90% of cases were found to have edema associated with them while only 14% of controls had edema associated with them and statistically this was found significant.
- Majority of patients in control (45%) had no proteinuria. Most of the patients in eclampsia and severe pre-eclampsia had proteinuria ≥ 3+.
- Mean LDH level was found to be 288.76±63.43IU/L in controls, 578.66±165.29 IU/L in mild pre-eclampsia, 912.80±542.48 IU/L in severe pre-eclampsia and 1103.85±546.33 IU/L in eclampsia. These findings were highly significant with p value < 0.001.



- 51.5% in eclampsia and 45.7% in severe pre-eclampsia belonged to 33-36 wks while 78.1% in mild pre-eclampsia delivered ≥ 37 wks. Statistically it was found significant with p value <0.001. 1 patient of eclampsia died undelivered at 37 wk gestation.
- LSCS rate was highest in eclampsia group comprising 66.7% followed by severe pre-eclampsia in which the percentage was 54.3%. When compared statistically it was found to be significant.



- Rate of still birth was highest in severe pre-eclampsia group which was 25.7% followed by eclampsia having 24.2% still birth. On applying Fisher Exact test the result was found to be highly significant.
- Platelets decrease as value of LDH increases being lowest in >800 group with mean 1.40±0.40.While other parameters serum bilirubin, AST, ALT, serum urea and serum creatinine were higher in >800 IU/L group indicating that as value of LDH increases it effects these parameters. Similar is the relation with severity of disease.

Table1: Correlation of Clinical variables according to Serum LDH levels

Variables	Serum LDH(IU/L)			P value
	≤600 (n=24)	601- 800 (n=25)	>800 (n=51)	
Maternal Age	26.46±4.59	24.36±4.19	25.06±4.37	0.233
Platelets (lac/ml)	1.70±0.29	1.55±0.30	1.40±0.40	0.003**
Serum Bilirubin (gm/dl)	0.90±0.35	1.17±0.40	2.16±2.41	0.007**
AST (IU/L)	29.83±8.27	35.48±9.95	68.31±96.07	0.040*
ALT (IU/L)	28.88±14.06	33.72±11.09	67.98±92.96	0.027*
Serum Urea (mg/dl)	30.96±6.65	32.44±10.69	42.49±20.13	0.004**
Serum Creatinine (mg/dl)	1.03±0.29	1.16±0.35	1.57±0.90	0.003**

- On statistical analysis it was found that higher levels of serum LDH is associated with high diastolic BP (P<0.001).

Table 2: Association of systolic and diastolic BP with LDH levels

SYSTOLIC BP (mmHg)	<600 IU/L	601 – 800 IU/L	> 800 IU/L	P value
< 140	0 (0%)	1 (4%)	1 (1.96%)	
140-159	19 (79.17%)	13 (52%)	6 (11.76%)	
≥ 160	5 (20.83%)	11 (44%)	44 (86.28%)	
Mean SBP (mmHg)	151.50±10.55	157.36±14.76	173.33±15.86	<0.001**
DIASTOLIC BP(mmHg)				
< 90	0 (0%)	0 (0%)	0 (0%)	
90 – 109	19 (79.17%)	13 (52%)	11 (21.57%)	
≥ 110	5 (20.83%)	12 (48%)	40 (78.43%)	
Mean DBP (mmHg)	101.08±7.76	107.84±9.75	113.53±9.00	<0.001**

- Various parameters of perinatal outcomes in respect to LDH level were studied. In LDH > 800 IU/L mean gestational age at the time of delivery was significantly less, 35.63 ± 2.76 in patients with LDH >800 IU/l, mean weight was also significantly less and was 2036.86± 594.66g. This observation indicates that there is reduction in the average weight of babies with higher level of LDH (P <0.001).

Table3: Comparison of perinatal outcome variables in relation to Serum LDH levels

Variables	Serum LDH			P value
	≤600	601-800	>800	
Gestational age (delivery)	37.58±2.24	37.12±1.67	35.63±2.76	0.002** (ANOVA test)
Birth Weight (g)	2671.46±481.14	2651.60±633.43	2036.86±594.66	<0.001** (ANOVA test)
Apgar Score at 1 min	6.54±1.47	5.92±1.91	4.32±2.53	<0.001** (ANOVA test)
Apgar Score at 5 min	8.46±0.93	7.88±1.94	5.68±3.44	<0.001** (ANOVA test)

Variables		Serum LDH(IU/L)			P value
		< 600	601-800	> 800	
Neonatal complication	Nil	62(83.7%)	13(52%)	12(24%)	<0.001** (Chi Square test)
	Present	12(16.9%)	12(48%)	38(76%)	

Alive		73(98.6%)		23(92%)		35(70%)		<0.001** (Chi Square test)
Death	IUFD	1(11.1%)	1(1.3%)	2(22.2%)	2(8%)	6(66.7%)	15(30%)	
	Neonatal death	0(0%)		0(0%)		9(100%)		

NICU admission of alive babies	No	23(95.83%)	17(68%)	22(43.14%)	0.001**
	Yes	1(4.17%)	6(24%)	19(37.25%)	

- High LDH levels were found to be significantly related to low mean Apgar scores at 1 min (P<0.001) and 5 min (P<0.001).
- The occurrence of neonatal complications (p<0.001) and perinatal death (p <0.001) were significantly higher in mothers who had increased serum levels of LDH.
- There were 2(8.3%) cases of maternal complications when LDH levels were normal. Complications were noted in 6 (24%) cases were noted when LDH levels (600-800 IU/L) and 24(47.1%) cases when LDH levels (>800 IU/L) subsequently. There was statistically significant increase in maternal complications with increasing LDH levels (p = 0.002).

Table 4: Comparison between maternal outcome and serum LDH values

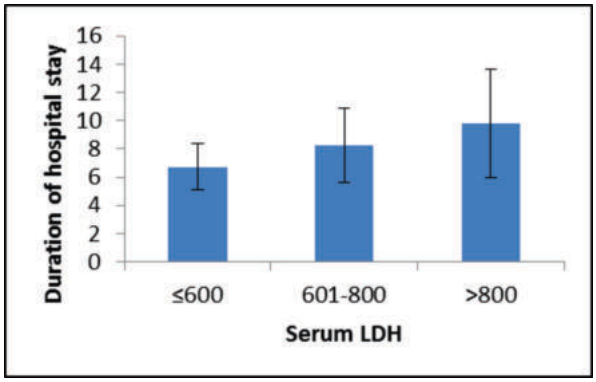
Maternal Complications	Serum LDH			Total (n=100)	P value
	≤600 (n=24)	601-800 (n=25)	>800 (n=51)		
Uneventful	22(91.7%)	19(76%)	27(52.9%)	68(68%)	0.002** (Chi square)
Present	2(8.3%)	6(24%)	24(47.1%)	8(8%)	

Maternal death	0(0%)	0(0%)	4(7.8%)	4(4%)	0.174 (Fischer exact test)

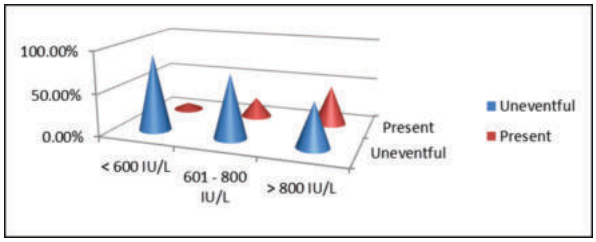
Mode of delivery	VD+VE	12(50%)	17(68%)	16(31.3%)	45(45%)	1 died undelivered
	LSCS	12(50%)	8(32%)	34(66.67%)	54(54%)	

Duration of hospital stay	6.71±1.63	8.24±2.65	9.80±3.86	0.001** (ANOVA test)

- Mean duration of hospital stay was highest in >800 IU/L LDH level and was statistically significant with p value 0.001.



- Out of 100 cases studied there were 4 maternal deaths (1 patient died undelivered) during the study and all were associated with high levels of serum LDH. 2 died due to pulmonary edema, 1 died due to ARF+HELLP and 1 died due to HELLP + DIC + pulmonary edema.



DISCUSSION:

Lactate Dehydrogenase (LDH) is mainly an intracellular enzyme. Its levels are increased in the scenario of increased

cell leakiness; hemolysis and cell death. Preeclampsia and eclampsia lead to a lot of cellular damage and death. So, serum LDH levels seem to be very promising and can be used to assess the severity of disease. These patients may be benefited by aggressive monitoring and treatment as secondary preventions.

Present study is a hospital based prospective study comprising 150 pregnant women. Out of which 50 were normotensive taken as control (Group 1), 32 were mild pre – eclampsia (Group 2a), 35 were severe pre-eclampsia (Group 2b) and 33 were eclampsia (Group 2c).

In the present study majority of the patients belonged to younger age group and were primi gravida. It was found that 28.1% in mild pre-eclampsia, 25.7% in severe pre-eclampsia and 33.3% in eclampsia were significantly (18-21yr) and 28.6% in severe pre-eclampsia were >30 yr. Pre-eclampsia is more common among extremes of reproductive age group and eclampsia is more common in younger patients. The mean age in all 4 groups was calculated to be 25.54±3.70 (group 1), 25.25±4.16 (group 2a), 25.89±4.78 (group 2b), 24.48±4.22 (group 2 c) respectively being highest in severe pre-eclampsia and lowest in eclampsia. 56.3% in mild, 62.9% in severe and 75.8% in eclampsia were primi gravida. Similar findings were also observed by Jaiswar et al(2011) [3], Sarkar PD et al (2013) [4], Munde SM et al(2014) [5], Umasatyasri Y et alet al(2015) [6], Sreelatha S et al(2015) [7].

In our study majority of patients in cases belonged to low socioeconomic class with 46.9% in mild, 57.1% in severe, 72.7% in eclampsia while majority of patients in control belonged to middle class probably because of lack of awareness, illiteracy, poverty, poor ANC, lack of antioxidants and vitamins in diet. This was found to be statistically significant (p< 0.001) on analysis. This is supported by study of Silva LMet al (2008) [8], Andrew L et al (2008) [9].

In this study edema was seen in majority of cases with 25(78.1%) in mild pre-eclampsia, 34(97.1%) in severe pre-eclampsia and 31(93.9%) in eclampsia while in control group only 7(14%) had edema and 43(86%) had no edema. Though the finding is significant it has no relation with severity of disease.

In present study mild pre-eclampsia group 23 had 1+, 9 had 2+ proteinuria. Amongst patients of severe pre-eclampsia, 25 had 3+ and 10 had 4+ proteinuria. In the eclampsia group, 14 patients had 3+, 2 patients had 4+ proteinuria, 1 patient had 1+, 1 patient had trace and 2 had no proteinuria. 45women in control group had no proteinuria, 4 had trace and 1 had 1+ proteinuria. Amount of protein in urine increases because of glomerular damage as the disease becomes severe reflected by higher BP, higher LDH, and higher urea and creatinine levels in the patients.

The mean blood urea levels of Group 1, 2(a), 2(b), 2(c) were 31.82±7.64 mg/dl, 29.72±5.93mg/dl, 44.51±16.65 mg/dl, 36.73±19.97mg/dl and serum creatinine levels were 0.73±0.24mg/dl, 1.04±0.30mg/dl, 1.26±0.48mg/dl and 1.70±1.01mg/dl respectively. Mean blood urea level was highest in patients of severe preeclampsia group and mean serum creatinine level was highest in patients of eclampsia group. This correlated well and significantly with high S.LDH levels being highest in >800 IU/L group with mean serum urea 42.49±20.13mg/dl, p value 0.004 and serum creatinine 1.57±0.90mg/dl, p value 0.003. Hypertensive disorders of pregnancy are commonly associated with decrease in renal function due to damage done by hypertension and wide spread endothelial dysfunction. The more is endothelial damage higher are the LDH levels. Thus higher LDH level shows more damage and renal compromise is reflected by the rising urea and creatinine levels. But most of these changes are reversible.

Indumati V et al (2014) observed mean blood urea (mg/dl) of 25.36 ± 6.68 in control group and 24.82 + 7.73 in pre-eclampsia/eclampsia, the finding was not significant with p= 0.6729. Mean serum creatinine (mg/dl) in control was 0.81 ± 0.22 and 0.98 + 0.27 in cases with p = 0.0002 making it significant [10].

Dr. Kant RH et al (2015) found similar finding in their study, mean S.Urea (mg/dl) 28.6±7.6 (study) and 15.6±3.2 (control) which was highly significant (p = 0.000). Mean serum creatinine (mg/dl) 0.8±0.5 (control) and 0.6±0.2 (cases) with p value 0.0002 [11]. Similar findings were seen in Munde SM et al (2014) [5].

The mean serum bilirubin levels in the four groups were 0.71±0.21, 0.79±0.22, 2.03±2.52 and 1.96±1.58 respectively. The mean AST levels in IU/L were 25.60±9.36, 27.59±3.80, 69.97±96.88, 53.18±67.91and mean ALT levels in IU/L were 25.08±7.89, 24.44±6.28, 69.91±82.00, 53.76±80.6825 in the respective groups. Serum bilirubin levels (p < 0.001), AST (p <0.002) and ALT (p <0.001) levels were highest in patients of severe pre-eclampsia followed by patients of eclampsia indicating endothelial dysfunction caused by factor released from ischemic placenta that causes damage to hepatocytes and with increase in severity of the disease, there is decrease in conjugation and hence rise in bilirubin levels and due intracellular damage ALT and AST are also raised showing extensive damage. The increase in level of bilirubin, AST and ALT also correlates to the increase in LDH levels. It was found in present study that mean value of above variables (2.16±2.41 p 0.007, 68.31±96.07 p 0.040, 67.98±92.96 p 0.027) was highest in > 800IU/L group of LDH and on analysis the finding was highly significant. Thus serum LDH can be used as a biochemical marker for the disease. Similar finding were quoted by Demir SC et al (2006) [12], Andrew L et al (2008) [9], Sonagra AD et al (2012) [13], Munde SM et al (2014) [5], Indumati V et al (2014) [10], Dr. Kant RH et al (2015) showing severe preeclampsia associated with fulminant rise in these markers [11].

In present study the mean platelet count in lakhs/ml in four groups was found to be 1.83±0.42, 1.70±0.26, 1.41±0.39 and 1.43±0.38 respectively. Mean platelet count was found to be lowest in severe pre-eclampsia group closely followed by that of eclampsia patients. As the severity of disease increases the platelet count decreases and this finding was statistically significant. Platelet count below 1lakh/ml in a patient of preeclampsia is an ominous sign and can be used as an independent predictor for severity of disease. The mean platelet count according to LDH levels were found to be 1.70±0.29 (<600IU/L), 1.55±0.30 (601 – 800 IU/l), 1.40±0.40 (>800 IU/L) with p value 0.003 as depicted in and they were found to be lowest in >800 IU/L group. There is negative correlation between mean Platelet value and LDH level, may be used to assess the severity of disease.

Munde SM et al (2014) reported in their study similar findings which were highly significant. The mean platelet count in control, mild and severe pre-eclampsia were found to be 220 ± 30.2, 205 ± 22.0 and 185.5 ±28.33 respectively being lowest in severe pre-eclampsia [5].

Dr. Kant RH et al (2015) also found similar results in their study. The mean platelets count (lac/mm3) was 1.4±0.4 in pre-eclampsia group and 1.6±0.5 in control (normotensive group). On analysis the findings were significant p = 0.018 [11].

In present study rate of LSCS was relatively higher in pre-eclampsia and eclampsia when compared with control group.

This might be explained by the fact that preterm termination was essential in patients with un-favorable Bishops score and to decrease morbidities and mortalities of mothers and babies. There was no correlation between mode of delivery and serum LDH levels. Similar findings were observed by Sreelatha S et al (2015) with LSCS rate of 90% in mild pre-eclampsia and 80% in severe pre-eclampsia [7].

In the present study the LDH levels were significantly raised with the severity of the disease ($p < 0.001$) Mean LDH±SD level in Groups 1, 2(a), 2(b), 2(c) were 288.76±63.43, 578.66±165.29, 912.80±542.48, 1103.85±546.33 respectively. Mean value of eclamptic patients was highest followed by patients of severe and mild pre-eclampsia. Women were divided according to the serum LDH levels into <600 IU/L, 601-800 IU/L, >800 IU/L. In control group all had LDH levels <600 IU/L. Out of 100 patients studied as cases, 24 women had LDH <600IU/L in which 19 cases had mild and 5 cases had severe pre-eclampsia, there was no case of eclampsia in this group. Out of 25 cases with LDH levels 601-800IU/L, 10 had mild, 7 had severe pre-eclampsia and 8 had eclampsia. Out of 51 cases with LDH >800IU/L, 3 had mild, 23 had severe pre-eclampsia and 25 had eclampsia. Majority of patients with severe preeclampsia and eclampsia had LDH levels >800IU/L.

Jaiswar et al (2011) observed mean LDH levels 278.33±119.25 IU/L in control, mild preeclampsia had 400.45±145.21 and severe pre-eclampsia had 646.95±401.64 IU/L. They found it to be significant with p value <0.001 [3].

Similar results were found by Sarkar PD et al (2013)[4], Munde SM et al (2014) [5], Umasatyasri Y et al (2015) [6], Sreelatha S et al (2015)[7], Dr. Kant RH et al (2015)[11].

In present study mean systolic BP was highest in patients of severe pre-eclampsia being 173.31±9.43 mmHg closely followed by patients of eclampsia, 170.00±20.43 mmHg. The mean diastolic BP was highest in severe pre-eclampsia being 116.86±6.24 mmHg and in eclampsia it was found to be 110.85±9.17mmHg. The values correlate well with the mean value of LDH levels in the groups. The greater the systolic and diastolic BP the more the damage leading to higher LDH levels. Hence LDH level can be used to assess the severity of disease.

The mean systolic blood pressures 3 groups based on LDH levels were 151.50±10.55, 157.36±14.76, 173.33±15.86 and mean diastolic blood pressure in 3 groups 101.08±7.76, 107.84±9.75, 113.53±9.00 respectively being highest in LDH value > 800 IU/L. Higher levels of serum LDH were associated with high mean systolic and diastolic BP were significantly higher ($p < 0.001$). Similar findings were also observed in various studied Jaiswar et al (2011) [3], Sarkar PD et al (2013) [4], Munde SM et al (2014) [5], Umasatyasri Y et al(2015) [6], Sreelatha S et al(2015) [7], Dr. Kant RH et al(2015) [11].

The perinatal outcomes in respect to LDH levels, have been studied in this study. In our study mean gestational age at time of delivery decreased with increase in severity of disease and was found to be lowest in severe pre eclampsia 35.86±2.73 wks followed by eclampsia 36.03±2.57 wks. This indicates that as severity of disease increases the more are the preterm delivery. The mean gestational age at the time of delivery in this study was significantly less in patients with increasing LDH levels ($p<0.001$). Mean gestational age at delivery in < 600 IU/L was 37.58±2.24wks, 601-800 IU/L was 37.12±1.67wks, >800 IU/L was 35.63±2.76 wks. This indicates increase in preterm deliveries in patients with higher LDH levels.

In Jaiswar SP et al study, the mean gestational age in the similar groups was 36.92 ± 3.44 wks (<600 IU/l), 34.77 ± 3.11 wks (600-800 IU/l) and 35.25 ± 3.23 wks (LDH >800 IU/l) respectively. They found it to be significant with p value was 0.025 [3].

In Sarkar PD et al study, the mean gestational age (wks) was 38.58±3.64 in group A (control), 36.11±1.86 in group B1 (mild pre-eclampsia) and 33.64 ±6.17 in group B2 (severe pre-eclampsia) with p value <0.0001 [4].

In present study the mean birth weight was significantly low in eclampsia group followed by severe pre-eclampsia. The mean birth weight was found to be significantly low with higher value of LDH being 2671.46±481.14gm (<600IU/L), 2651.60±633.43 gm (601-800 IU/L) and2036.86±594.66 (>800IU/L). The association of low birth weight of infants with increase in serum LDH levels was suggested by He S, et al (1995) in their study [14].This was in contrary to Qublan et al who did not find any significant association. In Jaiswar SP et al study they observed that there was significant association between low birth weight and increasing LDH levels ($p= 0.019$).This could have been partially due to higher incidence of premature births in this group [3]. In Umasatyasri Y et al(2015) the mean birth weight was found to be 2.73 ± 6.38 kg , 2.54 ± 7.48 kg, 2.28 ± 7.90 kg in similar LDH level groups [6].

The mean APGAR scores at 1 minute and 5 minutes was found to lowest in severe pre-eclampsia followed by eclampsia and the finding was highly significant ($p <0.001$). The APGAR score of babies at 1 and 5 min was 6.54±1.47 & 8.46±0.93 in <600IU/L LDH level. It was 5.92±1.91and 7.88±1.94 in 601-800IU/L group. At level >800 IU/L, mean APGAR at 1 min and 5 min was 4.32±2.53 and 5.68±3.44 respectively. Thus showing low levels of score in the newborn baby with increasing LDH levels ($p < 0.001$ and $P < 0.001$) at 1 and 5 min. Similar findings were reported by Jaiswar SP et al (2011) and Umasatyasri Y et al(2015) [3,6].

In present study FGR (fetal growth restriction) was found to be the most common complications in cases studied. As neonatal complications increase with severity of disease and increased serum LDH levels rate of NICU admission was found to be highest in eclampsia and >800 IU/L group.

In present study there were 1(2%), 1(3.1%), 9(25.7%) and 7(21.2%) perinatal deaths in Group 1, 2(a), 2(b) and 2(c) respectively. Rate of perinatal death was higher in cases with severe pre-eclampsia followed by eclampsia group and rate of neonatal complications were also highest in eclampsia group. These results were highly significant, thus increase in severity of disease is associated with increased perinatal morbidity and mortality. Out of total 18 deaths during study there were 11 intrauterine deaths, 7 early neonatal deaths and 1 patient died undelivered. Mild pre-eclampsia had 1(14.3%) neonatal death and no IUFD, severe pre-eclampsia had 4(36.4%) IUFD; 5(71.4%) neonatal death and eclampsia had 6(54.5%) IUFD; 1(14.3%) neonatal death. There was 1(9.1%) case of IUFD in control group. There was no relation between severity of disease and time of death.

According to Jaiswar SP et al (2011) study, significant increase in neonatal complications ($P= 0.003$), still births ($P< 0.001$) and perinatal deaths ($P= 0.003$) was noted [3].Umasatyasri Y et al(2015) noted that the occurrence of neonatal complications ($p = 0.33$) and perinatal deaths ($p = 0.79$) were higher in mothers who had increased serum levels of LDH but not statistically significant in their study ($p >0.05$) [6]. Similar findings were obtained in the present study when number of perinatal outcome was divided according to S.LDH levels it was found that majority of neonatal complications, IUFD and neonatal death were seen in > 800 IU/L group and on analysis it was found statistically significant $p < 0.001$. The high

stillbirth rate may be explained by delayed referral, poor ANC, illiteracy and poverty. Patients are referred from outside hospitals; our institute is a well-equipped and located near rural and tribal areas, receiving a large number of high risk patients from surrounding locations.

In present study 13(39.39%) in eclampsia, 13(37.14%) in severe pre-eclampsia and 6(18.75%) mothers had complications while only 1(2%) had complications. Pulmonary edema was the most common complication in eclampsia and severe pre-eclampsia group. Other complications seen were abruption, HELLP, renal failure, DIC, PPH etc. The mean duration of hospital stay was also higher in eclampsia and severe pre-eclampsia group. There were total 4 maternal deaths 1 in severe pre-eclampsia and 3(1 died undelivered) in eclampsia and all belonged to low socioeconomic status. Pulmonary edema, HELLP was the main causes of maternal death. Though the finding was not significant but increase in maternal morbidity and mortality was seen with increase in severity of disease. Maternal complications was highest in >800 IU/L LDH level with 47.1%. Higher value of serum LDH was associated with increased maternal complications. There was a significant increase in maternal morbidity with increasing value of LDH (p=0.002). There were 4 maternal deaths during study all 4 belonged to >800 IU/L LDH group. All the patients who died had serum LDH >2000 IU/L and the patient who died undelivered had LDH > 3000. Hence there is increase in maternal mortality with increasing level of LDH, though in present study this finding was not found to be significant (p=0.174) unlike other studies.

Same findings were observed in various studies. Martin et al (1999) study concluded that high serum levels of LDH (1,400 IU/l) had high predictive value for significant maternal morbidity [15]. Statistically significant relation between maternal complications and high LDH levels was concluded in Demir et al (2006) study [12]. Odendaal et al (2000) observed in his study that LDH levels were significantly higher in early onset preeclampsia group with abruption [16].

Jaiswar SP et al (2011) study showed significant co-relation between higher serum LDH levels and increased maternal complications like abruption placenta, renal failure HELLP syndrome, cerebrovascular accidents etc. On analysis with p value was <0.001. Patients with LDH levels > 800 IU/l had maternal mortality of 13.8% and this was a significant on analysis (P=0.006) [3].

Andrews L et al (2012) shared similar views. They studied that hypertensive mothers with LDH levels > 600IU/l resulted in 77.7% maternal deaths (out of these three mothers (42.8%) had LDH > 800 IU/l) and had 17.5% preterm deliveries. 37% patients with pre-eclampsia and raised liver function tests had maternal complications. 8(88.8%) of patients resulting in maternal deaths were from rural areas and low socioeconomic class and had not taken antenatal care. Thus they concluded that serum levels of LDH and AST can be used as markers to predict the complications in pre-eclampsia patients, early in pregnancy and thus help in better management and prevention of disease [9].

Thus, in our study LDH levels were found to have significant association with different maternal and fetal outcomes studied in patients of preeclampsia and eclampsia.

CONCLUSION:

This study was intended to correlate serum LDH level with maternal and fetal outcome in pre-eclampsia and eclampsia to know that whether it can be used as a biochemical marker or not. Since Pre-eclampsia is a multisystemic disorder which affects virtually all maternal organ system. There is evidence that endothelial cell and altered endothelial cell function play important role in pathogenesis of pre-eclampsia. There is extensive cellular damage in pre-eclampsia and LDH being intra cellular enzyme is released when there is cell injury, hemolysis and cellular death. In this study a close relation was seen between the LDH levels and severity of disease. So it can be used as a reliable biochemical marker to identify high risk patients for close monitoring in antenatal period and hence help in preventing complications. High risk pregnancy with increased level of LDH requires proper supervision during delivery. And as indicated by the study severe pre-eclampsia can have more severe and grave complications as compared to eclampsia. So it requires aggressive monitoring and follow-up. We found significant correlation between LDH levels and neonatal morbidity and mortality. Higher the level of LDH the more were the complication rate and poorer was the outcome. Proper management is necessary to decrease both maternal and fetal morbidity and mortality. Thus, it can be used as a potential added diagnostic test for early detection of the severity and occurrence of various maternal and fetal complications. Further studies will be required to predict that whether serum LDH is an independent factor or not.

Maternal complications		Serum LDH			Total (n=100)	
		≤600 (n=24)	601-800 (n=25)	>800 (n=51)		
Mode of delivery	VD+ VE	12(50%)	17(68%)	16(31.3%)	45(45%)	1 died undelivered
	LSCS	12(50%)	8(32%)	34(66.67%)	54(54%)	

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