

ELEVATED LEVELS OF SERUM LDH AND SERUM URIC ACID IN DETERMINING THE SEVERITY OF PRE-ECLAMPSIA MOTHERS

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ABSTRACT

Background: Pregnancy-related hypertension issues impact between 3% and 5% of pregnancies. Elevated circulating uric acid concentrations do not always indicate pre-eclamptic women, but they do seem to distinguish a subgroup of pre-eclamptic women who are more likely to experience maternal and fetal morbidities, which may have prognostic as well as diagnostic implications.

Aim: To determine the effects of serum LDH and serum uric acid levels in patients of pre-eclampsia mothers to determine the effects of serum LDH and serum uric acid levels in 250 pre-eclampsia mothers admitted in our tertiary care centre. **Materials and Methods:** We conducted a hospital-based observational study in the antenatal OPD, labour ward, and casualty. Patients underwent specialized and standard investigations. Using a commercial kit in the auto-analyzer (uricase technique), the uric acid level was approximated, and the LDH level was determined using the auto-analyzer's LDH isoenzyme kit. Serum LDH (140–280 U/L) and serum uric acid (3.1–6.3 mg/dl) were considered normal values. Association between the severity of preeclampsia and LDH and serum uric acid levels were checked. **Result:** The study analyzed 250 participants with preeclampsia. The majorities were between 25–30 years old (49.6%), and most were over 36 weeks pregnant (46.0%). About half were first-time mothers (53.0%). Only 12.0% had a previous history of preeclampsia, and most conceptions (71.0%) were spontaneous. Clinical symptoms varied, with 52.8% being asymptomatic. Laboratory results showed mean values for hemoglobin (11.8 g/dL), platelet count ($191.18 \times 10^3/\mu\text{L}$), and various liver and kidney function markers. Elevated serum LDH levels were significantly associated with the severity of preeclampsia, rising from 312.9 U/L in mild cases to 551.1 U/L in severe cases. Similarly, serum uric acid levels increased from 4.9 mg/dL in mild pre-eclampsia to 6.2 mg/dL in severe cases. **Conclusion:** The findings suggest that monitoring serum LDH and uric acid levels can be valuable in assessing the severity of pre-eclampsia and potentially guiding clinical management.

INTRODUCTION

Pregnancy-related hypertension issues impact between 3% and 5% of pregnancies. Together with hemorrhage and infection, they constitute the lethal trio, significantly increasing the morbidity and mortality rate among mothers.^[1,2,3] The incidence of pre-eclampsia was 10.3% and that of eclampsia was 1.9% in 2013, according to the National Epileptic Registry (antepartum being higher than 50%, around 13% postpartum). Even while early diagnosis and treatment have significantly decreased maternal deaths in affluent nations, such as India, 19% of

annual deaths in developing nations are still related to maternal deaths.^[4] The percentage of maternal deaths directly related to eclampsia is 4%–6%. 20% of instances result in perinatal mortality, of which 50% are still births. Prior to the emergence of clinical symptoms, preeclampsia's systemic inflammatory response causes endothelial dysfunction, which raises vascular reactivity.

The reversal of normal pregnancy's circulatory adaptations and an imbalance in sodium-volume homeostasis are caused by endothelial integrity loss.^[5] These widespread changes in the mother's organ systems result in often fatal consequences

such heart failure, liver failure, renal failure, eclampsia, placental abruption, and disseminated intravascular coagulation (DIC). Reduced birth weight, fetal growth restriction, spontaneous or iatrogenic preterm delivery, hyaline membrane disease, and an overall increase in neonatal intensive care unit (NICU) admissions are examples of fetal problems. As early as 10 weeks of gestation, hyperuricemia is one of the first signs of proteinuria, hypertension, and Pre-eclamptic pregnancies.^[2] This elevated level points to significant renal function deterioration that could happen soon.^[6]

Elevated circulating uric acid concentrations do not always indicate preeclamptic women, but they do seem to distinguish a sub group of pre-eclamptic women who are more likely to experience maternal and fetal morbidities, which may have prognostic as well as diagnostic implications.^[7] In determining the likelihood of renal involvement and fetal impairment, it is as significant to consider as proteinuria. Since lactate dehydrogenase (LDH) is an intracellular enzyme, high levels suggest hemolysis, cellular malfunction, and even cell death.^[8-10] In preeclampsia, hypoxia raises LDH activity and glycolysis, which raises lactate generation. There are five different isoforms of LDH. The isoenzyme LDH-A is found immunolocalized in fetal endothelium cells, whereas the isoenzyme LDH-B is mostly found in syncytiotrophoblasts. According to certain research, tiny for gestational age newborns and the development of hemolysis, elevated liver enzyme levels, and low

platelet levels (HELLP) syndrome are all predicted by elevated serum levels of LDH.

Aims and Objectives

To determine the effects of serum LDH and serum uric acid levels in patients of pre-eclampsia mothers. We conducted a hospital-based observational study in the antenatal OPD, labour ward, and casualty in Government Dharmapuri medical college and hospital between May 2022 to May 2024. As a part of this research proposal, we intended to determine the effects of serum LDH and serum uric acid levels in patients of preeclampsia mothers admitted in our tertiary care centre. After institutional Ethical Committee approval and informed written consent, around 250 pre-eclampsia mothers were selected based on the inclusion and exclusion criteria.

MATERIALS AND METHODS

Inclusion Criteria

- Antenatal mothers
- Gestation more than 20 weeks
- Pre-eclampsia mothers.

Exclusion Criteria

- Mothers with hypertension <20 weeks of gestation
- Multiple pregnancy.
- Patients with pre-existing medical disorders like gestational diabetes mellitus, overt diabetes mellitus, cardiac disease, thyroid disorder.

RESULTS

Table 1: General characteristics of the study participants (N=250)

Characteristics	Frequency (%)
Age group	
20-25 years	47 (18.8)
25-30 years	124 (49.6)
>30 years	79 (31.6)
Gestational age	
<28 weeks	64 (27.0)
28-36 weeks	143 (27.0)
>36 weeks	43 (46.0)
Parity	
Primi	162 (53.0)
Multi	88 (47.0)
Previous history of pre-eclampsia	
Yes	37 (14.8)
No	213 (85.2)
Conception	
Spontaneous	221 (71.0)
After infertility	29 (29.0)
Marriage	
Consanguineous	23 (13.0)
Non-consanguineous	227 (87.0)
Clinical features	
Pedaloedema	57 (22.8)
Headache	32 (12.8)
Vomiting/blurring of vision	16 (6.4)
Abdominal pain	13 (5.2)
Asymptomatic	132 (52.8)

The study involved 250 participants whose general characteristics were analyzed. The age distribution showed that nearly half of the participants (49.6%) were between 25 and 30 years old, while 18.8% were in the 20-25 age group, and 31.6% were older than 30 years. Regarding gestational age, 27.0% were less than 28 weeks, 27.0% were between 28 and 36 weeks, and 46.0% were over 36 weeks. Parity data indicated that 53.0% were primi (first-time mothers), and 47.0% were multi (had previous pregnancies). Additionally, 15% had a previous history of pre-eclampsia, while 85.0% did not. Further analysis revealed that 71.0% of the conceptions were spontaneous, with the remaining 29.0% occurring after infertility treatments. Marital status indicated that 13.0% of the participants were in consanguineous marriages, whereas 87.0% were in non-consanguineous marriages. Clinical features of the participants showed that 22.8% experienced pedal oedema, 12.8% had headaches, 6.4% had vomiting or blurred vision, 5.2% experienced abdominal pain, and a significant portion, 52.8%, were asymptomatic.

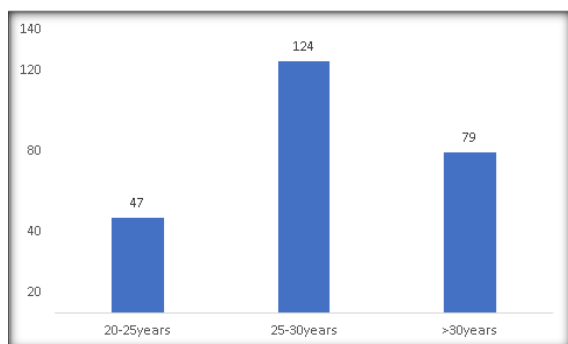


Figure 1: Age distribution of the participants

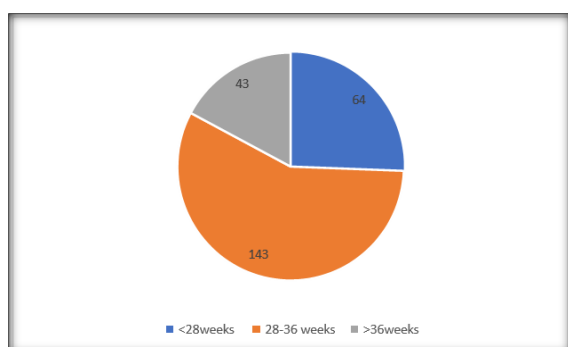


Figure 2: Gestational age distribution of the participants

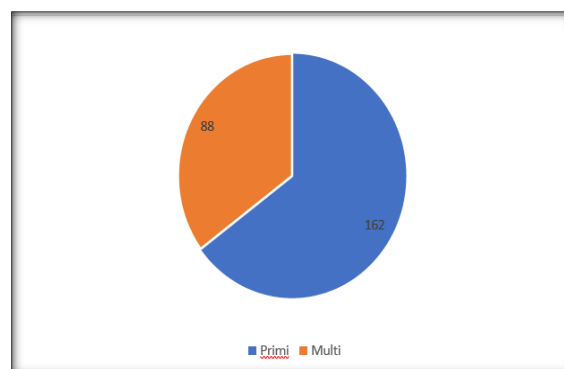


Figure 3: Parity among the participants

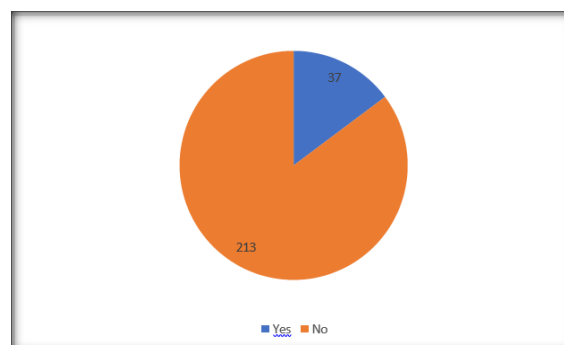


Figure 4: Previous h/o pre-eclampsia among the participants

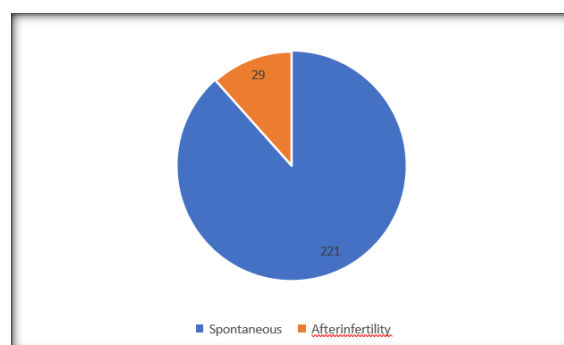


Figure 5: Conception among the participants

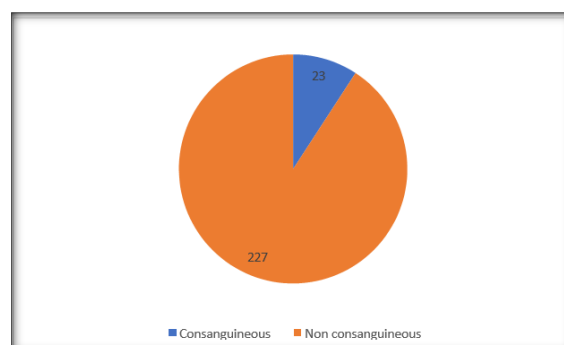


Figure 6: Type of marriage among the participants

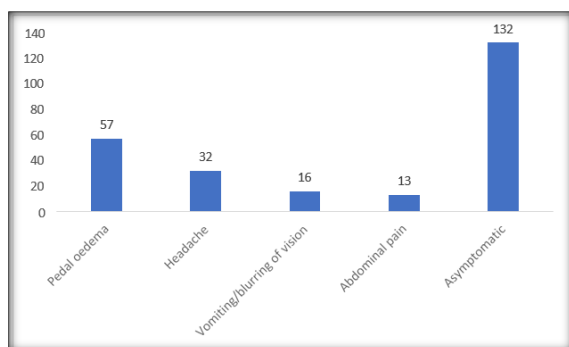


Figure 7: Clinical symptoms among the participants

Table 2: Lab investigations of the study participants (N=250)

Characteristics	Mean (SD)
Lab investigations	
Hb	11.8±1.62
Platelets	191.18±49.06
Direct bilirubin	0.23±0.08
Total bilirubin	0.6±0.22
ALT	28.7±20.3
AST	33.4±12.5
S.Creatinine	0.81±0.3
ALP	310.9±92.61

The lab investigations of the 250 study participants revealed the following mean values and standard deviations (SD) for various parameters. Hemoglobin (Hb) levels averaged 11.8g/d L with an SD of 1.62. The mean platelet count was 191.18 $\times 10^3/\mu\text{L}$, with an SD of 49.06. Direct bilirubin had a mean value of 0.23mg/dL (SD 0.08), while total bilirubin was 0.6mg/dL (SD 0.22). Alanine

Amino transferase (ALT) levels averaged 28.7 U/L, with an SD of 20.3, and aspartate amino transferase (AST) levels averaged 33.4 U/L, with an SD of 12.5. Serum creatinine levels had a mean of 0.81mg/dL with an SD of 0.3, and alkaline phosphatase (ALP) levels were 310.9 U/L (SD 92.61) [Table-2].

Table 3: Association between LDH levels and severity of pre-eclampsia among the study participants (N=250)

Severity of pre-eclampsia	LDH Levels	No of Study Participant	% Percentage	P-Value
Non Severe	312.9± 164.2	182	72.8%	<0.001
Severe	551.1± 189.1	68	27.2%	

The study explored the relationship between lactate dehydrogenase (LDH) levels and the severity of pre-eclampsia among the 250 participants. LDH levels were significantly associated with the severity

of the condition ($P < 0.001$). Participants with non severe pre-eclampsia had mean LDH levels of 312.9 U/L (SD 164.2), those with severe pre-eclampsia had mean levels of 551.1 U/L (SD 189.1) [Table-3].

Table 4: Association between serum uric acid levels and severity of pre-eclampsia among the study participants (N=250)

Severity of pre-eclampsia	Sr. Uric acid levels	No of Study Participant	% Percentage	P-Value
Non Severe	4.9±1.8	172	68.8	0.004
Severe	6.2 ± 1.4	78	31.2%	

Similarly, serum uric acid levels also showed a significant association with the severity of pre-eclampsia ($P = 0.004$). The mean uric acid levels for non severe and severe pre-eclampsia were 4.9

mg/dL (SD 1.8), and 6.2 mg/dL (SD 1.4) respectively. These findings suggest that both LDH and uric acid levels increase with the severity of pre-eclampsia [Table-4].

Table 5: Maternal and neonatal outcomes of the study participants (N=250)

Characteristics	Mean (SD)
Mode of delivery	
LSCS	83 (33.2)
NVD	159 (63.6)
Instrument delivery	8 (3.2)
Pregnancy outcome	

Preterm	92 (36.8)
Term	158(63.2)
Neonatal outcome	
Mother side	182(72.8)
NICU admission	68 (27.2)

Of the 250 mothers who were enrolled, we noted that around 64% delivered vaginally, while, 33% delivered through LSCS. Of the babies that were born, around 28% were preterm, and 21% required NICU admission post-delivery.[Table – 5]

5.1 Maternal Outcome: Variables

1. Gestational age of the participant when pregnancy was terminated
2. Participant Developing HELLP syndrome
3. Mode of Induction (Spontaneous & Induced preterm delivery)

Severity of pre- Eclampsia	GA of the participant when pregnancy was terminated	No. of participant	%of participant
Non Severe Pre-Eclampsia	>37weeks	112	44.8%
	<37weeks	70	28%
Severe Pre- Eclampsia	>37weeks	8	3.2%
	34-36weeks	22	8.8%
	<34weeks	38	15.2%

Table 5.1.1: Participants develops HELLP Syndrome

Severity of pre- Eclampsia	HELLP Syndrome	No.of participant	%of participant
Non Severe Pre- Eclampsia	Developing HELLP Syndrome	4	1.6%
Severe Pre- Eclampsia	Developing HELLP Syndrome	8	3.2%

Table 5.1.2: Mode of Induction (Spontaneous & Induced preterm delivery)

Severity of pre- Eclampsia	Preterm Delivery	No of participant	%of participant
Non Severe Pre-Eclampsia	Spontaneous	5	5.4%
	Induced	35	38%
Severe Pre-Eclampsia	Spontaneous	7	7.6%
	Induced	61	49%

5.2. NEONATAL OUTCOME: Variables are

1. Birth Weight
2. Fetal Growth Restriction
3. NICU Admission
4. APGAR Score at Birth

Table 5.2.1: Birthweight

Severity of pre- Eclampsia	Neonatal Outcome	No of Neonates Affected	% of Neonates Affected
Non Severe	Normal Birth Weight	143	65.2%
	Low Birth Weight	35	6%
Severe	Normal Birth Weight	2	0.8%
	Low Birth Weight	70	28%

Table 5.2.2: Fetal Growth Restriction (FGR)

Severity of pre- Eclampsia	Neonatal Outcome(FGR)	No of Neonates Affected	% of Neonates Affected
Non Severe	FGR	32	12.8%
Severe	FGR	54	21.6%

Table 5.2.3: NICU Admission

Severity of pre- Eclampsia	Neonatal Outcome(FGR)	No of Neonates Affected	% of Neonates Affected
Non Severe	NICU Admission	10	4%
Severe	NICU Admission	58	23.2%

Table 5.2.4: APGAR Score at Birth

Severity of pre- Eclampsia	Neonatal Outcome (APGAR Score atBirth)	No of Neonates Affected	% of Neonates Affected
Non Severe	<7	15	6%
	>7	163	65.2%
Severe	<7	70	28%
	>7	2	0.8%

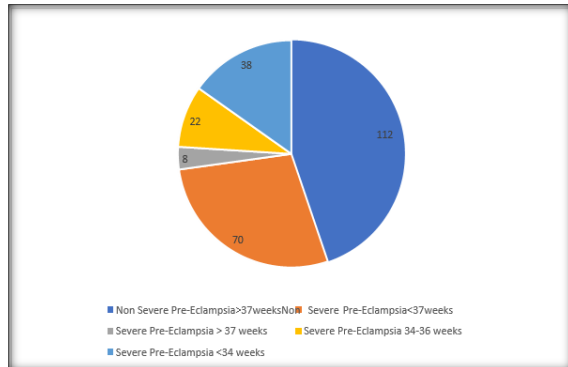


Figure 5.1: Maternal Outcome: Variables

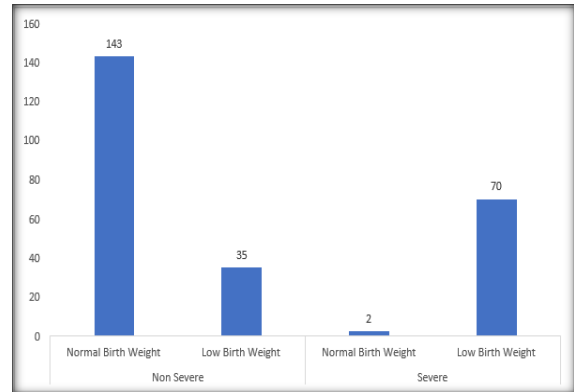


Figure 5.2.1: Birthweight

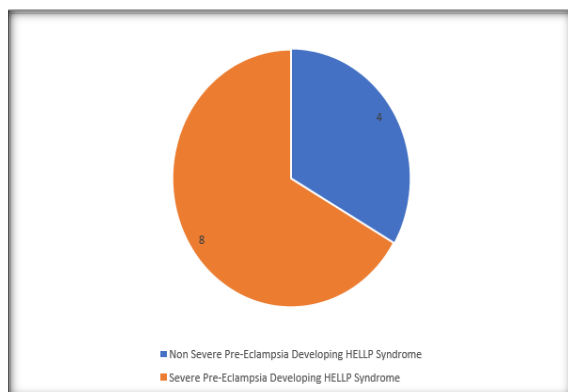


Figure 5.1.1: Participants develops HELLP Syndrome

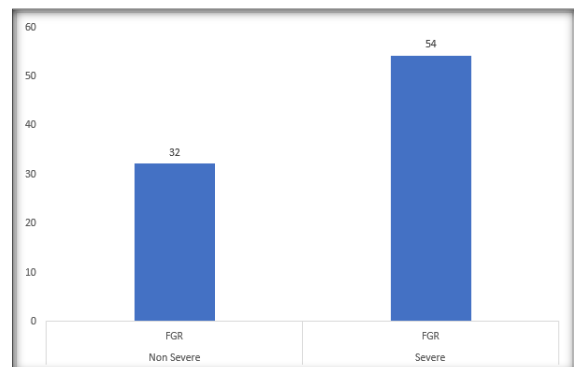


Figure 5.2.2: Fetal Growth Restriction (FGR)

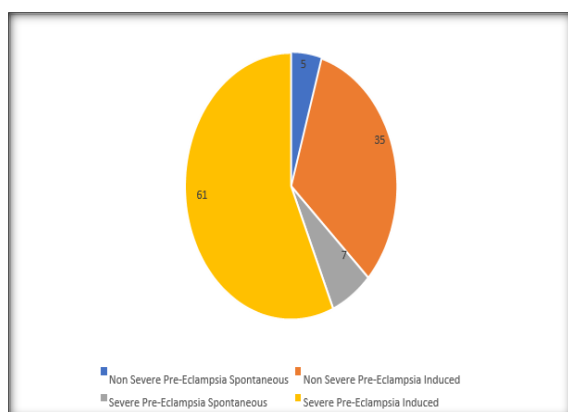


Figure 5.1.2: Mode of Induction (Spontaneous & Induced preterm delivery)

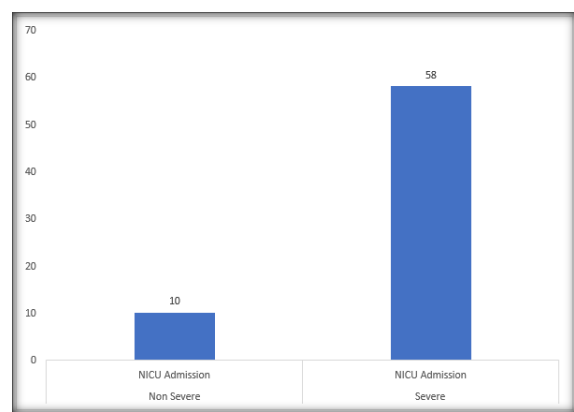


Figure 5.2.3: NICU Admission

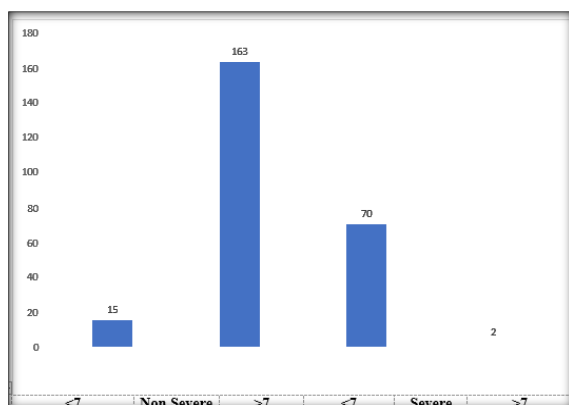


Figure 5.2.4: APGAR Score at Birth

DISCUSSION

Ninety-nine percent of all pregnancy-related birth-related deaths take place in low- and middle-income countries (LMICs) as a result of disparities in access to healthcare. Infections, significant bleeding (typically after delivery), high blood pressure throughout pregnancy (preeclampsia and eclampsia), and unsafe abortions are the main causes of problems. Because LMICs have a greater pregnancy rate than high-income countries, there is a larger chance of death during this time. This is especially important for teenagers under the age of 15, as 1 in 150 of them experience pregnancy-related problems.

Based on the study findings we have suggested the following recommendations

- Routine Screening:** Implement routine screening of serum LDH and uric acid levels in pregnant women, particularly those at high risk for preeclampsia, to identify and monitor disease severity early.
- Risk Stratification:** Use LDH and uric acid levels as part of a comprehensive risk stratification tool to categorize patients based on preeclampsia severity, aiding in tailored clinical management and intervention strategies.
- Targeted Interventions:** Develop and implement targeted therapeutic interventions aimed at reducing oxidative stress and endothelial dysfunction, thereby potentially lowering LDH and uric acid levels and improving maternal and fetal outcomes.
- Clinical Guidelines:** Update clinical guidelines to incorporate the measurement of serum LDH and uric acid levels in the routine evaluation and management of preeclampsia, emphasizing their role in predicting disease progression.

Further Research: Conduct large-scale, multicenter studies to further validate the utility of LDH and uric acid as biomarkers for preeclampsia severity and explore potential therapeutic targets to mitigate their effects.

CONCLUSION

The study analyzed 250 participants with preeclampsia. The majority were between 25-30 years old (49.6%), and most were over 36 weeks pregnant (46.0%). About half were first-time mothers (53.0%). Only 12.0% had a previous history of preeclampsia, and most conceptions (71.0%) were spontaneous. Clinical symptoms varied, with 52.8% being asymptomatic. Laboratory results showed mean values for hemoglobin (11.8 g/dL), platelet count ($191.18 \times 10^3/\mu\text{L}$), and various liver and kidney function markers. Elevated serum LDH levels were significantly associated with the severity of preeclampsia, rising from 312.9 U/L in mild cases to 551.1 U/L in severe cases. Similarly, serum uric acid levels increased from 4.9 mg/dL in mild preeclampsia to 6.2 mg/dL in severe cases. These findings suggest that both LDH and uric acid levels are indicative of preeclampsia severity and could be valuable in clinical assessment. Our study demonstrates that elevated serum LDH and uric acid levels are significantly associated with the severity of preeclampsia. These biomarkers increase progressively from mild to severe cases, reflecting the underlying patho-physiological processes of cellular damage, hemolysis, oxidative stress, and renal dysfunction.

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