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Original Research Article

A study on lactate dehydrogenase levels in hypertensive disorders of pregnancy and its correlation with fetomaternal outcome

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ABSTRACT

Background: Hypertensive disorders of pregnancy are one of the most common medical disorders seen during pregnancy. Lactate dehydrogenase (LDH) is an intracellular enzyme. The objective of this study was to compare lactate dehydrogenase levels in women with hypertensive disorders of pregnancy and normal pregnant women, to correlate lactate dehydrogenase levels with complications of hypertensive disorders of pregnancy and role of lactate dehydrogenase as an early predictor of hypertensive disorders of pregnancy.

Methods: A study was conducted in the department of obstetrics and gynecology at JJ group of hospitals, Mumbai, India for a duration of 18 months from January 2020 to June 2021. This study has a sample size of 500 antenatal patients. Necessary information such as their detailed clinical, and obstetric history, clinical examination, investigations was noted. LDH were measured at 12-16 weeks of pregnancy and at the time of delivery.

Results: In our study, the incidence of hypertensive disorders of pregnancy was 10.2%. There was no association between LDH levels at 12-16 weeks of gestation and development of hypertensive disorders of pregnancy. There was association between levels of lactate dehydrogenase levels at time of delivery and severity of hypertensive disorders in our study. Higher serum LDH levels were associated with increased incidence of maternal and fetal complications like abruption placenta, HELLP syndrome, IUGR, IUFD, prematurity and oligohydramnios in our study.

Conclusions: Hypertensive disorders of pregnancy are one of the medical conditions affecting pregnancy. Lactate dehydrogenase levels at 12-16 weeks of gestation is not early predictor of hypertensive disorders of pregnancy. Serum lactate dehydrogenase levels at time of delivery helps in prediction of severity of disease, adverse outcomes and complications of hypertensive disorders of pregnancy. Hence lactate dehydrogenase acts as prognostic factor in hypertensive disorders of pregnancy.

Keywords: Hypertensive disorders, Lactate dehydrogenase levels, Maternal outcome

INTRODUCTION

Hypertensive disorders represent the most common medical complication of pregnancy affecting between 7% and 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 worldwide, hypertensive disease remains a leading cause of direct maternal mortality. Together with haemorrhage and infection, hypertension

forms the deadly triad that contributes to morbidity and mortality during pregnancy and childbirth.²

In India, the incidence of preeclampsia is reported to be 8-10% among the pregnant women.^{3,4} Severe preeclampsia is frequently accompanied by hemolysis, which manifests as elevated serum lactate dehydrogenase levels and reduced haptoglobin levels.⁵ Lactate dehydrogenase is an intracellular enzyme and its levels are increased in these women with cellular death. The effects of LDH in

pregnancy related complications like preeclampsia is now gaining attention. Though cellular enzymes in the extracellular space have no metabolic function, they 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. So, serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease.⁶

Preeclampsia produces potentially lethal complications including placental abruption, hepatic failure, acute renal failure and cardiovascular collapse. The analysis of a combination of biomarkers particularly markers related to vascular dysfunction such as LDH may enrich the ability to predict and prevent preeclampsia in near future.⁷

The objective of this study was to compare lactate dehydrogenase levels in women with hypertensive disorders of pregnancy and normal pregnant women, to correlate lactate dehydrogenase levels with complications of hypertensive disorders of pregnancy and role of lactate dehydrogenase as an early predictor of hypertensive disorders of pregnancy.

Aims and objectives of the study

To evaluate LDH levels at 12 to 16 weeks of gestation as predictor of hypertensive disorders of pregnancy. To correlate levels of LDH and severity of hypertensive disorders of pregnancy. To find the association between LDH levels and complications of hypertensive disorders of pregnancy.

METHODS

A prospective study was conducted in the department of obstetrics and gynecology at JJ group of hospitals, Mumbai, India for a duration of 18 months from January 2020 to June 2021. 500 antenatal patients who were registered in first trimester and were meeting the inclusion and exclusion criteria, were enrolled for the study after obtaining consent.

Pregnant women were screened and monitor properly for development of hypertensive disorders using criteria that hypertension is diagnosed empirically when appropriately taken blood pressure exceeds 140 mmHg systolic or 90 mmHg diastolic on two occasions taken 4-6 hours apart.

From each patient 2 ml of venous blood was collected with disposable sterile syringe and needle after all aseptic precautions at 12-16 weeks of gestation and at time of delivery. The blood was collected from the antecubital vein and delivered into a plain bulb. LDH level was measured using automated analyzer. Calibration of instrument was done as recommended by International Committee for Standardization in Hematology and biochemistry.

Inclusion criteria

Pregnant women from 12 to 16 weeks gestation. Pregnant women willing to take part in study.

Exclusion criteria

Pregnant women with chronic hypertension. Pregnant women with pre existing diabetes mellitus type 1 or 2, epilepsy, renal or liver disease. Pregnant women who develop gestational diabetes mellitus during the pregnancy. Patient not willing to participate in the study.

Target sample size was minimum 500 cases.

Study participants or their family members gave consent to be part of this study. Approval of ethical committee was taken. A detailed history was taken, vitals of patients were noted, clinical examination and relevant laboratory investigation were performed on admission. Information about complications was noted. Microsoft Office Excel software was used to analyse the data.

RESULTS

Incidence

According to our study, the incidence of hypertensive disorders of pregnancy in patients during 18 months duration from January 2020 to June 2021 at a tertiary care centre is 10.2% which included gestational hypertension, preeclampsia and eclampsia.

Table 1: Incidence of hypertensive disorders of pregnancy in study population.

Total number of patients	500
Number of cases of hypertensive disorders of pregnancy detected	51
Incidence of hypertensive disorders of pregnancy	10.2%

In our study, lactate dehydrogenase levels between 101-200 U/l were found in 31.37% of hypertensive group and 40.76% of normotensive group. Lactate dehydrogenase levels between 201-300 U/l were found in 56.86% of hypertensive group and 49.22% of normotensive group. Lactate dehydrogenase levels between 301-400 U/l were found in 13.73% of hypertensive and 9.13% of normotensive group. Lactate dehydrogenase levels more than 400 U/l were found in 0% of hypertensive group and 0.66% of normotensive group. The mean LDH level was 232 U/l in hypertensive group and 217 U/l in normotensive group. There was no association between LDH levels at 12-16 weeks of gestation and development of hypertensive (p value =0.292032).

Table 2: Lactate dehydrogenase at 12-16 weeks of gestation.

LDH (U/L)	No. of hypertensive patients	Percentage	No. of normotensive patients	Percentage	P value
101-200	16	31.37	183	40.76	The chi-square statistic is 2.4618. The p value is 0.292032. The result is not significant at p<0.05
201-300	29	56.86	221	49.22	
301-400	7	13.73	41	9.13	
>400	0	0	3	0.66	
Median	140-363		110-510		
Mean	232		217		

Table 3: Lactate dehydrogenase levels at time of delivery and severity of hypertensive disorders.

Group	Minimum value of lactate dehydrogenase (U/l)	Maximum value of Lactate dehydrogenase (U/l)	Mean value of lactate dehydrogenase(U/l)	Number of patients	P value
Gestational hypertension	280	450	387.5	4	The t-value is-2.18263. The p value is 0.016942. The result is significant at p<0.05.
Non severe preeclampsia	280	648	367	38	
Severe preeclampsia	480	1180	616	8	
Eclampsia	980	980	980	1	
Normotensive patients	120	420	280	449	

Table 4: Association of lactate dehydrogenase at the time of delivery and complications of hypertensive disorders.

Complication	Minimum value of lactate dehydrogenase (U/l)	Maximum value of lactate dehydrogenase (U/l)	Mean value of lactate dehydrogenase (U/l)	Number of patients
Abruption	580	1180	469.33	3
HELLP syndrome	1180	1180	1180	1
IUFD	320	680	500	2
Eclampsia	980	980	980	1
IUGR	320	980	491	5
Prematurity	340	842	546	5

Table 5: Association of lactate dehydrogenase levels (U/l) with ICU admission.

No. of patients	Minimum value of lactate dehydrogenase (U/l)	Maximum value of lactate dehydrogenase (U/l)	Mean value of lactate dehydrogenase (U/l)	Percentage
Admitted to ICU=5	480	1180	800.5	9.80
Patients not admitted to ICU=46	280	880	478.78	90.20

In our study, the mean of lactate dehydrogenase value at time of delivery was 387.5 U/l in case of gestational hypertension, 367 U/l in cases of mild preeclampsia, 616 U/l in cases of severe preeclampsia and 980 U/l in case of eclampsia. The mean lactate dehydrogenase value in normotensive at the time of delivery was 280. There was association between levels of lactate dehydrogenase at time of delivery and severity of hypertensive disorders in our study (p value =0.016942).

In our study, 9.80% of hypertensive patients were admitted to ICU for management. The lactate dehydrogenase levels

were higher in patients admitted to ICU with mean lactate dehydrogenase levels of 800.5 U/l as compared to patients not admitted to ICU with mean lactate dehydrogenase levels of 478.78 U/l in hypertensive group.

DISCUSSION

Out of 500 patients, 51 were detected to have hypertensive disorders of pregnancy. Incidence of hypertensive disorders of pregnancy was found to be 10.2% which included gestational hypertension, preeclampsia and eclampsia. About 10% of pregnancies globally are

complicated by hypertensive diseases.⁸ In a study by Sengodan et al, the prevalence of hypertensive disorders in pregnancy was 10.4%.⁹

Lactate dehydrogenase levels at 12-16 weeks of gestation and hypertensive disorders of pregnancy

In our study, lactate dehydrogenase levels between 101-200 U/l were found in 31.37% of hypertensive group and 40.76% of normotensive group at 12-16 weeks of gestation. Lactate dehydrogenase levels between 201-300 U/l were found in 56.86% of hypertensive group and 49.22% of normotensive group at 12-16 weeks of gestation. Lactate dehydrogenase levels between 301-400 U/l were found in 13.73% of hypertensive group and 9.13% of normotensive group at 12-16 weeks of gestation. Lactate dehydrogenase levels more than 400 U/l were found in 0% of hypertensive group and 0.66% of normotensive group at 12-16 weeks of gestation. The mean LDH level was 232 U/l in hypertensive group and 217 U/l in normotensive group at 12-16 weeks of gestation. There was no association between LDH levels at 12-16 weeks of gestation and development of hypertensive (p value =0.292032). Hence lactate dehydrogenase level at 12-16 weeks of gestation is not a predictor of hypertensive disorders of pregnancy as there are no significant results. There was no significant difference in lactate dehydrogenase levels at 12-16 weeks of gestation between hypertensive group and normotensive group. Hence lactate dehydrogenase levels at 12-16 weeks of gestation is not early predictor of pregnancy induced hypertension as there are no statistically significant results in our study and no such similar studies has been done.

In our study, the mean of lactate dehydrogenase value at time of delivery was 387.5 U/l in case of gestational hypertension, 367 U/l in cases of non-severe preeclampsia, 616 U/l in cases of severe preeclampsia and 980 U/l in case of eclampsia. The mean lactate dehydrogenase value in normotensive at the time of delivery was 280. There was association between levels of lactate dehydrogenase at time of delivery and severity of hypertensive disorders in our study (p value =0.016942). There was association of higher levels of lactate dehydrogenase with severity of disease. Higher levels of lactate dehydrogenase are associated with more severe form of hypertensive disorders of pregnancy.

In a study by Jaiswar et al, it was found that most of the patients in non-severe preeclampsia group had levels <600 IU/l and in cases of severe pre-eclampsia, 58.3% had LDH levels less than 600 IU/l, 13.9% had LDH levels between 600 and 800 IU/l and 27.7% had LDH levels above 800 IU/l.¹⁰ In eclampsia group, majority of patients i.e., 69.4% had levels 800 IU/l. In this study, it was clearly observed that there was significant rise in the LDH levels with increasing severity of the disease.¹⁰ Similar results are found in our study.

Qublan et al found in their study that the mean LDH levels in normal controls was 299±79 IU/l, in patients with non-severe preeclampsia was 348 ±76 IU/l and in patients with severe preeclampsia was 774±69.61 IU/l.¹¹ Thus they demonstrated a significant association of serum LDH levels with severe preeclampsia (p<0.001).¹¹ Similar results are found in our study.

In our study, in cases of hypertensive group with complications, higher level of lactate dehydrogenase was found. The mean value of lactate dehydrogenase in case of maternal complications like abruption was 469.33 U/l, HELLP syndrome was 1180 U/l and eclampsia was 980U/l. The mean value of lactate dehydrogenase in case of fetal complications like IUGR was 500 U/l, IUGR was 491 U/l and prematurity was 546 U/l .

In this study by Jaiswar et al with marked elevations of serum LDH levels (>800 IU/l), complications were observed in 22.2% of cases.¹⁰ There was statistically significant increase in maternal complications with increasing LDH levels (p<0.001).¹⁰ Another observation in this study by Jaiswar et al was that there is reduction in the average weight of babies with higher level of LDH (p=0.019).¹⁰ The occurrence of neonatal complications (p=0.003), stillbirths (<0.001) and perinatal deaths (p=0.003) were significantly higher in mothers who had increased serum levels of LDH.¹⁰ The association of low birth weight of infants with increase in serum LDH levels was suggested by He et al in their study.¹²

Increase in the incidence of perinatal deaths was observed by Qublan et al in patients with increasing levels of serum LDH levels (p<0.001).¹¹ Intrauterine fetal death was seen in 4.8% of cases, intrauterine growth restriction in 33.9% and prematurity in 77.9%.^{2,3,8} Similar results are found in our study.

Severely pre-eclamptic 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, in the study of Qublan et al.¹¹

Catanzerite et al reported a subgroup of patients who had elevated levels of LDH manifested with hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome and were at a high risk for developing maternal mortality.¹³ Demir et al concluded that there was a statistically significant relation between maternal complications and high LDH levels.¹⁴

In our study, 9.80% of hypertensive patients were admitted to ICU for management. The lactate dehydrogenase levels were higher in patients admitted to ICU with mean lactate dehydrogenase levels of 800.5 U/l as compared to patients with hypertensive disorders not admitted to ICU with mean lactate dehydrogenase levels of 478.78 U/l.

In our study we have found that there is significant association between levels of lactate dehydrogenase at time of delivery with severity of hypertensive disorder like gestational hypertension, preeclampsia and eclampsia. Higher serum LDH levels were associated with increased incidence of maternal and fetal complications like abruption placenta, HELLP syndrome, IUGR, IUFD, prematurity and oligohydramnios in our study. There was a significant increase in maternal morbidity with increasing serum LDH levels.

CONCLUSION

Lactate dehydrogenase levels at 12-16 weeks of gestation is not early predictor of pregnancy induced hypertension as there are no statistically significant results in our study. Lactate dehydrogenase levels have significant association with various maternal and fetal outcomes in patients of gestational hypertension, preeclampsia and eclampsia. Serum lactate dehydrogenase levels helps in prediction of severity of disease, adverse outcomes and complications of pregnancy induced hypertension. Hence lactate dehydrogenase acts as prognostic factor in pregnancy induced hypertension.

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