

Study of Relation of Lactate Dehydrogenase Levels with Severity of Preeclampsia and its foetal Outcome

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Abstract: *Background:* Pre eclampsia is a multisystem disorder characterized by vascular endothelial dysfunction. Elevated levels of LDH indicates cellular damage and can be used as a biochemical marker to reflect complications and fetal outcome. *Aim:* To analyse the severity of preeclampsia and evaluate the outcome of baby by raised LDH levels. *Material and methods:* 100 patients with high blood pressure after 28 weeks of gestational age were included. The diagnosis of severe pre-eclampsia was made when a diastolic blood pressure was measured ≥ 110 mmHg on two or more occasions, or ≥ 120 mmHg on one or more occasions, in the context of significant proteinuria (≥ 300 mg/24 hours, or persistent $\geq 1+$ on dipstick). Serum LDH level was done twice weekly. A baseline ultrasound was performed. Reversed end-diastolic flow was an indication for delivery. *Observation and results:* In severe preeclampsia group 40% patients had LDH levels >800 IU/L 50% of babies had low birth weight with maternal serum LDH levels <600 IU/L. 66% of babies had low birth weight with maternal serum LDH levels >600 IU/L. *Conclusion :* Raised LDH levels can predict the occurrence of maternal and neonatal complications.

Keywords: preeclampsia, LDH levels, maternal, neonatal complications

1. Introduction

Hypertensive disease in pregnancy is one of the main reasons of maternal, fetal and neonatal morbidity and mortality. As preeclampsia is a multisystem disorder with different clinical characteristics, prevention, diagnosis and therapy of this disease requires close inter-disciplinary cooperation [1] Preeclampsia affects about 5 to 10% of all pregnancies. [2] The etiology of preeclampsia is unknown but thought to be related to hypoxia in the placenta [3] Preeclampsia is defined as hypertension associated with proteinuria, greater than 0.3 g/l in a 24 hr urine collection or 1+ by qualitative urine examination, after 20 weeks of gestation [4] Mild preeclampsia is defined as diastolic blood pressure less than 110 mmHg. Severe preeclampsia is defined as systolic blood pressure of 160 mmHg or more and diastolic blood pressure of 110 mmHg or more. [5] Preeclampsia and eclampsia becomes apparent at the last stage in the pregnancy usually in third trimester. [6] Lactate dehydrogenase (LDH) is most often measured to evaluate the presence of tissue damage. Dysfunction of endothelial cells can contribute to inappropriate vasoconstriction and platelet aggregation which are early signs of atherosclerosis, hypertension and coronary vasospasm. Acute clinical symptoms that endanger the life of fetus in preeclampsia correlate with distinct activity of aspartate transaminase (AST) and lactate dehydrogenase (LDH). [7] LDH is useful biochemical marker that reflects the severity and occurrence of complications of preeclampsia. [8] The present study was to evaluate the co relation of LDH level with severity of preeclampsia and fetal outcome.

Aim

- To analyse the severity of preeclampsia by raised LDH levels
- To evaluate the outcome of fetus in case of preeclampsia with raised LDH levels.

Inclusion criteria

- Antenatal patients with high blood pressure (BP) recordings
- Patients with proteinuria >0.3 gm per 24 hrs.

Exclusion criteria

- Patients with urinary tract infection
- Chronic hypertensives.
- Eclamptic patients.
- Patients with diabetes or any other medical and surgical disorders
- Multiple gestations

2. Material and Methods

The present clinical study was conducted after obtaining approval from institutional ethical committee. The present study was undertaken to evaluate the severity of preeclampsia and outcome of baby by raised LDH levels. All women presenting after 28 weeks of gestation, with high BP and with proteinuria >0.3 gm per 24 hrs were hospitalized. The diagnosis of severe pre-eclampsia was made when a diastolic blood pressure was measured ≥ 110 mmHg on two or more occasions, or ≥ 120 mmHg on one or more occasions, in the context of significant proteinuria (≥ 300 mg/24 hours, or persistent $\geq 1+$ on dipstick). Gestational assessment was based on the best available evidence, using

ultrasound, symphysis – fundal height measurement and the menstrual history. On admission, patients were monitored as follows: Six-hourly cardiotocograph (CTG) recording of fetuses ≥ 28 weeks of gestation. Fetal distress was defined as baseline variability less than 5 over 60 minutes, repeated late decelerations or both. Blood pressure was recorded at six hourly intervals. This frequency was increased to half-hourly if a diastolic blood pressure of ≥ 110 mm Hg, until control of the blood pressure had been achieved. When urine dipstick testing was inconclusive, a 24-hour collection of urine was done. Serum LDH level was done twice weekly. A baseline ultrasound was performed, to assess fetal weight and amniotic fluid volume, and to exclude the presence of fetal abnormalities or maternal ascites. Umbilical artery doppler was added if intrauterine growth retardation (IUGR) was suspected. The ultrasound was repeated every second week, to assess the growth. Reversed end-diastolic flow was an indication for delivery.

3. Observations and Results

Table 1: Distribution of Study Population (n=100)

Group	Frequency	Percentage
Severe Preeclampsia	34	34%
Mild Preeclampsia	33	33%
With One High BP reading	33	33%
TOTAL	100	100%

The study group was categorized according to the severity of preeclampsia as shown in TABLE 1. 34% of cases had severe preeclampsia and 33% had mild preeclampsia or only one high BP reading.

Table 4

LDH		Intrauterine Fetal Demise	Intrauterine Growth Restriction	NICU Admission	NIL	Total
<600 IU/L	No. Percent	0 (0%)	0 (0%)	0 (0%)	30 (100%)	30 (40%)
>600 IU/L	No. Percent	14.6 (33.33%)	14.6 (33.33%)	14.6 (33.33%)	0 (0%)	44 (60%)
TOTAL	No. Percent	24.6 (33.33%)	24.6 (33.33%)	24.6 (33.33%)	30 (100%)	74 (100%)

Association between LDH Levels in Preeclampsia and Neonatal Complications (N=100)

Association between LDH levels in preeclampsia and neonatal complications (n=100) is depicted in Table 4. Babies having maternal LDH levels <600 IU/L are

Table 2: Distribution of Patients in Each Group According To LDH Levels

Group	LDH <600	LDH 600-800	LDH >800	TOTAL
Severe Preeclampsia	14 (40%)	6 (20%)	14 (40%)	34 (100%)
Mild Preeclampsia	26 (80%)	7 (20%)	0 (0%)	33 (100%)
With One High BP Recording	33 (100%)	0 (0%)	0 (0%)	33 (100%)
Total	73 (73%)	13 (13%)	14 (13%)	100 (100%)

As shown in TABLE 2, 40% patients of severe preeclampsia group had LDH levels >800 whereas 0% patients in other two groups had LDH levels > than 800

Table 3

LDH		Low Birth Weight	Normal Birth Weight	Total
<600 IU/L	No Percentage	15 (50%)	15 (50%)	30 (40%)
>600 IU/L	No Percentage	29 (66%)	15 (34%)	44 (60%)
TOTAL	No Percentage	44 (60%)	30 (40%)	74 (100%)

Association between LDH Levels In Preeclampsia and Baby Weight (n=100)

As shown in table no 3, 50% of babies had low birth weight with maternal serum LDH levels <600 IU/L. 66% of babies had low birth weight with maternal serum LDH levels > 600 IU/L

showing no neonatal complications and babies having maternal LDH levels > 600 IU/L are showing 33.33% of IUFD, IUGR and NICU admissions.

Table 5

GROUP		IUFD	IUGR	NICU	NIL	TOTAL
Severe Preeclampsia	No. Percent	1 (4%)	1 (4%)	2 (6%)	30 (86%)	34 (100%)
Mild Pre-Eclampsia	No. Percent	0 (0%)	0 (0%)	3 (8%)	30 (92%)	33 (100%)
With One High BP Recording	No. Percent	0 (0%)	0 (0%)	0 (0%)	33 (100%)	33 (100%)
Total	No. Percent	1 (1%)	1 (1%)	5 (5%)	93 (93%)	100 (100%)

Association between three Groups and Neonatal Complications

Association between three groups and neonatal complications is shown in Table 5.

In severe pre eclampsia group there are 4% IUFD, 4% IUGR, 6% NICU admissions. In mild pre eclampsia there were no IUD, IUGR, 85% of NICU admissions and in group with one high BP recording there were no neonatal complications.

Table 6

Group		LSCS	Vaginal	Total
Severe Pre-Eclampsia	No. Percent	8 (24%)	26 (76%)	34 (100%)
Mild Pre-Eclampsia	No. Percent	7 (22%)	26 (78%)	33 (100%)
With One High BP Recording	No. Percent	3 (10%)	30 (90%)	33 (100%)
Total	No. Percent	18 (19%)	82 (81%)	100 (100%)

Association between each Group and Mode of Delivery (N=100)

As shown in table 6, in severe pre eclampsia 24% have undergone LSCS and in mild pre eclampsia 22%, and in group with one high BP recording 10% have undergone LSCS.

Table 7: Association between LDH Level and Type of LSCS is Shown in Table 7

LDH Levels		Emergency LSCS	Elective LSCS	Total
<600	No. Percent	3 (20%)	10 (80%)	13 (33.3%)
>600	No. Percent	10 (40%)	16 (60%)	26 (66.6%)
Total	No. Percent	13 (33.33%)	26 (66.66%)	39 (100%)

In patients with LDH levels <600 20% have undergone emergency LSCS.

In patients with LDH levels >600 40% have undergone emergency LSCS.

Table 8

TYPE OF LSCS		IUFD	IUGR	NICU	NIL	TOTAL
Emergency LSCS	No. Percent	1 (2.5%)	1 (2.5%)	1 (2.5%)	10 (25.6%)	13 (33.33%)
Elective LSCS	No. Percent	0 (0%)	0 (0%)	2 (5.1%)	24 (61.4%)	26 (66.66%)
Total	No. Percent	1 (2.5%)	1 (2.5%)	3 (7.6%)	34 (87%)	39 (100%)

Association between type of LSCS and Neonatal Complications (N=39) is Shown in Table 8

As shown in table 8

After emergency LSCS there were 2.5% of IUD, IUGR AND NICU admissions. After elective LSCS there were no IUD, IUGR, but 5.1% of NICU admissions.

Table 9

		>34 Weeks	<34 Weeks	Total
Severe PE	No. Percent	30 (30%)	4 (4%)	34 (34%)
Mild PE	No. Percent	32 (32%)	1 (1%)	33 (33%)
With One High BP Recording	No. Percent	33 (33%)	0 (0%)	33 (33%)
Total		95 (95%)	5 (5%)	100 (100%)

Association between three Groups and Gestational Ages at Termination (n=100)

Association between three groups and gestational ages at termination (n=100) is shown in table 9. In severe pre eclampsia, 4% of pregnancies were terminated before 34 weeks, and 1% in mild pre eclampsia and none in group with one high BP recording.

Table 10

LDH Levels		<34 Weeks	>34 Weeks	Total
<600	No. Percent	0 (0%)	73 (73%)	73 (73%)
>600	No. Percent	5 (5%)	22 (22%)	27 (27%)
TOTAL	No. Percent	5 (5%)	95 (95%)	100 (100%)

Association between LDH Levels and Gestational Age of Termination (N=100)

As shown in Table 10, in patients with LDH levels <600, 73% of pregnancies were terminated after 34 weeks and with >600 only 22% were terminated after 34 weeks.

4. Discussion

Pre eclampsia is an important disease of pregnancy with potentially severe consequences for mother and child. Its progression differs among patients. Severe preeclampsia can lead to grave complications like convulsions, HELLP SYNDROME, DIC, intracranial bleed, IUFD and even

maternal mortality. Acute clinical symptoms that endanger the life of fetus in preeclampsia correlate with distinct activity of AST and LDH.

Comparing LDH levels

On analyzing the data in the study conducted by Y. Umasatyasri^[9] et al, it was observed that there is significant rise in the LDH levels with increasing severity of the disease ($P < 0.001$ – statistically significant). In another study done by Qublan HS^[8], et al. they found that the mean LDH levels in normal controls was 299 ± 79 IU/l, in patients with mild preeclampsia was 348 ± 76 IU/l and in patients with severe preeclampsia was 774 ± 69.61 IU/l. Thus, they demonstrated a significant association of serum LDH levels with severe preeclampsia. This outcome was in accordance with the present study.

Mode of delivery:

While studying the mode of delivery of the patients, no significance was found in the 3 groups studied. In the severe preeclampsia group 92% patients with LDH >600 IU/L had undergone LSCS. No comparative study was available to study the mode of delivery.

Baby Weight:

According to the study by Y. Umasatyasri^[9] et al, there was reduction in the average weight of babies with higher level of LDH but not statistically significant ($p = 0.926$). In the present study, 50% of babies had low birth weight with maternal serum LDH levels <600 IU/L where as 66% of babies had low birth weight with maternal serum LDH levels > 600 IU/L. This indicates increase in preterm deliveries in patients with higher LDH levels. The association of low birth weight of infants with increase in serum LDH levels was suggested by He S^[10], et al. in their study. This was in contrary to Qublan HS^[8], et al. who did not find any significant association.

According to Jaiswar SP^[11], et al study, there were significant low birth weight babies in women with higher LDH levels. ($P = 0.019$)

In our study it was found that 50% of women with severe preeclampsia had low birth weight babies. But there was no significant difference in the LDH levels of patients with small for gestational age infants. 60% of patients with LDH levels >600IU/L had low birth weight babies.

He S, Brennen K^[10] et al reported that pre eclamptic women with small for gestational age infants had higher LDH concentrations than those in the appropriate for gestational age group.

Neonatal complications

In the present study, neonatal complications like IUFD, IUGR, and NICU care were higher in the severe preeclampsia group. Qublan Hussein S^[8] et al reported that perinatal mortality were increased in patients with LDH>800IU/L compared with those who had lower levels. In the study by Y. Umasatyasri^[9] et al, there were 5 intrauterine deaths. In the women with LDH levels in the range of 600–800 IU/l (24 cases), 12 cases had uneventful 3 had early neonatal death. In this group no still births and there were 3 intrauterine deaths. In the third group where LDH levels were markedly elevated (i.e., >800 IU/l) there were 11 cases out of which only 6 had uneventful outcome, whereas 2 had neonatal complications and 1 was early neonatal death.

Association between three groups and gestational ages at termination

In the present study in patients with LDH levels <600, 73% of pregnancies were terminated after 34 weeks and with >600 only 22% were terminated after 34 weeks, whereas in the study of Y. Umasatyasri^[9] et al, the mean gestational age at the time of delivery was 37.60 ± 2.76 weeks in cases with LDH levels <600 IU/l. It was less in patients with LDH level in between 600 and 800 IU/l, which was 36.71 ± 2.96 weeks and 36.27 ± 2.69 weeks in patients with LDH >800 IU/l.

5. Conclusion

Raised LDH levels can predict the occurrence of maternal complications and therefore can be used as a laboratory based evidence of endothelial damage in preeclampsia. LDH can act as a single predictor or in conjunction with other predictors as a good parameter to detect the severity of preeclampsia and the occurrence of neonatal complications.

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