

Study of maternal and perinatal outcomes among women with pregnancy induced hypertension with normal and high serum LDH levels

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Abstract

Background: Pregnancy induced hypertension (PIH) is a common complication in pregnancy, affecting more than 5-10% pregnancies worldwide. Previous studies have shown varying results for the ability of LDH to predict adverse maternal outcomes in PIH. This study aims to study of maternal and perinatal outcomes among women with pregnancy induced hypertension with normal and high serum LDH levels. **Material and Methods:** Present study was prospective, comparative study, conducted pregnant women between 18-35 years, singleton pregnancy, ≥ 20 weeks of gestation with pregnancy induced hypertension. Blood was collected for analysis along with routine blood investigations and LDH levels. **Results:** 200 patients were studied in present study. In our study with serum LDH < 600 with urine albumin 2+ was 16%, 1+ in 15%, nil in 11%, traces in 5% and 3+ in 4%. Serum LDH between 600 to 800 with urine albumin 1+ in 23%, 2+ and nil with 3% each. Serum LDH > 800 with urine albumin 1+ and 2+ is 9% each, with 3+ and nil in 1% each. p value is 0.001 which is statistically significant. In our study serum LDH < 600 had abruption with PPH, DIC, eclampsia and PPH in 2% each, with serum LDH 600-800 had PPH in 6.9% and with serum LDH > 800 had PPH in 5% cases. p value is 0.85 which is statistically not significant. In our study serum LDH < 600 had a IUGR in 7.8%, fetal distress in 5.9%, neonatal death and stillbirth in 3.9% each, IUD, LBW, MSL and premature births in 2% each. Serum LDH between 600-800 had IUGR and LBW in 3.4% each. Serum LDH with > 800 had IUGR in 15% and neonatal death and stillbirth in 5% each which is clinically significant. p value is 0.585 which is statistically not significant. **Conclusion:** Higher LDH levels are indicative of maternal and fetal complications. higher serum LDH levels more than 500 IU/L to 600 to 800 IU/L have closer association with severe preeclampsia. Pre-eclampsia patients with raised LDH levels should be closely monitored.

Keywords: Preeclampsia, eclampsia, LDH (lactate dehydrogenase), pregnancy induced hypertension.

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INTRODUCTION

Pregnancy induced hypertension (PIH) is a common complication in pregnancy, affecting more than 5-10% pregnancies worldwide.¹ Increased awareness and the widespread use of screening methods have led to increased recognition of the problem. In Asia the incidence of PIH is around 5-8%.² Preeclampsia is a clinical condition of pregnancy characterized by hypertension, and proteinuria. It is a multisystem disorder affecting nearly every organ and system in the human body. Abnormal placentation, endothelial dysfunction, immunological intolerance and oxidative stress are some of the causes attributed to the development of PIH.³ Hence PIH can lead to multiorgan

dysfunction. PIH is associated with increased maternal morbidity and mortality. It can lead to complications like eclampsia, placental abruption, acute renal failure, pulmonary oedema in the mother. It is also associated with increased foetal complications like growth restriction, foetal distress, hypoxic ischaemic encephalopathy and it may sometimes lead to perinatal mortality.⁴ Previous studies have shown varying results for the ability of LDH to predict adverse maternal outcomes in PIH. While some studies have found strong associations between levels of LDH and adverse outcomes, others have found only weak associations or none at all. No consensus on reproducible predictive parameters has been reached.⁵

This study aims to study of maternal and perinatal outcomes among women with pregnancy induced hypertension with normal and high serum LDH levels.

MATERIAL AND METHODS

Present study was prospective, comparative study, conducted in the Obstetrics and Gynaecology Department, Raichur Institute of medical sciences, Raichur which is a tertiary care centre, catering to both low risk and high-risk antenatal patients. Study duration was of 1 year (1st January 2018 to 31st December 2018). Study was approved by institutional ethics committee.

Inclusion criteria:

- Pregnant women between 18-35 years, singleton pregnancy, ≥ 20 weeks of gestation with pregnancy induced hypertension.

Exclusion Criteria:

- Pregnant women with essential hypertension or hypertension < 20 weeks gestation;
- Pregnant women with pre-existing diabetes mellitus,
- Pregnant women with renal disease, liver disorder,
- Pregnant women with hyperthyroidism, epilepsy, urinary tract infection, cardiovascular disease, smokers, alcoholics, Rh negative pregnancy, multiple gestation.

RESULTS

200 patients were studied in present study. The maximum number of patients of pre-eclampsia were from age group 20-24 years (51%), next being 25-29 years (31%).

Table 1: Distribution of age

Age(yrs.)	No. of patients	Percentage
<20	18	9
20-24	102	51
25-29	62	31
≥ 30	18	9

In present study maximum number of cases were primigravida (51%), G2 were (32%), G3 were (11%).

- Not willing to participate / follow up

All women eligible for the study were explained about the study. An informed consent was taken from all the patients for inclusion in the study.

Blood was collected for analysis along with routine blood investigations. LDH levels was estimated in Erba biochemical fully automated analyzer by using Kinetic UV test.

Normal Serum LDH Values

Non-pregnant women	First Trimester	Second Trimester	Third Trimester
115 to 211 IU/L	78 to 433 IU/L	80 to 447 IU/L	82 to 524 IU/L

Serum LDH value above the reference range is taken as raised.

All women included in the study were followed until delivery. LDH levels was done after inclusion in the study and patients were followed up till delivery. Management was done according to hospital protocol. All maternal complications like abruption, eclampsia, renal failure, hepatic failure, cerebrovascular accidents, HELLP syndrome [hemolysis, elevated liver enzymes, and low platelet count], pulmonary oedema, shock, postpartum haemorrhage, Disseminated intravascular coagulation are noted down. All perinatal complications including gestational age at the time of delivery, birth weight, APGAR at 1 and 5 min, Intra uterine death, Neonatal ICU admission, Hypoxic ischemic encephalopathy and perinatal mortality are noted down. All non severe preeclampsia women included in the study, LDH levels was done and followed till delivery. If patient of non severe preeclampsia changed to severe preeclampsia LDH levels was done again and followed as severe preeclampsia. Data was analyzed using SPSS software v.23.0. and Microsoft office 2007. All characteristics were summarized descriptively. For continuous variables, the summary statistics of mean \pm standard deviation (SD) were used. Chi-square (χ^2) test was used for association between two categorical variables. If the p-value was < 0.05 , then the results were considered to be statistically significant.

Table 2: Distribution of Gravida status

Gravida status	No. of patients	Percentage
Primi	102	51
G2	64	32
G3	22	11
≥G4	12	6

In our study maximum number of cases are > 38 weeks of gestation (49%), cases between 36-38 weeks were 27% and between 32-34 weeks were 15%.

Table 3: Distribution of Gestational age (weeks)

Gestational age (weeks)	No. of patients	Percentage
32-34	18	9
34-36	30	15
36-38	54	27
>38	98	49

In our study with serum LDH <600 with urine albumin 2+ was 16%, 1+ in 15%, nil in 11%, traces in 5% and 3+ in 4%. Serum LDH between 600 to 800 with urine albumin 1+ in 23%, 2+ and nil with 3% each. Serum LDH >800 with urine albumin 1+ and 2+ is 9% each, with 3+ and nil in 1% each. p value is 0.001 which is statistically significant.

Table 4: Urine albumin according to LDH

Urine albumin	LDH(IU/l)< 600		LDH(IU/l) 600 to 800		LDH(IU/l) > 800		p value
	N	%	N	%	N	%	
	1+	30	15	46	23	18	
2+	32	16	6	3	18	9	
3+	8	4	0	0	2	1	
Nil	22	11	0	0	2	1	
Traces	10	5	6	3	0	0	
Total	102	51	58	29	40	20	

In our study serum LDH <600 had abruption with PPH, DIC, eclampsia and PPH in 2% each, with serum LDH 600-800 had PPH in 6.9% and with serum LDH >800 had PPH in 5% cases. p value is 0.85 which is statistically not significant.

Table 5: Maternal outcome according to LDH

Maternal Outcome	LDH(IU/l)< 600		LDH(IU/l) 600 to 800		LDH(IU/l)> 800		p value
	N	%	N	%	N	%	
	Abruption with PPH	1	2.0%	0	0.0%	0	
DIC	1	2.0%	0	0.0%	0	0.0%	
Eclampsia	1	2.0%	0	0.0%	0	0.0%	
PPH	1	2.0%	2	6.9%	1	5.0%	

In our study serum LDH<600 underwent elective LSCS in 47.1%, NVD in 47.1%, emergency LSCS in 3.9% and forceps assisted vaginal delivery in 2%. Serum LDH 600-800 underwent NVD in 72.4%, elective LSCS in 24.1% and emergency LSCS in 3.4%. serum LDH >800 underwent elective LSCS in 55%, NVD in 40% and emergency LSCS in 5%. p value is 0.286 which is statistically not significant.

Table 6: Mode of delivery according to LDH

Mode of Delivery	LDH(IU/l)< 600		LDH(IU/l) 600 to 800		LDH(IU/l)> 800		p value
	N	%	N	%	N	%	
	EM.LSCS	4	3.9%	2	3.4%	2	
Instrumental delivery	2	2.0%	0	0.0%	0	0.0%	
Elective LSCS	48	47.1%	14	24.1%	22	55.0%	
NVD	48	47.1%	42	72.4%	16	40.0%	

In our study mean APGAR 1 mins with serum LDH 600-800 is 7.7, >800 is 7.5, <600 is 7.2 respectively. mean APGAR 5 mins with serum LDH 600-800 is 8.7, >800 is 8.5, <600 is 8.3. p value is 0.083 and 0.217 APGAR 1min and APGAR 5mins, hence statistically not significant.

Table 7: Mean APGAR according to LDH

Parameters	LDH(IU/l)< 600	LDH(IU/l) 600 to 800	LDH(IU/l)> 800	p value
APGAR 1MIN	7.2±1.2	7.7±0.6	7.5±0.7	0.083
APGAR 5MIN	8.3±1	8.7±0.6	8.5±0.6	0.217

In our study serum LDH <600 had a IUGR in 7.8%, fetal distress in 5.9%, neonatal death and stillbirth in 3.9% each, IUD, LBW, MSL and premature births in 2% each. Serum LDH between 600-800 had IUGR and LBW in 3.4% each. Serum LDH with >800 had IUGR in 15% and neonatal death and stillbirth in 5% each which is clinically significant. p value is 0.585 which is statistically not significant.

Table 8: Perinatal outcome according to LDH

Perinatal Outcome	LDH(IU/l)< 600		LDH(IU/l) 600 to 800		LDH(IU/l)> 800		p value
	N	%	N	%	N	%	
	Fetal distress	3	5.9%	0	0.0%	0	
IUD	1	2.0%	0	0.0%	0	0.0%	
IUGR	4	7.8%	1	3.4%	3	15.0%	
LBW	1	2.0%	1	3.4%	0	0.0%	
MSL	1	2.0%	0	0.0%	0	0.0%	
Neonatal death	2	3.9%	0	0.0%	1	5.0%	
Premature	1	2.0%	0	0.0%	0	0.0%	
Still birth	2	3.9%	0	0.0%	1	5.0%	

DISCUSSION

The placenta has a very significant role in the pathogenesis of PIH, therefore the one and only definitive treatment for the preeclampsia is delivery of the fetus. The main mechanisms involved in the placenta causing the disease are abnormal trophoblastic invasion, endothelial cell injury or activation, immune rejection of the placenta, compromised placental perfusion, altered vascular reactivity and imbalance between prostacyclin and thromboxane. In our study, the study age of most pregnancies occurred in age group 20-24years followed by 25-29 years. Similar findings were noted by Jaiswar *et al.*⁶ and Pallavi Singh *et al.*⁷. In our study, most of the patients were primigravida. Similar findings were noted by Pallavi Singh *et al.*⁷. In present study mean LDH in severe preeclampsia and eclampsia patients were 570.5 IU/L. Rubina Aziz *et al.*⁸ and Metin Ingec *et al.*⁹ noted mean LDH in severe pre-eclampsia and eclampsia patients as 348.34 IU/L and 1118 IU/L respectively. The mean LDH levels in the severe preeclampsia group were significantly higher compared to non-severe pre-eclampsia patients. Similar findings were noted by Metin Ingec *et al.*⁹. Kiren K Malik *et al.*¹⁰ studied the correlation of Lactic dehydrogenase levels with severity of preeclampsia. A total of 120 pregnant women with preeclampsia (60 with mild and 60 with severe preeclampsia) and 60 healthy normotensive controls were studied. The study showed a statistically significant increase in terms of LDH and liver enzymes ($p < 0.05$) in patients with severe preeclampsia. LDH levels >600IU/L were seen in 62% of women with severe preeclampsia compared to 20% in normotensives and patients with mild preeclampsia. In this study LDH concentrations >800 IU/L had significant increase in

frequency of epigastric pain and vomiting. In severe preeclampsia with LDH >800 IU/L women had significant increase in all complications noticed eclampsia being the most frequent one. Elevated levels of LDH, indicative of cellular damage, can be used as a biochemical marker because it reflects complications and fetal outcome. In a similar study by James N Martin *et al.*¹¹, to investigate the utility of an admission battery of findings and laboratory data in the discrimination of patients with or without HELLP syndrome at high risk for development of significant maternal morbidity, they found that the presence of nausea and vomiting, epigastric pain or both in association with values that are in excess of the cut-offs for lactate dehydrogenase, aspartate aminotransferase and uric acid concentrations. In a prospective study by Qublan *et al.*¹² 111 preeclampsia women and 60 normotensive controls were included in the study. The symptoms and complications of preeclampsia along with foetal outcome were analyzed according to the levels of LDH. A significant association of serum LDH levels with severe preeclampsia was demonstrated. Increase in the incidence of perinatal deaths was observed in patients with increasing levels of serum LDH levels. Intrauterine fetal death was seen in 4.8% of cases, intrauterine growth restriction in 33.9% and prematurity in 77.9%. Neonatal deaths were reported in 95.2% in severe preeclampsia group. Severely preeclamptic women with LDH levels of < 800 IU/l showed a significant increase in complications in terms of eclampsia, abruption placenta and various other complications compared to women who had lower serum LDH levels. The Qublan *et al.* Study concluded that Preeclampsia is a pregnancy-specific disease, and in its severe form, serious multisystem complications may occur and

elevated levels of lactic dehydrogenase, indicative the cellular damage and dysfunction, can be used as a biochemical marker because it reflects the severity of the disease, the occurrence of complications, and foetal outcome.¹² Serum LDH is the earliest marker in blood during hypoxia and oxidative stress. It is raised in cases of pre-eclampsia and eclampsia. Detection of high-risk patients with increased levels of LDH mandates close monitoring, prompt and correct management to decrease both maternal and foetal morbidity and mortality. Estimation of serum Lactate Dehydrogenase can be used as a prognostic marker for preeclampsia and eclampsia. Limitations of present study were sample size studied was small and a smaller number of eclampsia patients. Larger studies are required to document findings.

CONCLUSION

Higher LDH levels are indicative of maternal and fetal complications. higher serum LDH levels more than 500 IU/L to 600 to 800 IU/L have closer association with severe preeclampsia. Pre-eclampsia patients with raised LDH levels should be closely monitored.

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