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Original Research Article

Lactate Dehydrogenase: A Marker to Prognosticate the Pregnancy Outcomes in Pregnancy Induced Hypertension

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Abstract:

Introduction: Hypertensive disorders are the most dreaded pregnancy-specific medical complication leading to adverse maternal and fetal complications. Lactate Dehydrogenase assesses the extent of intracellular death. This aids to prognosticate the disease severity in pregnancy induced hypertension and also helps in decision making regarding the management protocols and thereby improving the maternal and perinatal outcomes.

Material and Methods: This prospective case study from November 2018-May 2020 was conducted on antenatal women with pregnancy induced hypertension and serum lactate dehydrogenase levels were correlated with maternal and fetal outcomes and the severity of progression of disease was observed.

Results: 39.3% cases among 150 subjects were observed to have LDH levels below 600 IU/L while 33.3% and 27.4% were reported with Serum LDH levels between 600-800 IU/L and above 800 IU/L respectively. No statistically significant difference was found with post-partum hemorrhage and admission to ICU but post-partum $MgSO_4$ had p value 0.002. There was a statistically significant difference when fetal parameters were studied in terms of APGAR at <7 mins, NICU admission, intrauterine fetal demise, prematurity and low birth weight with significant p value of 0.001, 0.007, 0.003, 0.014 and 0.002 respectively at serum lactate dehydrogenase concentrations of < 600, 600-800 and > 800 IU/L.

Conclusion: Higher serum lactate dehydrogenase levels in pregnancy induced hypertension indicate heightened risk of progression to adverse outcomes in terms of maternal and fetal morbidity and mortality.

Keywords: Pregnancy induced hypertension, Serum Lactate Dehydrogenase, Maternal outcomes, Fetal outcomes.

Introduction

Pregnancy Induced Hypertension accounts for the most dreaded maternal and fetal morbidity and mortality. [1] The basic underlying pathology in pregnancy induced hypertension remains as endothelial dysfunction and vasospasm resulting from increased circulating pressor substances and increased sensitivity of the vascular system to normally circulating pressor substances.

Pregnancy induced hypertension is considered a disease of theories and inspite of all advancements in medicine, its etiology is poorly understood till date. No single test can predict the onset of this condition. However, biomarkers like serum lactate dehydrogenase may be used to prognosticate the disease severity and adverse complications associated with this condition. Lactate Dehydrogenase is the enzyme responsible for conversion of pyruvic acid into lactic acid during the process of glycolysis intracellularly which is the major source of energy in the placenta. Normal lactate dehydrogenase values vary from 200 - 400 IU/L. [2] Studies have shown that placentas of preeclamptic pregnancies have higher LDH activity and gene expression than normal pregnancy. [2] Although pregnancy itself does not affect the Lactate Dehydrogenase levels but when the tissues are damaged by injury or any other cause, the levels of LDH increase increases in blood.

Hypoxia in preeclampsia further enhances glycolysis and thus increases Lactate Dehydrogenase activity. [3] The cellular enzymes in the extracellular space serves as an indicator of disturbance in cellular integrity induced by pathological conditions and thus detect cell damage or cell death. This forms

the basis for serum LDH to assess the extent of cellular death and thereby helps to assess the severity of disease. This also adds to aid in accurate decision-making regarding the management strategies to reduce the maternal and fetal morbidity and mortality.

The present study on antenatal women with pregnancy induced hypertension correlates serum lactate dehydrogenase (LDH) levels with maternal organ dysfunction and morbidities and perinatal outcomes.

Aim and Objectives: To study the correlation of serum lactate dehydrogenase levels with maternal and fetal outcomes in antenatal women with pregnancy induced hypertension and predict the severity of disease progression.

Material and Methods:

This prospective case study conducted on 150 antenatal women diagnosed with pregnancy induced hypertension attending the antenatal clinic (outpatient department) and those admitted in the ward and labour room in the department of Obstetrics and Gynaecology, Shri Ram Murti Institute of Medical Sciences, Bareilly from November 2018-May 2020.Singleton pregnancy with Gestation age >20 weeks, calculated from the first day of the last menstrual period and blood pressure ≥ 140/90 mm Hg taken on two occasion 4 hours apart were included in the study. After approval from Institutional Ethical Committee and informed written consent, patients who satisfy inclusion criteria were examined. The blood samples were drawn intravenously at the hospital after each patient had rested for 30 minutes and the plain blood samples were sent to the chemical pathology laboratory for analysis using fully automated biochemical analyser.

The study population was divided into 3 groups based on the levels of serum lactate dehydrogenase (group 1: < 600 IU/L, group 2: 600-800 IU/L and group 3: > 800 IU/L). The patients and babies were followed up till early postpartum and neonatal period and results were analysed on software IBM SPSS version 20.0.

Observations: 39.3% cases among 150 subjects were reported to have LDH levels below 600 IU/L while 33.3% and 27.4% were observed with Serum LDH levels between 600-800 IU/L and above 800 IU/L respectively. The mean age with serum LDH < 600 IU/L, 600-800 IU/L and > 800 IU/L was 25.5 ± 2.5 years, 24.7 ± 3.7 years 26.8 ± 4.3 years respectively with minimum age of 18 years and maximum 42 years. Body mass index more than 25 kg/m^2 was common with LDH levels > 800 IU/L.

Table 1: Demographic variables among the study population

Demographic variables	Serum Lactate Dehydrogenase (IU/L)		
	< 600 IU/L (n=59)	600 – 800 IU/L (n=50)	> 800 IU/L (n=41)
Age (years)	25.5 ± 2.5	24.7 ± 3.7	26.8 ± 4.3
Body Mass Index (kg/m^2)	24.1 ± 3.7	25.3 ± 2.5	27.9 ± 4.3
Parity	Primigravida (10.3%)	Primigravida (15.2%)	Primigravida (31.8%)
Socio-economic status	Lower (11.3%)	Lower (17.4%)	Lower (22%)
Booking status	Booked 23.3%	Booked 7.3%	Booked 6.7%
Period of Gestation at delivery	37 – 42 weeks	37 – 42 weeks	34 – 37 weeks
Mean Systolic Blood Pressure (mm Hg)	142.5 ± 1.4	150.9 ± 2.8	162.8 ± 3.7
Mean Diastolic Blood Pressure (mm Hg)	92.3 ± 2.4	102.9 ± 2.8	108.7 ± 3.9

Total 57.3% women were primigravidas in this study and maximum (31.8%) had LDH levels above 800 IU/L. Majority (ie. 50.7%) patients in the study population belonged to lower socio-economic status, and had LDH levels above 800 IU/L. it was sad to observe that only 37.3% of the total pregnancies were booked, among which only 6.7% booked pregnancies were observed in patients with LDH levels > 800 IU/L. 64.4% cases with lactate-dehydrogenase below 600 IU/L had mild preeclampsia against 35.6% with severe preeclampsia while among LDH levels between 600-800 IU/L and > 800 IU/L, 60% and 43.9% cases were observed to have mild preeclampsia respectively and 40% and 56.1% cases respectively were reported with severe preeclampsia.

Table 2: Correlation of Serum Lactate Dehydrogenase levels with Organ Dysfunction

Organ Dysfunction	Serum Lactate Dehydrogenase (IU/L)			p-Value
	< 600 IU/L	600 – 800 IU/L	> 800 IU/L	
Abnormal fundoscopy	11 (18.6%)	16 (32%)	20 (48.8%)	0.006
Abnormal liver function tests	24 (40.7%)	22 (44%)	29 (70.7%)	0.007
Abnormal renal function tests	21 (35.9%)	26 (52%)	35 (85.4%)	0.003
p-Value	0.854			

Among all the cases with abnormal fundoscopy, 48.8% had serum lactate dehydrogenase concentration > 800 IU/L. Similarly, the laboratory parameters for liver function tests and renal function tests were deranged more with higher lactate dehydrogenase concentration ie. 70.7% and 85.4% women respectively and this was statistically significant with p value of 0.007 and 0.003 respectively.

The mean serum bilirubin, SGOT, SGPT and serum alkaline phosphatase among cases with values of serum LDH above 800 IU/L was 2.9 ± 1.6 mg/dl, 169 ± 88.9 IU/L, 167 ± 55.2 IU/L and 236 ± 31.3 IU/L respectively and this was statistically significant with p value of 0.001.

A statistically significant change in renal function test (p value 0.003) was observed among patients of preeclampsia. The values for mean serum urea and serum creatinine among cases with serum LDH concentration > 800 IU/L was 55.9 ± 1.4 mg/dl and 2.5 ± 0.8 mg/dL.

Out of total 150 cases, 143 women delivered, only 7 patients among the entire study population with serum LDH levels < 600 IU/L were discharged antenatally. All cases of severe preeclampsia were delivered.

71.2% women delivered vaginally against 28.8% cases who underwent cesarean section with serum lactate levels < 600 IU/L while with those with serum LDH levels > 800 IU/L, 14.6% underwent vaginal delivery against 85.4% cases who underwent cesarean section and this was statistically significant (p-Value = 0.004).

Table 3: Correlation of Serum Lactate Dehydrogenase levels with Mode of Delivery

Mode of Delivery	Serum Lactate Dehydrogenase (IU/L)			Total
	< 600 IU/L	600 – 800 IU/L	> 800 IU/L	
Vaginal	37 (71.2%)	27 (54%)	6 (14.6%)	70
Caesarean	15 (28.8%)	23 (46%)	35 (85.4%)	73
p-Value	0.004			

Only 4 out of 150 cases had antepartum eclampsia. None had postpartum eclampsia. No case of post-partum MgSO4 and ICU admission was observed at serum lactate dehydrogenase concentration < 600 IU/L while at levels above 800 IU/L, 24.4% cases required postpartum $MgSO_4$, 7.3% cases had postpartum hemorrhage and 4.9% cases were admitted to ICU for management and this difference was statistically significant. No mortality was observed in either group.

Table 4: Correlation of Serum Lactate Dehydrogenase levels with Maternal Complications

Maternal Complications	Serum Lactate Dehydrogenase (IU/L)			p-Value
	< 600 IU/L	600 – 800 IU/L	> 800 IU/L	
Post-Partum Hemorrhage	0	1 (2.0%)	3 (7.3%)	0.095
Post-Partum $MgSO_4$	1 (1.7%)	4 (8%)	10 (24.4%)	0.002
Admission to ICU	0	2 (4%)	2 (4.9%)	0.298
Mortality	0	0	0	0.000

15% babies had birth weight < 2 kg, 35% babies had birth weight between 2-2.5 kg while 50% had birth weight above 2.5 kgs among cases with serum LDH > 800 IU/L. Among these 87% were live births while 13% were documented to be intrauterine fetal demise. The mean baby birth weight observed with serum LDH levels < 600 IU/L, 600-800 IU/L and > 800 IU/L was observed to be 3.12 ± 1.6 kg, 2.96 ± 1.4 kg and 2.31 ± 1.2 kg respectively.

Table 5: Correlation of Serum Lactate Dehydrogenase levels with Fetal Complications

Fetal Complications	Serum Lactate Dehydrogenase (IU/L)			p-Value
	< 600 IU/L	600 – 800 IU/L	> 800 IU/L	
APGAR < 7 at 5 mins (n=81)	12 (20.3%)	29 (58%)	40 (97.6%)	0.001
NICU Admission (n=12)	1 (1.7%)	3 (6%)	8 (19.5%)	0.007
IUFD (n=18)	2 (3.4%)	5 (10%)	11 (26.8%)	0.003
Prematurity (n=57)	9 (15.3%)	18 (36%)	30 (73.1%)	0.014
Low Birth Weight (n=76)	11 (18.6%)	27 (54%)	38 (92.7%)	0.002

There was a statistically significant difference when fetal parameters were studied in terms of APGAR at <7 mins, NICU admission, intrauterine fetal demise, prematurity and low birth weight with significant p value of 0.001, 0.007, 0.003, 0.014 and 0.002 respectively at serum lactate dehydrogenase concentrations of < 600, 600-800 and > 800 IU/L.

Discussion

Our study concluded primigravida with age of 25-27 years, unbooked antenatally, BMI > 25 kg/m2, belonging to lower socio-economic status were high risk candidates for adverse pregnancy outcomes associated with pregnancy induced hypertension and these risk factors were more common

among study population with LDH levels above 800 IU/L but comparing the study by Gupta et al. (2019), it was observed that maximum antenatal females were in age group 20-25 years followed by 25-30 years. Majority of women belonged to lower middle class followed by upper middle class and were nullipara and unbooked (62%). [4]

In the study by Deshmukhet al. (2020), the mean systolic blood pressure observed was 130.53 ± 17.32 mm Hg and mean diastolic BP was 87.72 ± 13.86 mm Hg with serum LDH levels below 600 IU/L, mean systolic and diastolic blood pressure 154.27 ± 7.69 mm Hg and 107 ± 7.27 mm Hg with serum LDH levels between 600-800 IU/L against mean systolic and diastolic blood pressure 160.52 ± 14.45 mm Hg and 109.48 ± 9.78 mm Hg was reported with serum LDH levels above 800 IU/L. This was similar to results of our study where mean systolic BP was 142.5 ± 1.4 mm Hg, 150.9 ± 2.8 mm Hg and 162.8 ± 3.7 mm Hg and the mean diastolic BP was 92.3 ± 2.4 mm Hg, 102.9 ± 2.8 mm Hg and 108.7 ± 3.9 mm Hg respectively with serum LDH levels < 600 IU/L, 600-800 IU/L and > 800 IU/L. [3]

Our study concluded that majority patients with higher levels of lactate-dehydrogenase underwent caesarean section (P <0.001), which was similar to the study by Deshmukhet al. (2020), who reported a significant association (P <0.001) between Lactate Dehydrogenase and route of delivery, 21.5% women underwent caesarean with lactate-dehydrogenase values above 800 IU/L while with lactate-dehydrogenase levels below 600 IU/L, 79.5% underwent vaginal delivery. [3]

In our study, it was observed that the incidence of post-partum hemorrhage, post-partum MgSO4 and admission to Intensive Care Unit was more in subjects with LDH >800 IU/L. Jaiswar et al. (2011), noted a significant increase in maternal morbidity with increasing serum LDH levels with p-Value <0.001). They tabulated 13.8% maternal mortality with lactate-dehydrogenase levels >800 IU/L (p-Value- 0.006). [5] Lavanya et al. (2022), found the incidence of post-partum hemorrhage in serum lactate-dehydrogenase values below 600 IU/L to be 2%, 6.9% and 5% with serum lactate-dehydrogenase between 600-800 IU/L and above 800 IU/L respectively. [6] Qublan et al. and Demir et al. also reported significant increase in perinatal and maternal complications with serum lactate-dehydrogenase above 800 IU/L compared to women who had lower serum lactate-dehydrogenase levels. [7,8]

Andrews et al. (2016), in his study observed the mean gestational age at delivery was 37.21 ± 2.73 weeks in women with lactate-dehydrogenase levels below 600 IU/L and 36.61 ± 1.82 weeks when lactate-dehydrogenase levels were between 600-800 IU/L and 36.13 ± 1.12 weeks in women with lactate-dehydrogenase levels above 800 IU/L. The mean birth weight was 2.76 ± 0.24 kg in women with lactate-dehydrogenase levels below 600 IU/L, 2.52 ± 0.56 kg and 2.27 ± 0.25 kg in women with lactate-dehydrogenase levels between 600-800 IU/L and women with >800 IU/L respectively. [9] These results were similar to our study wherein period of gestation at delivery was 37 – 42 weeks with LDH levels below 800 and above was 34-37 weeks and the mean baby birth weight among patients with serum LDH levels < 600 IU/L, 600-800 IU/L and > 800 IU/L was observed to be 3.12 ± 1.6 kg, 2.96 ± 1.4 kg and 2.31 ± 1.2 kg respectively.

Sreelatha S et al. (2015), stated that the increased LDH level correlates with severity of pregnancy induced hypertension and has got poor perinatal outcome and thus, it can be considered as one of the biochemical marker. [10]

We concluded that there was a statistically significant difference when fetal parameters were studied in terms of APGAR at <7 mins, NICU admission, intrauterine fetal demise, prematurity and low birth weight with rising levels of LDH in our study and this was similar to Jha N et al (2015), who reported that the mean APGAR score was significantly (p-value <0.05) reduced at 5 (6.25 ±1.37) with higher serum lactate-dehydrogenase levels.

Increase in the incidence of perinatal deaths was observed by Dave et al. (2016) with rising values of serum lactate-dehydrogenase levels (P < 0.001). Intrauterine fetal death was seen in 4.8% of cases, intrauterine growth restriction in 33.9% and prematurity in 77.9% and neonatal deaths were reported in 95.2% in severe preeclampsia group. [11]

Similarly, Deshmukhet al. (2020), showed significant increase in neonatal complications (p-Value-0.003) and the proportion of NICU admission was 7.95%, 50% and 25.93% respectively among the less than 600 IU/L LDH level, 600 to 800 IU/L LDH level and >800 IU/L LDH level and this difference in the proportion of NICU admission across the three group was statistically significant (P value <0.001). [3] Jaiswar SP et al (2011), Dave A et al. (2016) and Jha N et al. (2015), found a similar association in their study and this can well be explained on the basis of hypoxic and unfavorable intrauterine environment with rising levels of LDH and hence a poor perinatal outcome. [5,11,12]

In the present study, lactate-dehydrogenase has been evaluated as a prognostic biochemical marker for disease severity in pregnancy induced hypertension. Detection of high-risk patients with increased levels of lactate-dehydrogenase mandate close monitoring, prompt management to prevent both maternal and fetal morbidity and mortality.

Conclusion

There is significant association between high serum lactate-dehydrogenase levels in preeclamptic patients with adverse effects on mother and baby. Since the level of serum lactate dehydrogenase has been observed to have considerable clinical implications in the course of pregnancy and on maternal and perinatal outcomes, the early detection of even minor degree of raised serum lactate-dehydrogenase level is important to improve both maternal and fetal morbidity and mortality. Serum lactate-dehydrogenase levels in patients with preeclampsia are seen to have associated with severity of the disease. Higher serum lactate dehydrogenase levels in pregnancy induced hypertension indicate heightened risk of progression to adverse maternal and perinatal outcomes.

Limitations: This is a very small study confined to single hospital, thus large randomized control trials are needed before establishing its efficacy as predictor of adverse maternal and fetal outcomes.

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