



STATUS OF LACTATE DEHYDROGENASE LEVELS IN PATIENTS WITH PREGNANCY INDUCED HYPERTENSION: A PROSPECTIVE OBSERVATIONAL STUDY

Obstetrics & Gynaecology

Asima Hassan*

PG Student, Department of OB&G, GMC Srinagar, Jammu and Kashmir, India
*Corresponding Author

Syed Masuma Rizvi

Professor Department of OB&G, GMC Srinagar, Jammu and Kashmir, India

Rahiq ul Makhtoom

Resident, Department of OB&G, GMC Srinagar, Jammu and Kashmir, India

ABSTRACT

Background: Obstetricians continue to face a therapeutic challenge when treating pregnancy-specific conditions like pregnancy-induced hypertension (PIH), a multi-system disease. Preeclampsia is a multisystem condition that complicates 5-8% of pregnancies. The present study has been aimed to find out the possible association of PIH and its complications with serum LDH levels. **Methods:** This observational prospective study was carried out with effect from October 2021 to October 2022 on 200 antenatal women who attended our department of obstetrics and gynecology at Lalla ded hospital, Srinagar. Lactate dehydrogenase (LDH) levels assessed in 200 antenatal women with PIH, who were classified into groups according to the severity of their gestational hypertension. **Results:** We observed that patients with mild, moderate and severe gestational hypertension or mild preeclampsia had normal LDH levels than in patients with severe preeclampsia with end organ changes and eclampsia. Out of 20 patients with severe preeclampsia, 70% patients had >800 serum LDH levels and 30% had 600-800 serum LDH levels and out of 4 patients with eclampsia; 87.5% had >800 serum LDH levels and 12.5% had 600-800 serum LDH levels. The assessment of various complications according to serum LDH levels among PIH patients revealed that, hypertensive retinopathy, HELLP syndrome, abruption placentae were significantly associated with LDH levels. **Conclusion:** The present study demonstrated Higher LDH levels were seen in severe preeclampsia and eclampsia patients. The development of HELLP syndrome was significantly associated with higher LDH levels. Vigilant monitoring and timely intervention may reduce maternal and perinatal complications.

KEYWORDS

Lactate dehydrogenase, preeclampsia, pregnancy.

INTRODUCTION

Obstetricians continue to face a therapeutic challenge when treating pregnancy-specific conditions like pregnancy-induced hypertension (PIH), a multi-system disease. Preeclampsia is a multisystem condition that complicates 5-8% of pregnancies.¹ In India the incidences is reported to be 8-10% of pregnancies. Its pathogenesis is poorly understood, and it is currently regarded as a disease of theories.² More and more data point to the importance of endothelial cells and altered endothelial cell activity in the pathophysiology of preeclampsia. More than 4 million women across the world develop this disorder every year & an estimated 5000 to 76000 women die of this condition every year. It is the leading cause of maternal ICU admissions & cause 15-20% maternal death world-wide.³ It is defined as systolic BP ≥ 140 mmHg & diastolic BP ≥ 90 mmHg. PIH is a major cause of maternal, fetal & newborn morbidity & mortality, refers to one of the following conditions.

- Pre-existing hypertension
- Gestational hypertension & preeclampsia
- Pre-existing hypertension plus superimposed gestational hypertension with proteinuria and
- Unclassified hypertension

PIH is generally understood to be immunological and inflammatory condition that involves the process of placentation. It is thought to arise from problems with the process of placentation where by trophoblast cells fail to fully activate transformation of uterine spiral arteries at about 12 to 16 weeks gestation, resulting in placental ischemia. This relative ischemia and lowered placental perfusion could cause the release of damaging factors (e.g., oxidized lipids, cellular debris, antiangiogenic factors) into maternal blood stream resulting in inflammation and oxidative stress. LDH is a marker seen in blood during hypoxia & oxidative stress. It is a useful marker that reflects the severity of PIH. Test is easily available so screening of all cases of PIH with LDH level must be done. LDH is an intracellular enzyme that breaks down lactate. The placenta's main source of energy is glycolysis. Preeclampsia's hypoxia promotes glycolysis even more while raising LDH activity. Studies have indicated that compared to healthy pregnancy, preeclampsia placentas have greater levels of LDH activity and gene expression.^{4,5} Increased lactate generation is caused by trophoblasts' increased LDH isoenzyme activity in response to hypoxia. A crucial component of embryonic stem cells, basic fibroblast growth factor, is known to be indirectly induced and upregulated by

LDH levels.^{6,7} The present study has been aimed to find out the possible association of PIH and its severity with serum LDH levels.

METHODS

This observational prospective study was carried out on 200 antenatal women who attended our department of obstetrics and gynecology at LDH, Srinagar. Lactate dehydrogenase (LDH) levels assessed in 200 individuals with PIH, who were classified into groups according to the severity of their gestational hypertension: mild, moderate, severe gestational hypertension, mild preeclampsia, severe preeclampsia with end organ changes, and eclampsia. Proper recommendation was obtained from institutional ethical committee. The patients booked before 20wks and have crossed 20 weeks with systolic BP ≥ 140 mmHg and diastolic BP ≥ 90 were included in the study group. The patient's hypertensive before 20 weeks of pregnancy and patients having urinary tract infections, chronic infections like cardiac, renal, liver, thyroid disease etc with major obstetric complications like APH, Twin, polyhydramnios were excluded in the study.

All individuals underwent a comprehensive and in- depth clinical assessment. Regular prenatal examinations were performed on all women. The enzymatic technique was used on the autoanalyzer to assess serum LDH levels.

Methods of estimation of serum LDH

The estimation of serum LDH was done with modified IFCC method (IFCC Method 1994) devised by Wacker et al., 1980 and Van der Linde 1982. It is based on the reduction of pyruvate to lactate in the presence of NADH by the action of lactate dehydrogenase. The rate of oxidation of NADH to NAD is measured as a decrease in absorbance which is proportional to LDH activity in the sample.

Normal Serum LDH levels in pregnancy

Non-pregnant: 115-221 IU/L, first trimester: 78-433 IU/L, 2nd trimester: 80-447 IU/L 3rd trimester: 82-524 IU/L

Statistical Methods:

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean $\pm$ SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by

bar and pie diagrams. Chi-square test was employed for determining relationship between levels of serum LDH and severity of PIH. A P-value of less than 0.05 was considered statistically significant.

RESULTS

In this study, the results of the study will be described

Table 1: Age distribution of study patients

Age (Years)	Number	Percentage
25-30	117	58.5
31-35	56	28.0
> 35	27	13.5
Total	200	100

Mean±SD=29.5±6.23 (25-39 Years)

Table 1, reflects the age distribution of PIH patients, wherein we found that the average age of studied patients was (29.5±6.23) years with majority of patients (58.5%) belonging to the age interval of (25-30) years.

Table 2: Showing parity of study patients

Parity	Number	Percentage
Nulliparous	130	65.0
Para 1	45	22.5
Para 2	20	10.0
Para 3	5	2.5
Total	200	100

We observe that majority of PIH patients were nulliparous accounting for 65%, followed by (22.5%) patients with para 1, (10%) patients with para 2, and (2.5%) patients with para 3.

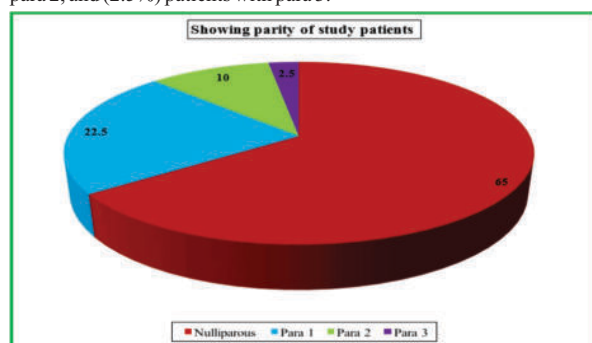


Table 3: Severity of PIH in study patients

Severity of PIH	Number	Percentage
Mild gestational hypertension	21	10.5
Moderate gestational hypertension	59	29.5
Severe gestational hypertension	51	25.5
Mild preeclampsia	41	20.5
Severe preeclampsia	20	10.0
Eclampsia	8	4.0
Total	200	100

Table 3, displays the severity of PIH patients in studied patients wherein we found that 29.5% patients had moderate gestational hypertension, followed by 25.5% patients with severe gestational hypertension, 20.5% patients with mild preeclampsia, 10.5% with mild gestational hypertension, 10% with severe preeclampsia and 4% patients with eclampsia.

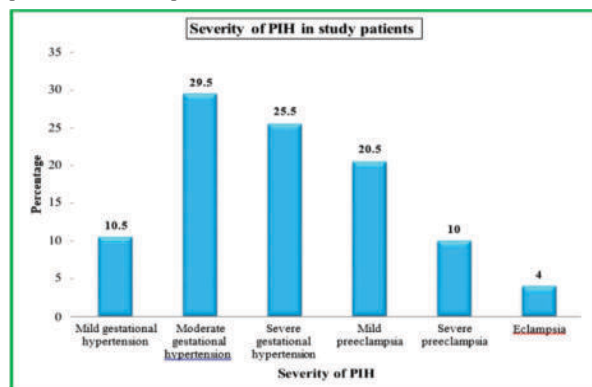


Table 4: Gestational age at diagnosis of hypertension

Gestational age (Weeks)	Number	Percentage
< 28	5	2.5
28-32	24	12.0
33-37	141	70.5
≥ 38	30	15.0
Total	200	100

we observe that gestational age at the diagnosis of hypertension among studied patients in most of the cases was (33-37) weeks, accounting for 70.5% followed by 15% patients who were diagnosed for hypertension at ≥ 38 weeks of gestation, 12% patients were diagnosed at 28-32 weeks of gestation and 2.5% patients at <28 weeks of gestational age.

Table 5: Relationship between levels of serum LDH and severity of PIH

Severity of PIH	Serum LDH Levels			Total
	< 600	600-800	> 800	
Mild gestational hypertension	21 (100%)	0 (0%)	0 (0%)	21
Moderate gestational hypertension	59 (100%)	0 (0%)	0 (0%)	59
Severe gestational hypertension	51 (100%)	0 (0%)	0 (0%)	51
Mild preeclampsia	41 (100%)	0 (0%)	0 (0%)	41
Severe preeclampsia	0 (0%)	7 (30%)	13 (70%)	20
Eclampsia	0 (0%)	1 (12.5%)	7 (87.5%)	8
Total	172	8	20	200

Chi-square=199.26; P-value<0.001 (Statistically Significant)

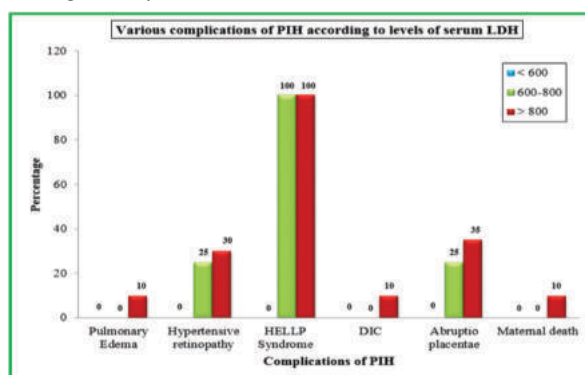
Table 5, show the relationship between serum LDH levels and severity of PIH. We observed that patients with mild, moderate, severe gestational hypertension and mild preeclampsia had normal LDH levels. However; out of 20 patients with severe preeclampsia, 70% patients had >800 serum LDH levels and 30% had 600-800 serum LDH levels and out of 8 patients with eclampsia; 87.5% had >800 serum LDH levels and 12.5% had 600-800 serum LDH levels. Evidently, association between serum LDH levels and severity of PIH was highly significant.

Table 6: Various complications of PIH according to levels of serum LDH

Complications	< 600	600-800	> 800	P-value
Pulmonary Edema	0 (0%)	0 (0%)	2 (10%)	0.152
Hypertensive retinopathy	0 (0%)	2 (25%)	6 (30%)	<0.001*
HELLP Syndrome	0 (0%)	8 (100%)	20 (100%)	<0.001*

*Statistically Significant Difference (P-value<0.05)

The assessment of various complications according to serum LDH levels among PIH patients was made, wherein we found that, hypertensive retinopathy, HELLP syndrome, abruption placentae were significantly associated with LDH levels.



DISCUSSION

In the present study, we have comprehensively analyzed patient's data on the basis of demographic parameters, history and clinical aspects. The average age of studied patients was (29.5±6.23) years; with majority of patients (58.5%) belonging to the age interval of (25-30) years. In a study by Saxena S et al, and Parmar M et al majority of PIH patients were belonging to the age group of 21-25 years, which is slightly smaller than what we observed in the present study.^{8,9} The reason might be attributed to the delaying marital age trend in our region. In the present study, nulliparous patients made up the majority

of PIH patients (65%), followed by (22.5%) patients with first parity. Likewise to this; in a retrospective study carried out in southeast Nigeria by Umegbolu EI et al., nulliparous women had a greater incidence of PIH.¹⁰ The incidence of PIH was also reported higher in the nulliparous population, according to Sibai and Cunningham's global survey.¹¹ After 20 weeks of pregnancy, a woman with a history of normal blood pressure is considered to have gestational hypertension if her systolic blood pressure is 140 mm Hg or higher, her diastolic blood pressure is 90 mm Hg or higher, or both, on two separate occasions that are at least 4 hours apart.¹² Severe gestational hypertension is defined as a systolic BP of 160 mm Hg and/or more, a diastolic BP of 110 mm Hg and /or more. Preeclampsia is a multisystem progressive disorder characterized by the new onset of hypertension and proteinuria or the new onset of hypertension and significant end organ changes with or without proteinuria after 20 weeks of gestation or postpartum in a previously normotensive patient. Eclampsia is defined as onset of general tonic clonic seizures in a woman with preeclampsia that cannot be attributed to other causes.

We evaluated the severity of PIH in the studied participants and observed that 29.5% had moderate gestational hypertension, followed by 25.5% with severe gestational hypertension, 20.5% with mild preeclampsia, 10% with mild gestational hypertension, 10% who had severe preeclampsia, and 4% who had eclampsia. The incidence of PIH increases with increasing gestational age and is irregularly distributed throughout late pregnancy. A majority of instances of prenatal hypertension and almost half of PIH cases happen at term (37 weeks' gestation). Contemporary to this; we also observed that the diagnosis of hypertension among studied patients in most of the cases (70.5%) was made between (33- 37) weeks of gestation, followed by 15% patients who were diagnosed for hypertension at ≥ 38 weeks of gestation, 12% patients were diagnosed at 28-32 weeks of gestation. Likewise to this, Sajitha et al in their study reported that the average gestational age at presentation was 32.7 weeks, which is comparable to our study.¹³ Severe preeclampsia is frequently linked to early-onset PIH.¹⁴ Preeclampsia typically develops after the 20th week of pregnancy in the vast majority of patients; however, recently a case from Japan was reported with typical preeclampsia symptoms developing after the 19th week of pregnancy.¹⁵ It was determined that there is a substantial correlation between the severity of PIH and serum LDH levels. Patients with mild, moderate, severe gestational hypertension and mild preeclampsia were found to have normal LDH levels. Out of 20 patients with severe preeclampsia, 70% patients had >800 serum LDH levels and 30% had 600-800 serum LDH levels and out of 8 patients with eclampsia; 87.5% had >800 serum LDH levels and 12.5% had 600-800 serum LDH levels. Evidently, association between serum LDH levels and severity of PIH was highly significant. Consistent to this, Qublan et al and Kharb S et al also reported a significant association of LDH levels with severe preeclampsia.^{16,17} Studies by Jaiswar et al, Hazari et al, and Gandhi et al. also reported similar association.^{18,20} Qublan et al demonstrated in their study the mean LDH levels were 299 IU/l in controls, 348 IU/l in patients with moderate preeclampsia cases, and 774 IU/l in patients with severe preeclampsia, which infers that there is a significant rise in the LDH levels in preeclampsia patients as compared to control group.¹⁶ In their study, Gupta et al found that LDH levels below 600 IU/l were found in 66% of patients with mild preeclampsia and 36.73% of patients with severe preeclampsia, while LDH levels above 800 IU/l were found in 9.8% of mild preeclampsia patients and 30.61% of severe preeclampsia patients.²¹ Severe preeclampsia was shown to have considerably greater LDH levels than moderate preeclampsia. These results are comparable with our study; however, unlike to our study they did not reported any case of eclampsia higher serum LDH levels.

In the present study, the assessment of various complications according to serum LDH levels among PIH patients was made, wherein we found that, hypertensive retinopathy, HELLP syndrome, abruptio placentae were significantly associated with LDH levels. Two patients (20%) with serum LDH levels above 800 experienced maternal death. Two patients (20%) showed signs of pulmonary edema, while two (10%) of the patients with serum LDH levels above 800 showed signs of DIC complications. Around (35%) individuals with LDH levels above 800 and one (25%) patient with LDH levels between 600 and 800 had an abruptio placenta. About (25%) of the patients with serum LDH between 600 and 800 and (30%) of the patients with LDH above 800 were found to have hypertensive retinopathy. In other likewise studies by Kharb S et al, Gupta et al and Demir et al the authors also reported a significant association of the

development of hypersensitive retinopathy, HELLP syndrome and abruptio placentae with exceeded serum LDH levels.^{17,21,22}

CONCLUSION

The present study demonstrated patients with severe preeclampsia with end organ changes and eclampsia were found to have considerably higher lactate dehydrogenase levels. The development of HELLP syndrome was significantly associated with higher LDH levels. Vigilant monitoring and timely intervention may reduce maternal and perinatal complications.

Declaration by Authors

Ethical Approval: Approved

Acknowledgement: None

Source of Funding: None

Conflict of Interest:

The authors declare no conflict of interest.

REFERENCES:

- Lain KY, Roberts JM. Contemporary concepts of the pathogenesis and management of preeclampsia. *Jama*. 2002;287(24):3183-6.
- Jan AK, Jamil M. Management of Pre-Eclampsia and Eclampsia. *JPMI* 2000;14(1):7-19.
- Das R, Biswas S. Eclampsia: The Major Cause of Maternal Mortality in Eastern India. *Ethiop J Health Sci*. 2015 Apr;25(2):111-6. doi: 10.4314/ejhs.v25i2.2. PMID: 26124617; PMCID: PMC4478261.
- Tsoi SC, Zheng J, Xu F, Kay HH. 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;22:317-22.
- Burd LI, Jones MD Jr, Simmons MA, Makowski EL, Meschia G, Battaglia FC, et al. Placental production and foetal utilisation of lactate and pyruvate. *Nature* 1975;254:710-1.
- Semenza GL. Targeting HIF-1 for cancer therapy. *Nat Rev Cancer* 2003;3:721-32.
- Pepper MS, Belin D, Montesano R, Orci L, Vassalli JD. Transforming growth factor-beta 1 modulates basic fibroblast growth factor-induced proteolytic and angiogenic properties of endothelial cells *in vitro*. *J Cell Biol* 1990;111:743-55.
- Saxena S, Srivastava PC, Thimmaraju KV, Mallick AK, Dalmia K, Das B. Socio-demographic profile of pregnancy induced hypertension in a tertiary care centre. *Religion*. 2014;47(67.14):51.
- Jena P, Mohapatra S. A retrospective study of socio-demographic factors in pregnancy induced hypertension in a tertiary care hospital in eastern India. *Inter J Clin Obstet Gynaecol*. 2019;3(1):78-81.
- Umegbolu EI, Ogamba JO. Incidence of gestational hypertension among pregnant women (2006-2015) in Enugu State, Southeast Nigeria: a retrospective study. *Inter J Comm Med Pub Health*. 2017;4(2):357.
- Sibai BM, Cunningham FG. Prevention of preeclampsia and eclampsia. In Lindheimer MD, Roberts JM, Cunningham FG editors; Chesley's Hypertensive Disorders of Pregnancy. 3rd edition, Elsevier, New York; 2009:215.
- Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. *Am J Obstet Gynecol* 2000;183:S1-22. (Level III)
- Sajith M, Nimbargi V, Modi A, Sumariya R, Pawar A. Incidence of pregnancy induced hypertension and prescription pattern of antihypertensive drugs in pregnancy. *Int J Pharma Sci Res*. 2014;23:4.
- The Internet Journal of Gynecology and Obstetrics. Clinical Evaluation of Hypertension and Proteinuria in patients who developed preeclampsia. 2005; 5
- Jun Zhang, Jonathan Zeisler, Maureen C. Hatch, and Gertrud Berkowitz. Epidemiology of pregnancy-induced hypertension. *Epidemiology Revised*, 1997; 19:218-232.
- Qublan HS, Amarun V, Bateinen O, Al-Shraideh Z, Tahat Y, Awamleh I, et al. LDH as biochemical marker of adverse pregnancy outcome in severe preeclampsia. *Med Sci Monit* 2005;11(8):393-7.
- Kharb S, Bhandari N, Singh A, Gupta A. Lactate dehydrogenase and maternal and perinatal outcome in preeclamptic women. *Arch Med Health Sci* 2019;7:163-6.
- Jaiswar SP, Amrit G, Rekha S, Natu SN, Mohan S. Lactic dehydrogenase: A biochemical marker for preeclampsia-eclampsia. *J Obstet Gynaecol India* 2011;61(6):645-8.
- Hazari NR, Hatolkar VS, Munde SM. Study of serum hepatic enzymes in preeclampsia. *Int J Curr Med Appl Sci* 2014;2(1):1-8.
- Gandhi M, Chavda R, Saini HB. Comparative study of serum LDH and uric acid in hypertensive versus normotensive pregnant woman. *Int J Biomed Res* 2015;6(1):25-8.
- Gupta A, Bhandari N, Kharb S, Chauhan M. Lactate dehydrogenase levels in preeclampsia and its correlation with maternal and perinatal outcome. *Int J Reprod Contracept Obstet Gynecol* 2019;8:1505-10.
- Demir C, Evruke C, Ozgunen FT, Urunsak IF, Candan E, Kadayifci O. Factors that influence morbidity and mortality in severe preeclampsia, eclampsia and hemolysis, elevated liver enzymes, and low platelet count syndrome. *Saudi Med J*. 2006;27(7):1015-8.