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Adverse obstetrical and perinatal outcome with increasing levels of lacate dehydrogenase enzymes in patients of preeclampsia and eclampsia

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Abstract
Objectives: To correlate the severity of the disease, maternal and perinatal outcome with lactate dehydrogenase (LDH) levels in serum in patients of preeclampsia and eclampsia.
Methods: It was prospective observational study done in Obstetrics and Gynaecology department of Government Medical College and Rajindra Hospital, Patiala. Study was done from January 2017 to December 2017. 200 Pregnant patients were included in the study. There were 50 patient of mild pre eclampsia, 50 patients of severe pre eclampsia, 50 patients of eclampsia and 50 normotensive patients were taken as controls.
Results: LDH levels were significantly elevated in women with pre eclampsia and eclampsia. As the severity of disease increased, LDH levels increased. Higher LDH levels had significant Correlation with high blood pressure as well as poor maternal and perinatal outcome.
Conclusions: High serum LDH levels correlate well with severity of disease and poor
Maternal and foetal outcome in patients of preeclampsia and eclampsia.

Keywords: Lactic Dehydrogenase, Pre eclampsia, Eclampsia, Maternal outcome, foetal outcome

Introduction
Pre eclampsia and eclampsia complicate 6-8% [1] of all pregnancies and lead to various maternal and foetal complications [2]. These are multisystem disorders and lead to lot of cellular death [3]. So serum LDH levels can be used to access the extent of cellular death and there by severity of disease in this group of patients [4]. This can be further used as help in making decision, regarding the management strategies to improve the maternal and foetal outcome.

Aims and Objectives
-To study serum LDH levels in the normal pregnant woman and in women with pre eclampsia and eclampsia
-To study the correlation of maternal and perinatal outcome with serum LDH levels.

Methods
This was a prospective observational study conducted in department of Obstetrics and Gynaecology in Government medical college and Rajindra Hospital, Patiala from 1 January 2017 to December 2017. 200 Pregnant women were enrolled in this study.

They were divided into
Group I - Healthy normotensive pregnant women.
Group II - Patients of pre eclampsia and eclampsia
This was further subdivided into following subgroups
Mild pre eclampsia
Severe pre eclampsia
Eclampsia

Subjects were also divided according to serum LDH levels as follows
1. <600 IU/L
2. 600 - 800 IU /L
3. >800 IU/L

Maternal and foetal outcome were noted

Exclusion Criteria

Those excluded were patients with hypertension at or < 20 weeks gestation, Preexisting diabetes mellitus, renal disease, Liver disorder, thyroid disorder, epilepsy.

Results

Total 200 Patients were studied. Out of which 50 patients with normal blood pressure served as control, remaining 150 patients were included with Preeclampsia and eclampsia. Out of these 150 patients, 50 patients were of mild pre eclampsia, 50 of severe pre eclampsia and 50 of eclampsia.

Table 1: Distribution of age and parity

Group	Normotensive	Mild Preeclampsia	Severe Preeclampsia	Eclampsia
Number	50	50	50	50
Age	Number (%)	Number (%)	Number (%)	Number (%)
<20 Years	1 (2%)	0	1 (2%)	2 (4%)
21-25 Years	13 (26%)	18 (36%)	23 (46%)	27 (54%)
26-30 Years	27 (54%)	19 (38%)	17 (34%)	14 (28%)
31-35 Years	7 (14%)	9 (18%)	8 (16%)	3 (6%)
>35 Years	2 (4%)	4 (8%)	1 (2%)	4 (8%)
Parity				
Nulliparous	26 (52%)	31 (62%)	28 (56%)	37 (74%)
Multiparous	24 (48%)	19 (38%)	22 (44%)	13 (26%)

In this study, in normotensive patients 2% patients belonged to less than 20 years of age, 26% patients were between 21-25 years of age, 54% patients were between 26-30 years, 14% patients were between 31-35 years and 4% patients were > 35 years of age. In patients with mild pre eclampsia 36% patients belonged to 21-25 years of age, 38% patients belonged to 26-30 years of age, 18 %patients belonged to 31-35 Years of age, 8% of patients belonged to >35 years. In patients with severe preeclampsia, 2% patients belonged to < 20 years, 46% patients belonged to 21-25 years, 34% patients belonged to 26-30 years, 16% patients belonged to 31-35 years, 2% patients belonged to >35 years of age. In patients with eclampsia 4% patients were of < 20 years age, 54% patients were of 21-25 Years, 28% patients were of 26-30 Years of age, 6% patients were of 31-35 years age and 8% patients were of > 35 years. In this study, 52% patients were nulliparous in normotensive patients. 62% patients were nulliparous in mild preeclampsia patients. In severe preeclampsia patients 56% patients were nulliparous and 74% patients were nulliparous in eclampasia patients. (Table1)

Table 2: Correlation of LDH Levels in different groups

LDH Levels	Normotensive	Mild Preeclampsia	severe preeclampsia	Eclampsia
< 600 IU/L	48 (96%)	37(74%)	1 (2%)	0
600-800 IU/L	1(2%)	11(22%)	33(66%)	17(34%)
>800 IU/L	1 (2%)	2 (4%)	16 (32%)	33 (66%)
Mean ldh levels (iu/l) ± standard deviation	298.20 ±79.825	468.06 ±121.505	712.80 ±417.701	1248.10 ±748.355
LDH levels (IU/L)	<600	600-800	>800	
Number of patients	86	62	52	

In the present study, in patients with normal blood pressure, 96% patients had LDH levels < 600 IU/L, 2% patients had LDH levels 600-800 Iu/L, 2% patients had LDH levels > 800 IU/L. In patients with mild preeclampsia 74%patients had LDH levels < 600 IU/L, 22% patients had LDH levels 600-800 IU/L, 4% patients had LDH levels > 800 IU/L.

In patients with severe preeclampsia 2% patient had LDH levels < 600 IU/L, 66% patient had LDH levels 600-800 Iu/L, 32% patients had LDH levels >800 IU/L. In patients with eclampsia, not even a single patient had LDH levels <600 IU/L, 34% patients had LDH levels 600-800 IU/L, 66% patients had LDH levels > 800 IU/L. Out of these 66% patients, 2 patients had their blood pressure less than 140/90mm hg, but they developed convulsions.

Mean LDH levels in normotensive patients was 298.20 ± 79.825 IU/L, in mild preeclampsia was 468.06 ± 121.505 IU/L, in severe preeclampsia was 712.80 ± 417.701 IU/L, in eclampsia was 1248.10 ± 748.355 IU/L. As the LDH levels increased the severity of disease increased.

Out of 200 patients, 86 patients had LDH levels <600 IU/L, 62 patients had LDH levels 600-800 IU/L, 52 patients had LDH levels >800 IU/L [Table 2]

Table 3.1: Association of systolic Blood pressure with LDH levels.

LDH levels (IU/L)	Blood pressure (mm/Hg)			
	< 140	140-160	>160	Total
	Number (%)	Number (%)	Number (%)	
<600	48(55.8%)	37(43%)	1(1.2%)	86
600-800	1(1.6%)	20(32.3%)	41(66.1%)	62
>800	3(5.7%)	5(9.6%)	44(84.6%)	52

Table 3.2: Association of diastolic Blood pressure with LDH levels

LDH levels (IU/L)	Blood pressure (mm/hg)			
	< 90	90 -110	>110	Total
	Number (%)	Number (%)	Number (%)	
< 600	48(55.8%)	38(44.1%)	0	86
600-800	1(1.6%)	20(32.2%)	41(66.1%)	62
>800	3(5.7%)	12(23.1%)	37(71.1%)	52

Out of 86 patients with LDH levels < 600 IU/L, 48 (55.8%) patients had normal systolic BP, 37 (43%) patients had systolic BP 140-160 mm Hg, 1 (1.2%) patients had systolic BP > 160mm Hg. Out of 62 patients with LDH levels 600-800 IU/L, 1 (1.6%) patients had systolic BP<140 mm Hg, 20 (32.3%) patients level

had systolic BP 140-160 mm of Hg, 41 (66.1%) had systolic BP > 160 mm Hg. Out of 52 patients of LDH levels > 800 IU/L, 3 (5.7%) patients has systolic BP < 140 mm Hg. Out of these 3 patients, 2 patients presented with eclampsia. 5 (9.6%) patients had systolic BP 140-160 mm Hg, 44 (84.6%) patients had systolic BP > 160 mm Hg

Out of 86 patients with LDH levels < 600 IU/L, 48 (55.8%) patients had diastolic BP < 90 mm Hg, 38 (44.1%) patients had diastolic BP 90-110 mm Hg and not even single patients had diastolic BP > 110 mm Hg. Out of 62 patients with LDH levels 600-800 IU/L. 1 (1.6%) patients had got diastolic BP < 90 mm Hg, 20 (32.2%) patients had got diastolic BP 90-110 mm Hg and 41 (66.1%) had got diastolic BP > 110 mm Hg. At LDH levels > 800 Iu/L there were 3 (5.7%) patients had got diastolic BP <90 mm Hg, 12 (23.1%) patients had diastolic BP 90-110 mm Hg, 37 (71.1%) patients had got diastolic BP > 110 mm Hg (Table-3)

Table 4: Maternal complication depending on LDH levels

S. LDH (IU/L)	< 600	600-800	> 800
No. of patients	86 (%)	62 (%)	52 (%)
Abruption	1 (1.16%)	2. (3.22%)	7 (13.5%)
DIC	0	1(1.61%)	6 (11.54%)
Intracranial hemorrhage	0	0	2 (3.84%)
HELLP syndrome	0	3(4.8%)	5 (9.61%)
Acute renal failure	0	2(3.22%)	4 (7.69%)
Pulmonary Oedema	0	1 (1.61%)	4 (7.69%)
PPH	1 (1.16%)	2 (3.22%)	5 (9.61)
Maternal Death	0	0	2 (3.84%)
Total number of patients with complication	2 (2.3%)	11 (17.74%)	33 (63.50%) (and 2 maternal deaths)

DIC-Disseminated Intravascular Coagulation. Hellp-Hemolysis Elevated Liver Enzymes Low Platelet Count. PPH-Post Partum Hemorrhage

In the present study, patients with LDH levels < 600 IU/L, 2 (2.3%) patients out of 86 patients developed complications in the form of abruption placentae and PPH. Out of 62 patients with LDH levels 600-800 IU/L, 11 (17.74%) patients devolved complication in the form of, 2 (3.22%) patients developed abruption, 1 (1.61%) patients developed DIC, 3 (4.8%) patients developed HELLP syndrome, 2 (3.22%) of patients developed acute renal failure, 1 (1.61%) of patients developed pulmonary oedema. 2 (3.22%) of patients developed PPH.

Out of 52 patients with LDH levels > 800 IU/L, 33 (63.5%) patients developed complication in the form of, 7 (13.5%) patients developed abruption placentae, 6 (11.54%) patients developed DIC, 2(3.84%) patients developed intracranial hemorrhage, 5, (9.61%) patients developed HELLP syndrome, 4 (7.69%) patients developed acute renal failure, 4 (7.69%) developed pulmonary Oedema. PPH developed in 5 (9.6%) patients. There were 2 maternal deaths in patients with LDH levels > 800 IU/L (Table-4)

Table 5: Foetal complications depending on LDH levels

S.LDH (IU/ L)	< 600	600-800	>800
Total patients	86	62	52
Mean births weight (kg) ±standard deviation	2.621 ±0.468	2.135±0.540	1.71± 0.689
Live births	83 (96.5%)	47(75.8%)	34(65.4%)
Intrapartum death	3 (3.48%)	15 (24.19%)	18 (34.6%)
Neonatal death	1(1.16%)	3 (4.8%)	6(11.5%)
Neonatal complications	5 (5.8%)	12(19.3%)	15(28.8%)

The mean birth weight was 2.621 ± 0.468 kg in patients with LDH levels < 600 IU/L, 2.135 ± 0.540 kg in patients with LDH levels 600-800 IU/L, 1.71 ± 0.689 kg in patients with LDH levels >800 IU/L. There were 96.5% live births in patients with LDH levels <600 IU/L. Out of which one baby died of neonatal septicemia. There were 3 (3.48%) intrapartum deaths in this group, thus making total perinatal mortality 4.65%. In patients with S. LDH 600-800 IU/L, there were 75.8% live births, out of which 3 babies died in neonate period, due to prematurity, foetal growth restriction, meconium aspirations. There were 15 (24.1%) Intra partum death thus making total perinatal mortality (29%). In patients with LDH > 800 IU/L, there were 34 (65.4%) live births. Out of which 6 (11.5%) died in neonate period mainly due to prematurity, foetal growth restriction. There were 18 (34.6%) intrapartum deaths thus making total perinatal mortality (46.1%) (Table-5)

Discussion

Pregnancy induced hypertension is one of the leading cause of maternal and neonatal morbidity and mortality. The exact etiology of these hypertensive disorders is unknown. There are many theories proposed to explain etiology of preeclampsia but the most accepted theory states that there is an incomplete trophoblastic invasion of uterine arteries causing placental ischemia which results in the release of many antiangiogenic Proteins from placenta causing endothelial dysfunction [5]. This finally results in hypertension, increase in vascular permeability, activation of coagulation cascade and damage to renal filtering mechanism causing new onset proteinuria [6, 7]. These changes will cause an increase in serious maternal and foetal risk. Even today the major complications in pregnancy arise due to late detection of these hypertensive disorders or worsening of milder form of hypertension to severe form. Currently many advances in treatment to reduce the impact of these hypertensive disorders have been made, prevention of these disorders with a reliable screening tool still remains to be a constant challenge to the obstetrician. Thus there appears a need to have a marker to predict the severity of disease that shall be studied.

In this study, we studied LDH levels in pregnancy and its efficacy in correlation with severity of hypertensive disorders,

maternal and neonatal outcome. In the present study 54% patients of eclampsia and 46% patients of severe pre eclampsia belonged to 21-25 years of age group. 56% patient with severe preeclampsia were nulliparous and 74% patients of eclampsia were nulliparous. Similar findings were also observed by Jaiswar *el al*. [8], where majority of patients belonged to age group of 20-30 years and were nulliparous.

In the present study mean LDH levels of normotensive patients was 298.20 ± 79.885 IU/L, mean LDH levels of mild preeclampsia was 468.06 ± 121.505 IU/L, mean LDH levels of severe preeclampsia was 712.80 ± 417.701 IU/L, mean LDH levels of eclampsia patients was 1248.10 ±748.355 IU/L. Similar types of result were observed by. Jaiswar *et al*. [8] where mean LDH level in control was 278.33 ± 119.25 IU/L, in mild pre eclampsia was 646.95 ± 401.64 IU/L and in eclampsia it was 1648.10 ± 190.29 IU/L. In present study, we observed a significant rise in LDH levels with increasing severity of the disease (P<0.001-statistically significant). Qublan HS, *et al*. [4] in their study also demonstrated a significant association of serum LDH levels with severe preeclampsia (P<0.001)

The systolic and diastolic blood pressure were significantly higher in patients with rising LDH levels. In present study, in normotensive patients 96% had LDH levels < 600 IU/L, in mild pre eclampsia 74% of patients had LDH levels < 600 IU/L. In severe preeclampsia only 2% patients had LDH levels < 600 IU/L. In eclampsia patients not even single patient had LDH levels <600 IU/L. In normotensive patients 2% patients had LDH levels 600-800 IU/L, in mild preeclampsia 22% patients had LDH levels 600-800 IU/L, in severe preeclampsia 66% patients had LDH levels 600-800 IU/L, in eclampsia patients 34% patients had LDH levels 600-800 IU/L. In normotensive patients 2% patients had LDH levels >800 IU/L, 4% patients with mild preeclampsia had LDH levels >800 IU/L, 32% patients with severe preeclampsia had LDH levels > 800 IU/L, and 66% patients with eclampsia had LDH levels >800 IU/L. The same results were also observed by Qublan *et al*. [4].

In the present study, it was noted that with increase in LDH level, there was significant increase in maternal complications. The patients with LDH levels < 600 IU/L, 2 (2.3%) patients out of 86 patients developed complications in the form of abruption placentae and PPH. Out of 62 patients with LDH levels 600-800 IU/L, 11 (17.74%) patients developed complications in the form of 2 (3.22%) patients developed abruption, 1 (1.61%) patients developed DIC, 3 (4.8%) patients developed HELLP syndrome, 2 (3.22%) patients developed acute renal failure, 1 (1.61%) patients developed pulmonany oedema. 2 (3.22%) patients developed PPH. Out of 52 patients with LDH level > 800 IU/L, 33 (63.5%) patients developed complications in the form of, 7 (13.5%) patients developed abruption placentae, 6 (11.54%) patients developed DIC. 2 (3.84%) patients developed intra cranial hemorrhage, 5 (9.6%) patients developed HELLP syndrome, 4 (7.69%) patients developed acute renal failure, 4(7.69%) patients developed pulmonary oedema. PPH developed in 5 (9.6%) of patients. There were 2 maternal deaths in patients with LDH level > 800 IU/L. Demir *et al*. [9] concluded that high LDH level was associated with increased maternal mortality. Similar type of observation about maternal morbidity was also made by Qublan *et al*. Jaiswar *et al*. and Catan zerite *et al*. [4, 8, 10]. In the present study the increase in LDH level was associated with adverse perinatal outcome. The mean birth weight in LDH level < 600 IU/L was 2.621 ± 0.468kg as compared to 2.135±0.540 kg in patients with LDH level 600-800 IU/L and 1.71±0.689 kg in patients with LDH level > 800 IU/L. The same observation was also made by He *et al*. [11]

In patients with LDH level <600 IU/L there were 3.48% intra partum deaths with one baby died in early neonates period so making total perinatal mortality 4.65%. In patients with LDH level 600-800 IU/L, there were 24.1% intra partum deaths and 3 babies out of 47 live births died in early neonate period so making total perinatal mortality (29%). In patients with LDH level >800 IU/L there were 18(34.6%) intra partum death. Out of 34 live births 6 babies died in early neonate period so making total perinatal mortality 46.1%. Similar observation was made by Jaiswar *et al*, [8] study showed a significant increase in neonatal complications (P=0.003), still births and perinatal deaths (P<0.001) with increasing serum LDH level. In present study, a significant increase in neonatal complications (P<0.001) and perinatal deaths (P<0.001) was observed.

Conclusion

Preeclampsia is a multisystem disorder specific to pregnancy and has many complications. It leads to poor maternal and foetal outcome. The observations of the present study showed that serum LDH levels increased in preeclamptic patients compared to controls. Also, the maternal and foetal outcome was poor in patients with high serum LDH levels. Therefore, serum LDH levels can be used as a biochemical marker and prognostic indicator of the severity of the disease and its influence on the maternal and the foetal outcome. Proper monitoring of serum LDH levels in a high risk pregnant woman may help in early diagnosis and early intervention of the disorder and may also help in preventing maternal and foetal complications.

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