Original Research Article

Serum lactate dehydrogenase level in pre-eclampsia and its correlation with maternal and fetal outcome

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ABSTRACT

Background: Hypertensive disorders are the most common medical disorders during pregnancy. It increases maternal and perinatal morbidity and mortality. The incidence is 7 to 10%. Identifying high risk patients and close monitoring can reduce the complications. Lactate dehydrogenase is a useful biochemical marker and can be used to evaluate maternal complications like Disseminated intravascular coagulation (DIC), HELLP syndrome (Haemolysis, elevated liver enzymes and lowered platelets), pulmonary edema, renal failure and fetal complications like Fetal growth restriction (FGR) APGAR score ≤7 at 5 min and Neonatal intensive care unit (NICU) admissions. The objective of this study was to estimate serum Lactate dehydrogenase levels (LDH) in pre-eclampsia patients and study the correlation between increased LDH levels and maternal and fetal outcome.
Methods: It was a prospective study from October 2015 to May 2017 at M. S. Ramaiah medical college and hospitals, Bangalore.
Results: The incidence of maternal and foetal complications was increased with higher serum LDH levels. With serum LDH >than 600 IU/l the incidence of HELLP syndrome, DIC, pulmonary edema was statistically significant. It also correlated with increased creatinine levels and decreased platelets with p value<0.001. The foetal complications including FGR NICU admission and Apgar score <7 at 5 min was statistically significant. The liver enzymes and serum creatinine correlated with increased LDH levels.
Conclusions: Maternal and foetal complications are increased with raised LDH levels, and it can be used as a biochemical marker to achieve a better outcome.

Keywords: Abruptio placenta, Disseminated intravascular coagulation, Foetal growth restriction, HELLP syndrome, Lactate dehydrogenase, Pre-eclampsia

INTRODUCTION

Hypertensive disorders complicate 5-10% of all pregnancies and together they are one family of the deadly triad- along with haemorrhage and infection-that contribute greatly to maternal morbidity and mortality. Of these disorders, the preeclampsia syndrome either alone or superimposed on chronic hypertension is the most dangerous.[1] Although the precise aetiology of preeclampsia is not clear, defective placentation and endothelial dysfunction are considered the core features of preeclampsia.[2]

Many theories have suggested that endothelial dysfunction caused by factors released from ischaemic placenta, may be a factor for disease pathogenesis.[3]

The complications of preeclampsia include: abrupt placentae, HELLP syndrome, DIC, liver failure, renal failure, retinal detachment and cerebral haemorrhage. The foetal complications include FGR, Intrauterine foetal demise, Apgar score <7 at 5 min and NICU admissions.

In the absence of effective screening modalities, clinical risk factors can help us to be vigilant.[4] Early detection of pre-eclampsia is imperative and non-invasive diagnostic methods based on biomarkers holds promise.[5] Lactate dehydrogenase (LDH) is a glycolytic enzyme involved in the reversible conversion of pyruvate to lactate when absolute or relative anoxemia is present.[6] Elevated levels of LDH indicate intracellular death and leakage of enzyme from the cell. High levels were found in association with severe preeclampsia.

LDH is a useful biochemical marker that reflects the severity of preeclampsia and the occurrence of complications of preeclampsia.[7] Serum LDH estimation and monitoring may help to decrease complications in preeclampsia and thereby help in improving maternal and foetal outcome.

The purpose of this study was to analyse if serum LDH levels can be used as a prognosticator in the management of preeclampsia.

Objectives

The objectives of this study were (a) to estimate serum LDH levels in preeclampsia patients; and; (b) to study the correlation between increased serum LDH levels and maternal and foetal outcome.

METHODS

This was a prospective study at the department of obstetrics and gynecology M. S. Ramaiah medical college and Hospitals from October 2015-May 2017.

All pregnant women with BP recording of >140/90 mmHg and proteinuria after 20 weeks of gestation attending antenatal clinic and those who were admitted at Ramaiah Hospitals were enrolled. The sample size was 115.

The lab method used was quantitative measurement of serum LDH was done by ELISA kit based on the principal that it catalyses the reaction between pyruvate and NADH. Based on LDH level, the patients were divided into two groups. Group 1 with serum LDH value <600 IU/l and group 2 with serum LDH >600 IU/l. Incidence of maternal complications like abruption placentae, eclampsia, HELLP syndrome, DIC, liver failure, renal failure, retinal detachment and cerebral haemorrhage were studied Incidence of foetal complications like FGR, Intra Uterine foetal demise (IUFD), Apgar score <7 at 5 min and NICU admission were studied in each group.

Inclusion criteria

All patients with gestational age >20 weeks and BP>140/90 mmHg along with proteinuria were included in the study.

Exclusion criteria

High BP recordings before 20 weeks gestation were excluded from the study.

Pre-existing medical conditions such as- diabetes mellitus, renal disorders, liver disorders, connective tissue disorders, cardiac disease, musculoskeletal disorders, haemolytic anaemia, epilepsy and thrombophilia.

Statistical analysis

Descriptive and inferential statistical analysis was carried out in the present study. 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. The following assumptions on data was made.

Chi square/Fischer exact test was used to find the significance of study parameters on categorical scale between the two groups. Non-parametric setting for qualitative data analysis and Fischer exact test used when cell samples were small.

The statistical software namely SPSS 18.0, and R environment version 3.2.2 were used for the analysis of the data and Microsoft word and excel have been used to generate graphs and tables.

RESULTS

Age, gravidity, period of gestation, mode of delivery, maternal and fetal complications were studied. Between October 2015 to May 2017, all patients with preeclampsia who fulfilled the inclusion criteria were studied.

In our study 43.9% were between 19-24 years of age and 36.8% were between 25-29 years. This showed that 80.7% were below 30 years of age. Unbooked patients accounted for 60.5% and booked patients accounted for 39.5%. Ours being a tertiary center we have a larger number of unbooked referrals.

It was seen that hypertension was more prevalent among Primigravidae which accounted for 65.8%.

It was seen that 36% were between 28-32 weeks of gestation and 37.7% were between 33-36 weeks.

Antepartum eclampsia accounted for 11.4%, HELLP syndrome 8.7% and abruption 7.9% of the cases.

The mode of delivery was LSCS in 51.8 % and vaginal delivery in 48.2%. Serum LDH levels >600 IU/l was seen in 16.7% of the cases. It was seen that, 49.1% of the newborns were <1.5 kg. Most of the cases were induced before term in order to prevent maternal complications. FGR was seen in 39.1% and NICU admissions were noted in 54.4% of study population. With increased serum LDH levels, maternal complications were seen to be higher. The overall incidence of HELLP syndrome in the present study was 8.7% and serum LDH was elevated in 73.3% of this population. This correlated with p value<0.001. The overall incidence of DIC was 1.7% with 15.8% of this population having elevated LDH, this corresponded with p value<0.004 significant. The overall incidence of pulmonary edema in this study was 2.6% with 10.5% of this population having elevated LDH levels. This corresponded with p value<0.072 significant.

Table 1: Age distribution.

Age in years	Number of patients (N=115)	Percentage (%)
19-24	50	43.9
25-29	43	36.8
30-34	16	14.0
35-40	6	5.3

Table 2: Booked verses unbooked.

Type	Number of patients (N=115)	Percentage (%)
Booked	46	39.5
Unbooked	69	60.5

Table 3: Gravidity distribution.

Gravidity distribution	Number of patients (N=115)	Percentage (%)
Primigravida	75	65.8
Multigravida	40	34.2

Table 4: POG of patients.

POG (in weeks)	Number of patients (N=115)	Percentage (%)
28-32	41	36
33-36	43	37.7
37-40	31	26.3

Table 5: Maternal complications.

Maternal complications	Number of patients (N=115)	Percentage (%)
HELLP syndrome	10	8.7
DIC	2	1.7
Pulmonary edema	3	2.6
Abruption	9	7.9
Antepartum eclampsia	13	11.4

Table 6: Mode of delivery.

Mode of delivery	Number of patients (N=115)	Percentage (%)
Vaginal delivery	56	48.2
Lower segment caesarean section (LSCS)	59	51.8

Table 7: Serum LDH levels.

Serum LDH levels	Number of patients	Percentage (%)
<600	96	83.4
>600	19	16.7

Table 8: Birth weight.

Birth weight (kg)	Number of neonates	Percentage (%)
<1.5	56	49.1
1.5-2.5	49	42.1
>2.5	10	8.8

Table 9: Fetal outcome.

Fetal outcomes	Number (N=115)	Percentage (%)
FGR	45	39.1
NICU admissions	62	54.4
IUFD	08	7
Apgar≤7 at 5 min	46	40.4
Still birth	08	7
Meconium stained liquor	36	31.6
RDS	15	13.2
Neonatal death	08	7
Stable	37	32.2

Table 10: Complications in relation to serum LDH levels.

Complications	Serum LDH				P value (Fisher exact test)
	<600 IU/l		>600 IU/l		
	N	%	N	%	
HELLP syndrome	0	-	10	73.7	<0.001 significant**
DIC	0	-	2	15.8	0.004 significant*
Pulmonary edema	1	1.1	2	10.5	0.072 significant+
Abruption	6	6.3	3	15.8	0.171 insignificant

Note: +-significance (p value: 0.05<p<0.10); *-moderately significant (p value: 0.01<p<0.05); and **-strongly significant (p value: p≤0.001).

DISCUSSION

Pre-eclampsia is considered to be an idiopathic multisystem disorder that is specific to human pregnancy.[8] Preeclampsia may be life threatening for both mother and child increasing both foetal and maternal morbidity and mortality.[8] The haemodynamic alteration, activation of the coagulation cascade with micro thrombi results in perinatal as well as maternal complications.[9]

Early prediction and management will prevent complications. The timing of delivery is critical.

In recent times, several research studies have suggested serum LDH as a potential indicator of preeclampsia and serum LDH levels have been observed to increase with the severity of the ailment.[3,8,11]

The multiorgan dysfunction in severe preeclampsia caused by vascular endothelial damage including maternal liver, kidney, lungs, nervous system, blood and coagulation system will lead to excessive LDH levels in serum due to cellular dysfunction.[14]

Young age and primigravida are well known risk factors for developing pre-eclampsia.[16]

Numerous risk factors for preeclampsia have been suggested but only some have been established in multivariant models that permit simultaneous control for possible cofounders.[17]

The neonatal outcome has been linked to neonatal intensive care facilities and gestational age at birth.[18]

Preeclampsia and foetal growth restriction remain an important cause of morbidity and mortality.[19]

Placental growth factor (PlGF) is a pro angiogenic factor and from as early as 11-13weeks gestation, low levels are associated with the later development of pre-eclampsia. sFlt-1 (Soluble fms-like tyrosine kinase 1) is anti-angiogenic and levels elevated as much as 5 weeks prior to the clinical onset of the disease. Both have been evaluated as diagnostic tests but neither has sufficient sensitivity to be of use in clinical practice.[20]

In the present study, age factor did not have any significant correlation, though majority were less than 30 years. The unbooked patients in our hospital accounted for 60.5%, indicating that majority were referrals (Table 2). Primigravidae accounted for 65.8% (Table 3). This was similar to the study by Hak et al where primigravida accounted for 74%.[3]

In our study, 26.3% were between 37-40 weeks of gestation (Table 4). In a study done by Doddamani et al 53% were term gestation.[13]

The incidence of severe preeclampsia was 64% in our study. In a study by Hak et al severe pre-eclampsia was found in 40% of the cases.[3] Depending on the severity of the maternal and foetal condition, delivery was planned. 51.8% underwent Caesarean section and 48.2% delivered vaginally (Table 6). In a study by Hak et al 46.4% underwent LSCS.[3] In a study by Anupama et al 42.8% underwent LSCS.[11] In our study, the major indication for LSCS was foetal distress, with other contributing factors being pathological NST and abnormal Doppler.

In our study, the maternal complications were antepartum eclampsia (11.4%), HELLP syndrome (8.7%), abruptio placenta (7.9%), pulmonary oedema (2.6%) and DIC (1.7%) (Table 5). There was no maternal mortality.

Serum LDH level was >600 IU/l in 16.7% and <600 IU/l in 83.4% (Table 7).

In our study 54.4% of the new born were shifted to NICU and 39% had FGR (Table 9). In a study by Hall et al, 40.4% were shifted to NICU.[18] In our study, 7% of the patients presented with IUFD, 7% had still birth. 7% had neonatal mortality. 49.1% of the new born were <1.5 kg, 42.7% were between 1.5-2.5 kg, 8.8% were >2.5 kg (Table 8).

In our study, serum LDH was >600 IU/L in 16.7% of the patients. HELLP syndrome was seen in 8.7% with p value 0.001 which was statistically significant (Table 10). This was similar to a study by Hak et al where HELLP syndrome was seen in 6.9%.[3] Urvashi et al reported HELLP syndrome around 9%.[8]

DIC was seen in 1.7% of our patients and correlated with serum LDH level >600 IU/l with p value 0.004 which was statistically significant. Urvashi et al reported similar findings.[8]

Pulmonary oedema was seen in 2.6% of our patients and correlated with p value of 0.072 which was statistically significant.

In our study with serum LDH >600 IU/l the patients had serum creatinine between 0.71 mg/dl with p value of 0.001which was statistically significant. The other parameters like urine albumin, platelet count also correlated with increased serum LDH levels.

The incidence of FGR was 39.1% in the present study and 84.2% were in the group with serum LDH >600 IU/l and p value<0.001 which was significant.

NICU admissions and APGAR score <7 at 5 min were also more in the group with LDH>600 IU/l which was statistically significant.

Mean AST and ALT values were higher in the group with LDH>600 IU/l with p value<0.001 which was significant.

There was no maternal mortality in our study.

Limitations

Investigations for thrombophilia were not done.

CONCLUSION

Pre-eclampsia is a multisystem disorder which is specific to pregnancy and has multifactorial etiology. Preeclampsia is associated with complications and can increase both maternal and perinatal morbidity and mortality. Elevated LDH levels correlated with maternal complications like HELLP syndrome, DIC, Pulmonary edema, thrombocytopenia and renal failure. Elevated LDH level correlated with fetal complications like FGR, APGAR <7 at 5 min and NICU admission. Serum LDH is a useful biochemical marker and can be monitored to prevent complications in preeclampsia, hence leading to a better outcome for both mother and the newborn.

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