

“TO STUDY SERUM LDH AND SERUM URIC ACID LEVELS IN NORMOTENSIVE AND PREECLAMPTIC-ECLAMPTIC PREGNANT WOMEN AND ITS CORRELATION WITH FETO-MATERNAL OUTCOME.”

ELETI MANILA REDDY¹, MANJUSHA AGRAWAL²

¹Post Graduate Resident, Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Deemed to be University

Email: manilareddyeleti444@gmail.com

Mobile: 9701060038

²Professor of Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Deemed to be University

Email: badnemanju@gmail.com

Mobile: 9823114705

Corresponding author's name and address:

Eleti Manila Reddy, Sawangi, Meghe

Corresponding author's email id: manilareddyeleti444@gmail.com

Corresponding author's contact no.: 9701060038

Type of Article: Original Article

Conflict of Interest: **None**

Funding: Nil

Abstract:

BACKGROUND: A major health problem is hypertension during pregnancy. This complicates In India, around 5 to 10 percent of pregnancies occur. Preeclampsia is a disorder whose pathogenesis is still not clearly understood. One theory suggested that the cause of PE is, endothelial dysfunction is brought about by certain factors released from ischemic placenta leading to poor uterine and placental perfusion. Preliminary executive research suggests that serum LDH and uric acid are abnormal in women with preeclampsia-eclampsia and usual in women with normotension. **AIM AND OBJECTIVES:** We aim to study the correlation between serum lactate dehydrogenase levels and serum uric acid levels in in normotensive pregnant women and preeclamptic-eclamptic pregnant women together with their feto-maternal performance. The objectives of the study to compare and correlate serum lactate dehydrogenase and

serum uric acid levels in normotensive and preeclamptic-eclamptic women with fetal-maternal outcome. MATERIALS AND METHODS: This is a prospective observational study and will be conducted in the obstetrics and gynaecology department, AVBRH, DMIMS (Deemed to be University, Wardha), situated in the rural area of Wardha district in over 230 patients for period between 2020-23. This study will include antenatal patients of age 18 - 35yrs, gestation 28-40 weeks, normotensive and preeclampsia-eclampsia women and will exclude mothers with hypertension < 20 weeks of gestation (Chronic Hypertension), multiple pregnancy, pre-existing Diabetes Mellitus, liver disorder, renal disorder, epileptic disorder, thyroid disorder, Heart Disease, leukaemia, haemolysis and hepatitis.

EXPECTED RESULTS: We expect that there will be significant difference in maternal and fetal outcome based on serum lactate dehydrogenase and serum uric acid concentration in normotensive and preeclamptic -eclamptic pregnant women.

KEYWORDS: Preeclamptic women, Eclamptic women, normotensive women, serum LDH, serum uric acid.

INTRODUCTION:

Hypertension is a major health issue during pregnancy. One of the leading causes of maternal and perinatal morbidity and mortality is hypertension. It complicates one tenth of pregnancies in India. (1)

A big health concern is hypertension during pregnancy. It is one of the most important causes of perinatal morbidity and mortality. Around 5 to 10% of births in India are complicated by hypertension. Fetal growth retardation and prematurity are closely associated with hypertension. Preeclampsia is a disorder whose pathogenesis is still not clearly understood. One of the theories suggested for the cause of PE is that, endothelial dysfunction is brought about by certain factors released from ischemic placenta leading to poor uterine and placental perfusion. Lactate production and High glucose consumption is normally present in human placenta and glycolysis is a major energy pathway. Hypoxia boosts metabolic pathways, thereby further enhancing glycolysis and increasing LDH activity that transforms pyruvate to lactate. LDH is an intracellular cytoplasmic enzyme which is highly sensitive, is of diagnostic significance in several disorders and serves as an indicator of disturbance of cellular integrity in pathological conditions. Studies have associated elevated levels of LDH in PE with complications such as abruption placenta, Hemolysis Elevated Liver Enzymes Low Platelet count (HELLP) syndrome and renal failure. The state of hypoxia in PE causes increased oxidative stress with reduced antioxidant capacity. Due to placental hypoxia the purine catabolism increases which results in increased production of uric acid. This is one of the reasons for increased uric acid levels besides trophoblast breakdown and cytokine release. Besides the increased production, the levels of uric acid are increased in PE due to decreased excretion. (2)

Eclampsia is a disorder in which one or more convulsions, often accompanied by coma, occur in pregnant women suffering from elevated blood pressure and presenting a threat to the health of mothers and infants. The activity of gene expression and lactate dehydrogenase is higher in preeclampsia placentas than in normal pregnancy.

In trophoblasts, hypoxia induces LDH isoenzyme activity, resulting in higher production of lactate. LDH typically has five isoforms and is most susceptible to hypoxia among all LDH4 that is seen in placenta with preeclampsia. Cellular

damage and dysfunction are indicated by elevated levels of LDH, so lactate dehydrogenase can be used as a biochemical marker because it reflects the severity of the disease, the occurrence of complications and the fetomaternal outcome.(3)

A potent mediator of inflammation is uric acid. Uric acid activates monocytes to develop IL-1 β , IL-6, TNF-alpha pro-inflammatory cytokines. Endothelial dysfunction is caused by uric acid, which can facilitate hypertension, vascular disease, and renal disease. There is a link between uric acid levels and disease incidence, complications, and fetomaternal outcome. (4) There is a substantial rise in serum lactate dehydrogenase and uric acid levels in hypertensive and hypertensive pregnant women relative to normal pregnant women in the analysis of serum lactate dehydrogenase and serum uric acid concentrations in hypertensive pregnant women. To predict disease incidence, serum lactate dehydrogenase and uric acid are effective and inexpensive markers.(1)

Therefore this analysis will compare the levels of serum lactate dehydrogenase and serum uric acid in preeclampsia-eclampsia and normal pregnancy and correlates its values with fetomaternal outcome.

RATIONALE:

To assess the extent of cell death and thus the fetomaternal outcome, serum lactate dehydrogenase and serum uric acid levels can be used. In order to improve maternal and fetal outcomes, monitoring of serum lactate dehydrogenase and serum uric acid levels during pregnancy may help in deciding the management strategy. In this study, serum lactate dehydrogenase and serum uric acid levels in normotensive and preeclamptic-eclamptic pregnant women will be shifted and their values will be correlated with fetomaternal outcome.

AIM:

We aim to research the association with fetal and maternal outcomes of serum lactate dehydrogenase and serum uric acid levels in normotensive and Preeclamptic and eclamptic pregnant women.

OBJECTIVES:

1. To study the serum lactate dehydrogenase and uric acid levels in normotensive pregnant woman.
2. To study serum lactate dehydrogenase and uric acid levels in preeclampsia-eclampsia women.
3. Comparison of serum lactate dehydrogenase and uric acid concentrations in normotensive and preeclamptic-eclamptic pregnant women.
4. To correlate serum LDH levels with fetomaternal outcome.
5. To correlate serum uric acid levels with fetomaternal outcome

MATERIALS AND METHODS:

Study Design- Prospective Observational study

Setting: The thesis will be performed at Acharya Vinoba Bhave Rural Hospital(AVBRH), a tertiary care teaching hospital located in the rural area of Wardha District, in the Department

of Obstetrics and Gynaecology. The research will be performed after approval by the Ethical Committee of the Institute (applied for).

Participants: We will include antenatal patients of age 18 - 35 yrs, gestation 28-40 weeks, normotensive and preeclampsia-eclampsia women at AVBRH, Sawangi. Documented written consent will be received from all participants.

Study Population:

In this study 115 participants from each group will be taken after Ethical clearance from the institutional ethical committee. Before enrolling the patient into the study, every women will be explained the type and the nature of study and informed consent will be taken.

FORMULA:

$$n = \frac{Z_{\alpha/2} \cdot P \cdot (1-P)}{d^2}$$

WHERE,

$Z_{\alpha/2}$ is the level of significance at 5%

i.e. 95% confidence interval = 1.96

P = Prevalence of HT disorder in pregnancy = 8% = 0.08

d = Desired error of margin = 5% = 0.05

$$n = \frac{1.96^2 \times 0.08 \times (1-0.08)}{0.05^2}$$

= 115 patients needed in each group

Level of Significance: 5% (95% CI)

Power of the test: 80%

Side of the test: Two Sided

INCLUSION CRITERIA:

1. Antenatal patients of age 18 - 35 yrs.
2. Gestation 28-40 weeks
3. Normotensive and preeclampsia-eclampsia women

EXCLUSION CRITERIA:

- 1) Mothers with Hypertension < 20 weeks of gestation (Chronic Hypertension)
- 2) Multiple pregnancy
- 3) Preexisting Diabetes Mellitus
- 4) Liver disorder
- 5) Renal disorder
- 6) Epileptic disorder
- 7) Thyroid disorder
- 8) Heart Disease
- 9) Leukemia
- 10) Hemolysis
- 11) Hepatitis
- 12) Pancreatitis

METHODOLOGY: Study will be conducted in Department of Obstetrics and Gynaecology in AVBRH, Sawangi Meghe Wardha.

This research will be performed from October 2020 to October 2022 for a period of two years. Data for the study will be collected from 230 patients attending the Datta Meghe Medical College, Sawangi Department of Obstetrics and Gynaecology at Acharya Vinoba Bhave Rural Hospital. It involves 115 pregnant women in group A who are normotensive and 115 preeclamptic-eclamptic women in group B with the same gestational age. After meeting inclusion and exclusion requirements, they will be included.

STUDY GROUP:

Study group of 115 participants from each group of gestation 28-40 weeks.

Study group A- Normotensive pregnant women. (control n=115)

Study group B- Preeclamptic-eclamptic women.(case n=115)

In addition, the research group was subdivided into the following subgroups:

- 1) MILD PREECLAMPSIA: Blood Pressure of $\geq 140/90$ to $< 160/110$ mmHg
- 2) SEVERE PREECLAMPSIA: Blood Pressure of $\geq 160/110$ mmHg.
- 3) ECLAMPSIA: Preeclamptic patients with 1 or more episode of Generalized Tonic Clonic Seizures.

Study Population is also divided according to LDH and Uric Acid levels:

Subjects were also classified into the following classes, according to serum lactate dehydrogenase levels:

- <600 IU/l
- 600-800IU/l
- >800 IU/l

Subjects were also classified into the following classes, according to serum uric acid levels:

- <6mg/dll
- >6 mg/dl

A total of 230 subjects full filling the inclusion criteria will be admitted and monitored in the pre-labor room. A detailed history will be taken to exclude any contraindications for the intervention. General examination, systemic examination, including thorough obstetric examination will be done including a detailed per abdominal and per vaginal examination. 1 ml of venous blood sample was taken from the antecubital vein in a plain bulb under all aseptic precautions. Sample was allowed to clot for 30 minutes and then subjected to centrifugation in a clinical centrifuge machine at 3 thousand rpm for 3 mins to separate the serum. The separated serum was used to estimate serum LDH and uric acid levels.

EXPECTED RESULTS:

We expect that there will be significant difference in maternal and fetal outcome based on serum lactate dehydrogenase and uric acid levels in normotensive and preeclamptic - eclamptic pregnant women.

DISCUSSION:

Maternal and perinatal morbidity and mortality are linked to hypertension in pregnancy. A number of studies reflected on the magnitude of this problem globally(5,6,7). Hence identification of this entity is very important. Serum levels of lactate dehydrogenase & uric acid were high in preeclamptic group when compared to normotensive group. The preeclampsia group was subdivided further into mild and severe groups. When the serum LDH & uric acid levels were compared between these groups, it was found that their levels were almost doubled in the severe PE women as compared to normal and it was also high in comparison to mild PE group. This suggests that these parameters are associated with the severity of the disease. Uric acid is a purine degradation agent catalysed by the Xanthine Oxidase enzyme (XO). Poor uterine and placental perfusion in preeclampsia yields a state of hypoxia. This promotes increased XO activity resulting in increased production of uric acid through maternal, fetal or placental tissue breakdown. This associated with the production of ROS is implicated as a contributor to oxidative stress in PE. Alternatively, hypovolemia which is an early change in PE, brings about increased uric acid reabsorption which in turn causes increased serum uric acid concentrations. In the pathophysiology of PE, hypoxic condition in the placenta leads to oxidative stress which in turn increases anaerobic glycolysis are higher in placentas of preeclamptic women as compared to normal pregnant women. It is also known that vascular endothelial dysfunction is the central pathogenic cause for PE. This dysfunction causes increased sensitivity of the vasculature to vasoactive substances which in turn leads to reduction of perfusion and loss of fluid from the intravascular compartment leading to multi organ failure. Multi organ dysfunction leads to excessive LDH leakage and brings about an increase in LDH activity in serum. Correlation studies were carried out between serum LDH & uric acid concentrations and severity markers of PE i.e. SBP and proteinuria in order to confirm the findings. A positive association of serum LDH levels with SBP & proteinuria was observed in both mild and severe PE groups. On the other hand,

correlation analysis of severity parameters with serum uric acid levels presented a negative association the exception being with proteinuria in severe cases of PE.(2)

A number of related studies were reviewed. Yadav et. al. compared serum lipid profile of women with preeclampsia and normotensive pregnancy(8). Khanna et. al. studied on serum uric acid levels in acute stroke(9). Articles related to pregnancy and various diagnostic tests were reported(10,11,12). Shrivastava and Master reported on Fetal Growth Restriction (13).

CONCLUSION:

The results of my research would suggest that serum LDH and UA are accurate and inexpensive markers in preeclamptic eclamptic women to predict severity and maternal and fetal outcome.

Limitation of this study is that it only includes association of serum levels of LDH and uric acid with preeclampsia and eclampsia but it has not included the treatment of preeclampsia and eclampsia to prevent fetomaternal complications.

The scope of this study is to get first-hand information about association of levels of serum LDH and uric acid in preeclamptic-eclamptic women as compared to normotensive women. This research would help to figure out the causal link between the levels of serum LDH and uric acid and Preeclamptic-eclamptic women and can develop valuable data based on which effective screening; early diagnosis and proper treatment can be done to prevent fetomaternal complications.

REFERENCES:

- [1] Joseph, L., George, M., Alex, A., 2016. A REVIEW ON ESTIMATION OF SERUM LDH AND URIC ACID IN HYPERTENSIVE VS NORMAL PREGNANT WOMAN AND ITS CORRELATION WITH MATERNAL OUTCOME in A TERTIARY CARE HOSPITAL. IJTA 32, 35–37. https://doi.org/10.20530/IJTA_32_35-37
- [2] Mendez, D., Kunder, M., Shashidhar, K.N., M, M., 2019. Correlation of serum lactate dehydrogenase and uric acid levels with severity parameters of preeclampsia. International Journal of Clinical Biochemistry and Research 6, 315–320. <https://doi.org/10.18231/j.ijcbr.2019.069>
- [3] Dave, A., Maru, L., Jain, A., 2016. LDH (Lactate Dehydrogenase): A Biochemical Marker for the Prediction of Adverse Outcomes in Pre-eclampsia and Eclampsia. J Obstet Gynaecol India 66, 23–29. <https://doi.org/10.1007/s13224-014-0645-x>
- [4] Meena, R., Pachori, P., Chaudhary, S., Chandrakanta, 2019. Level of serum uric acid in patients with preeclampsia compared to controls and its relation to fetomaternal outcome. International Journal of Reproduction, Contraception, Obstetrics and Gynecology 8, 2471–2474. <https://doi.org/10.18203/2320-1770.ijrcog20192452>.
- [5] Vos, Theo, Stephen S Lim, Cristiana Abbafati, Kaja M Abbas, Mohammad Abbasi, Mitra Abbasifard, Mohsen Abbasi-Kangevari, et al. “Global Burden of 369 Diseases and Injuries in 204 Countries and Territories, 1990–2019: A Systematic Analysis for the Global Burden of Disease Study 2019.” *The Lancet* 396, no. 10258 (October 2020): 1204–22. [https://doi.org/10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9).
- [6] Wang, Haidong, Kaja M Abbas, Mitra Abbasifard, Mohsen Abbasi-Kangevari, Hedayat Abbastabar, Foad Abd-Allah, Ahmed Abdelalim, et al. “Global Age-Sex-Specific Fertility, Mortality, Healthy Life Expectancy (HALE), and Population Estimates in 204 Countries and Territories, 1950–2019: A Comprehensive

Demographic Analysis for the Global Burden of Disease Study 2019.” *The Lancet* 396, no. 10258 (October 2020): 1160–1203. [https://doi.org/10.1016/S0140-6736\(20\)30977-6](https://doi.org/10.1016/S0140-6736(20)30977-6).

- [7] Lozano R, Fullman N, Mumford JE, Knight M, Barthelemy CM, Abbafati C, et al. Measuring universal health coverage based on an index of effective coverage of health services in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020.
- [8] Yadav, S., M. Agrawal, C. Hariharan, D. Dewani, K. Vadera, and N. Krishna. “A Comparative Study of Serum Lipid Profile of Women with Preeclampsia and Normotensive Pregnancy.” *Journal of Datta Meghe Institute of Medical Sciences University* 13, no. 2 (2018): 83–86. https://doi.org/10.4103/jdmimsu.jdmimsu_70_17.
- [9] Khanna, S., A. Inamdar, S. Kumar, and A.V. Basat. “Study of Serum Uric Acid Levels in Acute Stroke.” *International Journal of Pharmaceutical Research* 11, no. 4 (2019): 2041–44. <https://doi.org/10.31838/ijpr/2019.11.04.508>.
- [10] Kshirsagar, P.C., A. Tembhare, and P. Palsodkar. “Evaluation of Serum Ferritin Level in Anaemic & Nonanemic Pregnant Women & Its Correlation with Maternal and Perinatal Outcome.” *International Journal of Pharmaceutical Research* 11, no. 4 (2019): 2075–79. <https://doi.org/10.31838/ijpr/2019.11.04.515>.
- [11] Nakade, M., M.L. Jungari, R. Ambad, and G. Dhingra. “Status of Vitamins and Minerals in Pregnancy: Still a Point of Concern in Central India.” *International Journal of Current Research and Review* 12, no. 14 Special Issue (2020): 45–49. <https://doi.org/10.31782/IJCRR.2020.4549>.
- [12] Phatak, S., D. Shrivastav, G. Marfani, S. Daga, K. Madurwar, and S. Samad. “Transvaginal Sonography and Elastography Evaluation of Ectopic Pregnancy.” *Journal of Datta Meghe Institute of Medical Sciences University* 14, no. 2 (2019): 86–89. https://doi.org/10.4103/jdmimsu.jdmimsu_13_19.
- [13] Shrivastava, D., and A. Master. “Fetal Growth Restriction.” *Journal of Obstetrics and Gynecology of India* 70, no. 2 (2020): 103–10. <https://doi.org/10.1007/s13224-019-01278-4>.