Original Article

Association of High Serum LDH Levels and Fetal Outcome in Pre Eclamptic Women

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Abstract

Objective: To determine the association of high serum LDH levels and fetal outcome in pre-eclamptic women.
Study Design: Prospective, cohort study.
Methodology: This study was carried out at Department of Obstetrics & Gynecology, Bahawal Victoria Hospital, Bahawalpur, starting from 1st January 2018 to 30th June 2018. A total of 266 pre-eclamptic patients, 18 to 35 years of age were included. Patients with chronic liver disease, multiple pregnancies, eclampsia, diabetes mellitus, renal disease, and heart disease were excluded. Group A (exposed) included the females with serum LDH levels ≥600 IU/L while Group B (unexposed) included the pregnant females with serum LDH levels <600 IU/L. All patients were followed until they were delivered and final fetal outcome i.e. alive birth and intrauterine death (yes/no) were noted.
Results: Mean age was 24.83 ± 2.68 years. Mean gestational age was 31.65 ± 3.43 weeks. The mean parity was 2.49 ± 0.86. In my study, live births and intrauterine deaths were seen in 67 (50.38%) and 22 (16.54%) preeclamptic women with serum LDH ≥600 IU/L (group A) compared to 93 (69.92%) and 08 (6.08%) preeclamptic women with serum LDH <600 IU/L (group B) which has shown p-value of 0.001 and relative risk of 0.72 which is significant and shows a positive association between higher serum LDH levels and adverse fetal outcome.
Conclusion: Higher serum LDH levels are associated with adverse fetal outcome in women with pre-eclampsia.
Key Words: Preeclampsia, lactate dehydrogenase, intrauterine death.

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Introduction

Preeclampsia is considered as one of the most common medical disorder of pregnancy. It is characterized by raised blood pressure, protein in urine and/or edema, usually appears after 20 weeks of pregnancy.[1] It results in increase rate of maternal and perinatal morbidity and mortality worldwide, but especially affecting developing countries. In India, about 7-10% of all antenatal patients are affected by preeclampsia according to hospital record.[2] Regarding etiology of preeclampsia, defective placentation and endothelial dysfunction are considered important features, although the exact mechanism causing preeclampsia is not known.[3] It is a disease that involves various organs in the body including kidneys, liver, brain, clotting system but placenta is primarily involved.[4] Since preeclampsia is

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a disease with multisystem organ dysfunction' it results in a variety of clinical symptoms, and there are various methods for prevention, diagnosis and treatment and this requires multidisciplinary approach.[5] In early pregnancy, more fat is accumulated in the body due to lipogenesis. While increased breakdown of fat depots occurs in late pregnancy and play an essential role in development of fetus. So, dyslipidemias occurring in early pregnancy, in turn, increase the risk of preeclampsia. The exact pathophysiology of this disease is still unknown although there are many studies which have been carried out to know the pathophysiological mechanisms behind the disease.[3]

There is increasing evidence that endothelial dysfunctions play a major role in etiology of preeclampsia. Serum lactate dehydrogenase (LDH) and serum gamma glutamyl transferase (GGT) are most often measured for evaluation of tissue damage that occurs due to endothelial injury.[6] Generalized vasoconstriction and aggregation of platelets occur due to endothelial damage and these are early signs of raised blood pressure .Lactate Dehydrogenase (LDH) is an enzyme which is produced mainly inside the cell and is involved in interconversion of pyruvate and lactate inside the cells. Its levels are several times higher inside the cells as compared to plasma.[7] Serum LDH is deranged in affected person, therefore the total serum LDH is highly sensitive but it is not specific test. LDH isoenzymes can be measured to improve diagnostic accuracy. This can be further used as guide in decision making, and in managing patients resulting in improved maternal and fetal outcome.[7-9] In a study, live births and intrauterine deaths were seen in 56.52% and 4.3% preeclamptic women with serum LDH <600 IU/L compared to 51.43% and 14.29% preeclamptic women with serum LDH ≥600 IU/L.[9] As pre-eclampsia is a severely dangerous form of hypertensive disorder in pregnancy that is associated with significant maternal and fetal risks, so, its precise diagnostic and therapeutic guidelines are required. As there was no local study available which indicates the association between serum LDH levels and fetal outcome, so this study was carried out to know how high serum LDH levels affect fetal outcome.

Methodology

This study was carried out at the Department of Obstetrics & Gynecology, Bahawal Victoria Hospital, Bahawalpur, from 1st January 2018 to 30th June 2018. A total of 266 pre-eclamptic patients, 18 to 35 years of age were included. Patients with chronic liver disease, multiple pregnancies, eclampsia, diabetes mellitus, renal disease and heart disease were excluded. Group A (exposed) included the females with serum LDH levels ≥600 IU/L while Group B (unexposed) included the pregnant females with serum LDH levels <600 IU/L. All the patients were followed until they were delivered and final fetal outcome i.e. alive birth and intrauterine death (yes/no) were noted. Statistical analysis was carried out using SPSS version 20.0,

Results

18 to 35 years of patients were included in the study with average age of 24.83 ± 2.68 years. The average age of women in group A was 25.26 ± 2.96 years and in group B was 24.56 ± 2.31 years. Most of the patients 139 (52.26%) were between 18 to 25 years of age as shown in Table I.

Table I: Age distribution for both groups (n=266)

Age (years)	Group A (n=133)	Group B (n=133)	Total (n=266)
	Patients (%)	Patients (%)	Patients (%)
18-25	56 (42.11%)	83 (62.41%)	139 (52.26%)
26-35	77 (57.89%)	50 (37.59%)	127 (47.74%)
Mean ± SD	**25.26 ± 2.96**	**24.56 ± 2.31**	**24.83 ± 2.68**

Average gestational age was 31.65 ± 3.43 weeks. The mean gestational age in group A was 32.53 ± 3.47 weeks and in group B was 30.85 ± 3.40 weeks. Most of the patients 239 (89.85%) were between 29-36 weeks of gestational age as shown in Table II. The mean parity was 2.49 ± 0.86 (Table III). Mean parity in group A was 2.57 ± 0.65 and in group B was 2.51 ± 0.77. Mean height was 1.32 ± 0.51 meter and the mean weight was 71.09 ± 8.28 kg. The mean BMI in group A was 32.57 ± 3.65 kg/m2 and in group

Table II: Distribution of patients according to Gestational age in both groups.			
Gestational Age (weeks)	**Group A (n=133)**	**Group B (n=133)**	**Total (n=266)**
	Patients (%)	**Patients (%)**	**Patients (%)**
29-36 weeks	115 (86.47%)	124 (93.23%)	239 (89.85)
>36 weeks	18 (13.53%)	09 (6.77%)	27(10.15)
Mean ± SD	**32.53 ± 3.47**	**30.85 ± 3.40**	**31.65 ± 3.43**

Table III: Parity for both groups (n=266)			
Parity	**Group A (n=133)**	**Group B (n=133)**	**Total (n=266)**
	Patients (%)	**Patients (%)**	**Patients (%)**
0-2	66 (49.62)	61 (45.86%)	127 (47.74%)
3-4	67 (50.38)	72 (54.14%)	139 (52.26%)
Mean ± SD	**2.49 ± 0.86**	**2.57 ± 0.65**	**2.51 ± 0.77**

Table IV: BMI for both groups (n=266)			
BMI (kg/m2)	Group A (n=133)	Group B (n=133)	Total (n=266)
	Patients (%)	**Patients (%)**	**Patients (%)**
≤30	51 (38.35%)	53 (39.85%)	104 (39.10%)
>30	82 (61.65%)	80 (60.15%)	162 (60.90%)
Mean ± SD	**32.49 ± 3.86**	**32.57 ± 3.65**	**32.51 ± 3.77**

Table-V: Percentage of patients according to h/o previous pre-eclampsia for both groups (n=266)			
h/o previous pre-eclampsia	**Group A (n=133)**	**Group B (n=133)**	**Total (n=266)**
Yes	56 (42.11%)	61 (45.86%)	117 (43.98%)
No	77 (57.89%)	72 (54.14%)	149 (56.02%)

B was 32.57 ± 3.65 kg/m2 as shown in Table IV. Distribution of patients according to h/o previous pre-eclampsia is shown in Table V. In my study, live births and intrauterine deaths were seen in 67 (50.38%) and 22 (16.54%) preeclamptic women with serum LDH ≥600 IU/L (group A) compared to 93 (69.92%) and 08 (6.08%) preeclamptic women with serum LDH <600 IU/L (group B) as shown in Table VI which has shown p-value of 0.001 and relative risk of 0.72 which is significant and shows a positive association between higher serum LDH levels and adverse fetal outcome.

Table VI: Comparison of Fetal outcome between both Groups.					
		Group A (n=133)	**Group B (n=133)**	**P-value**	**RR**
		Patients (%)	Patients (%)		
Alive birth	Yes	67 (50.38%)	93(69.92%)	**0.001**	**0.72**
	No	66 (49.62%)	40 (30.09%)		
Intrauterine Death	Yes	22 (16.54%)	08 (6.02%)	**0.007**	**0.89**
	No	111 (83.46%)	125 (93.98%)		

Discussion

According to American College of Obstetrician and Gynaecologists, pre-eclampsia is defined as hypertension greater than 140/90mm hg 4 hours apart associated with proteinuria more than 0.3 gm/dL in a 24 hours urine collection or more than 1 gm/l or +1 on urine dipstick examination.[10] Eclampsia is defined as onset of new-onset grand mal seizures in a woman suffering from preeclampsia. Serum LDH is an enzyme produced mainly inside the cell. It causes interconversion of Pyruvate and Lactate inside the cell.[11] In pre-eclampsia & eclampsia massive intracellular death occurs, so it's a very good marker to detect disease severity. So, this study has been carried out to know the effect of raised serum LDH levels on fetal outcome in pre-eclamptic women.

In a study, live births and intrauterine deaths were seen in 56.52% and 4.3% preeclamptic women with serum LDH <600 IU/L compared to 51.43% and 14.29% preeclamptic women with serum LDH ≥600 IU/L.

Qublan et al[12] showed an increase in perinatal death in patients with increasing levels of serum LDH levels (P < 0.001). 4.8% of cases having Intrauterine fetal death, 33.9% of cases having intrauterine growth restriction and in 77.9% cases, prematurity was reported. In 95.2% of cases with severe preeclampsia group, neonatal death was observed.

In another study, perinatal death was seen in 77.7% of women with LDH more than 800 IU/L as compared to 20.6% with LDH 600-800 IU/L and 6.25% in women with LDH <600 IU/L which is statistically very significant (p<0.001). Raised level of LDH was associated with reduction in the average weight of babies although not statistically significant.[13]

Jaiswar SP, et al[14] concluded in a study a significant increase in neonatal complications (P = 0.003), stillbirths (P < 0.001) and perinatal deaths (P = 0.003). Their study showed that LDH levels were much higher in women with preeclampsia and eclampsia and raised LDH levels had significant association with the progression of the disease which results in poor maternal and perinatal outcome. Bera S et al showed LDH is a good parameter to predict severity of PIH and bad fetal outcome.[5]

In another study, total of 110 cases were studied during the study period, 40 were normal pregnant women and remaining 70 were PIH cases. Out of the 70 PIH cases, 15 (21.5%) were mild preeclampsia, 35 (50.0%) were severe preeclampsia and 20 (28.5%) were eclampsia. Maternal mortality occurred in 06 cases (8.5%). Perinatal mortality was seen in 28 (40.0%), Out of these, 20 (71.4%) were stillbirth and 08 (28.6%) were neonatal deaths. Raised level of LDH was seen in more severe disease (172.37±28.09) normotensive, (356.33±24.47) mild preeclampsia, (609.91±136.92) severe preeclampsia and (854.05±247.45), eclampsia (P<0.0001). Perinatal deaths occurred in 28 cases, out of these 06 (21.5%) had LDH levels less than 600 IU/l, 8 (28.5%) had LDH levels between 600-800 IU/l and 14 (50%) were with LDH levels >800 IU/l.7

Another study concluded that high levels of LDH was associated with reduced birth rate and poor apgar score. Also this was concluded in a study that gestational age decreases with raised LDH levels which was mainly due to induction of labour at an earlier gestational age in patients with raised LDH levels.[8] In this study, neonates had IUGR in antenatal period with LDH level between 600 to 800 IU while 2.8% had Doppler changes, 2.8% was affected by septicemia and 11.4% had IUD. Thus, raised LDH level is associated with increase in perinatal complication including perinatal death. Gupta JSP[15] also concluded that average gestational age was significantly reduced in patients with high LDH levels. Malerewicz et al, also concluded that acute clinical symptoms that are fatal for fetal life in Preeclampsia are associated with the activity of LDH.[16]

It is found that LDH-A isoenzyme is immunolocalized primarily in the fetal endothelial cells while LDH-B isoenzyme is predominantly present in syncytiotrophoblasts. As compared with normal pregnancy, preeclamptic patients have 1.6 fold increased level of LDH-A activity.[17] This may also be concluded that endothelial dysfunction at uteroplacental vessels can result in hypoperfusion of growing fetus & may result in raised LDH isoform.[18]

Conclusion

This study concluded that raised serum LDH levels are associated with poor fetal outcome in women with pre-eclampsia. So, we suggest that LDH levels should be measured in every woman with pre-eclampsia so that perinatal morbidity and mortality can be reduced.

References

1. Gandhi M, Chavda R, Sain HB. Comparative study of serum LDH and uric acid in hypertensive versus normotensive pregnant woman. Int J Biomed Res. 2015;6(01):25-28.
2. Sarkar PD, Sogani S. Evaluation of serum lactate dehydrogenase and gamma glutamyl transferase in preeclamptic pregnancy and its comparison with normal pregnancy in third trimester. Int J Res Med Sci. 2013;1:365-368.
3. Munde SM, Hazari NR, Thorat AP, Gaikwad SB, Hatolkar VS. Gamma glutamyl transferase and lactate dehydrogenase as biochemical markers of severity of preeclampsia. Int J Med Health Biomed Bioeng Pharma Eng. 2014;8(1):50-53.
4. Lolo Mission JF, Caughey L. Hypertensive disease of pregnancy and maternal mortality. Current Operation Obst Gynae. 2013;25(2):124-132.
5. Bera S, Gupta S, Saha S, Kunti S, Soumi Biswas S, Ghosh D. Study of liver enzymes especially lactate dehydrogenase to predict foetal outcome in pregnancy induced hypertension. Sch J App Med Sci. 2014;2(5A):1569-1572.
6. Purnima DS, Jonal S. Evaluation of serum LDH and gamma glutamyl transferace in preeclamptic pregnancy in 3rd. trimester. Int J Res Med Sci. 2013;1(4):365-368.
7. Andrews L, Patel N. Correlation of serum lactate dehydrogenase and pregnancy induced hypertension with its adverse outcomes. Int J Res Med Sci. 2016;4:1347-1350.
8. Hak J, Nisa N, Gupta S. LDH levels in pregnancy and its association with severity of the disease and feto-maternal

outcome in pre-eclampsia and eclampsia. JK Sci. 2015;17(3):110-113.
9. Umasatyasri Y, Vani I, Shamita P. Role of LDH (Lactate dehydrogenase) in preeclampsia – eclampsia as a prognostic marker: an observational study. Int Archive Integ Med. 2015;2(9):88-93.
10. American College of Obstetrician and Gynaecologists. Women's Health Care Physicians. Hypertension in Pregnancy. Chapter -2, Establishing the Diagnosis of Preeclampsia and Eclampsia. 2013; 19.
11. Clinical enzymology and biomarkers. In: Vasudevan D, Sree kumari S, Vaidyanathan K; Textbook of biochemistry, 6th edn. Jaypee Brothers, New Delhi 2011; 146-159.
12. Qublan HS, Amarun V, Bateinen O. LDH as biochemical marker of adverse pregnancy outcome in severe preeclampsia. Med Sci Monit. 2005;11:393–397.
13. Vinitha PM, Chellatamizh M, Padmanaban S. Role of serum LDH in preeclampsia as a prognostic factor – a cross sectional case control study in tertiary care hospital. Int J Reprod Contracept Obstet Gynecol 2017;6:595-598.
14. Jaiswar SP, Amrit G, Rekha S, Natu SN, Mohan S. Lactic Dehydrogenase: A biochemical marker for preeclampsia-eclampsia. JOGI. 2011;61(6): 645-648.
15. Gupta JSP, Sachan A, Nates R, SN Shali SN, Mohan. J Obst Gynaecol India. 2011; 61(6): 645-648.
16. Malerwicz A, Gruszka O, Raquala J. The usefulness of routine laboratory tests in evaluationn of sudden threat of pregnant women and fetus in pre-eclampsia. Ginekol POL 2006;77(4): 276-284.
17. Herrera E, Gomez DC, Lasuncion MA. Lipid metabolism in pregnancy. Biol Neonate. 1987; 52(2):70-77.
18. Tsoi S, Zheng J, Xu F, Kay H. Differential expression of lactate dehydrogenase isozymes (LDH) in human placenta with high expression of LDH-A(4) isozyme in the endothelial cells of pre-eclampsia villi. Placenta. 2001; 22(4): 317-322.