Original Research Article

Correlation of Biochemical Markers of Serum Uric Acid and Lactate Dehydrogenase in Preeclampsia With Feto-Maternal Outcomes

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Abstract

Introduction: Hypertensive disorders complicate 5-10% of all pregnancies worldwide. There are controversies aboutthe association between serum biomarkers and the severity of disease in the literature. AIM: To evaluate serum biomarkers uric acid(UA) and lactate dehydrogenase(LDH) in preeclamptic women and their prognostic role in maternal and fetal outcomes. **Materials And Methods**: Prospective study. A total of 52 women with preeclampsia were subjected to UA and LDH estimation and followed up in the obstetrics and gynecology department, NRIGH, Chinakakani, Andhra Pradesh from July 2019 to December 2019. **Results:** Out of 52 cases, 31(59.5%) and 21(40.2%) had non-severe and severe preeclampsia. 13 women had elevated LDH and 25 had elevated UA, out of which 7(13.4%) had both. Complications observed were more in women with LDH > 600U/L and serum UA ≥ 6mg%.Out of 7 patients with eclampsia, both were elevated in 3, isolated elevation of LDH in 2 cases. 6 had PRES; only 1 had an elevation of both, isolated elevation of UA and LDH in 2 each. Out of 4 patients with thrombocytopenia, 3 had an elevation of both and 1 had an elevation of UA. Only 1 of 52 cases had retinal detachment with the elevation of both markers. 4 out of 8 ICU admission had both markers elevated. All 3 patients who developed pulmonary edema had elevated UA, and only 1 had elevated LDH. Fetal morbidity like preterm delivery, LBW, IUGR, NICU admission were more in elevated UA while IUFD was more in elevated LDH women. **Conclusion:** As ours is a small study group, we cannot conclude which biomarker is better, but both UA and LDH may be reliable in preeclampsia and its prognosis as per our study findings. CLINICAL SIGNIFICANCE: Monitoring serum UA and LDH levels during antenatal period may help in early intervention and help prevent maternal and fetal morbidity and mortality due to preeclampsia.

Keywords: Preeclampsia, hypertensive disorders of pregnancy, Lactate dehydrogenase, Uric acid.

Introduction

Hypertensive disorders of pregnancy remain the most intriguing and significant unsolved problems in obstetrics. These disorders complicate 5-10% of all pregnancies worldwide and are associated with increased maternal & perinatal morbidity and mortality, particularly in developing countries [1].A WHO secondary analysis in low and middle-income countries reported preeclampsia incidence to be in the range of 2–15% in India[2].

The National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy (NHBPEP) recommends classification of hypertension during pregnancy as

1) Gestational hypertension
2) Pre-eclampsia, eclampsia
3) Chronic hypertension and
4) Preeclampsia superimposed on chronic hypertension [3].

Gestational hypertension is defined as new-onset hypertension (systolic BP of 140 mm Hg or more or diastolic BP of 90 mm Hg or more, or both on two occasions at least 4-6 hours apart but within 7 days) without proteinuria or any other systemic features of preeclampsia after 20 weeks of gestation, during labour or in 1st 24-hour postpartum in previously normotensive non proteinuric women[4]. Preeclampsia is gestational hypertension plus proteinuria greater than 0.3g/dl in a 24-hour urine collection or dipstick 2+ or women with gestational hypertension without proteinuria with following features:

- ·Thrombocytopenia (platelet count <100,000 x 10^9/L)
- ·Impaired liver functions (twice upper limit of normal)
- ·Severe persistent right upper quadrant or epigastric pain
- ·Renal insufficiency (serum creatinine>1.1mg/dl)
- ·Pulmonary edema
- ·New onset headache unresponsive to acetaminophen or visual disturbances [4].

Preeclampsia is a multi-system disorder and results in cell death leading to end organ failure. The exact pathophysiology of this disease is unknown. Defective placentation with abnormal trophoblastic invasion of uterine vessels and endothelial cell activation and dysfunction is considered the main etiopatho-genesis [1].Investigations include hematocrit, platelet count, liver function test (LFT), lactate dehydrogenase(LDH), serum uric acid(UA), coagulation profile, serum bilirubin and urine albumin levels. There are controversies for association between these parameters and severity of disease in literature [5]. LDH is an intracellular enzyme and is responsible for interconversion of lactate and pyruvate in the cells. Its level is increased in hemolysis and cellular death. So LDH level measurement can thereby indicate the severity of disease[6][7].Uric acid is an end product of purine metabolism.It is filtered through glomeruli and almost completely reabsorbed in proximal convoluted tubules (PCT) by both active and passive carrier mediated process. It is actively secreted into the tubules. About 85% of total excreted uric acid is from tubular secretion. Hyperuricemia is one of the earliest biochemical manifestations of preeclampsia. This

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can be due to reduced uric acid clearance due to reduced glomerular filtration rate and reduced tubular secretion in preeclampsia [7].Understanding the pathogenesis and early identification of the patients at risk will help in preventive care and early therapeutic interventions, which helps to reduce the morbidity and mortality during pregnancy and the long-term problems associated with preeclampsia. So there is a need to assess the markers. This study was done to evaluate the serum biomarkers like LDH and UA in antenatal women with preeclampsia and their prognostic role in maternal and fetal outcomes.

Materials and Methods

A total of 52 pregnant women with preeclampsia were studied prospectively in the department of obstetrics and gynaecology, NRI general hospital, Chinakakani, Andhra Pradesh, over six months from July 2019 to December 2019. All Pregnant women were screened for hypertension and those diagnosed as preeclampsiawere taken for further evaluation. The demographic details, gestational age, obstetrics history, complaints, blood pressure recordings and investigations were noted. Institutional ethical committee acceptance was taken before the start of the study.

Inclusion Criteria

1. Antenatal women diagnosed with preeclampsia
2. Singleton pregnancy
3. Primi / Multigravida
4. Pregnant women of age 18-45 years
5. Gestational age >20 weeks
6. Willing to participate in the study.

Exclusion Criteria

1. H/o chronic hypertension
2. Diabetes mellitus
3. Multiple gestation
4. Smoking
5. Alcoholism

a. Liver, cardiac or renal diseases

6. Connective tissue disorders
7. Vascular disorders

Sample Collection

Under aseptic precautions, 3-5 ml of blood was drawn in a plain vial. The serum was separated by centrifugation. Estimation of UA is by enzymatic calorimetric method using RX IMOLA Fully Auto Analyzer. Estimation of LDH is by DGKC UV method using RX IMOLA Fully Auto Analyzer.

Statistical Analysis

Quantitative variables were expressed in terms of means and standard deviations and qualitative data in terms of percentages. Data was presented with suitable graphical methods.

Results

During the study period, 52 pregnant women with preeclampsia were followed up, out of which 31(59.6%) and 21(40.3%) women had non-severe and severe preeclampsia. Data regarding parity, age, period of gestation, systolic and diastolic blood pressures, LDH and uric acid levels,maternal and neonatal complications are given in tables.

Table 1: Age

Age(years)	Number(n)	Percent(%)	Mean±SD
18-29	47	90.3	23.27±3.08
30-45	5	9.6	33.8 ±3.89

Table 2:Parity

	n	%
Primi	30	57.6
Multi	22	42.3

Table 3: Period of gestation at delivery

POG(weeks)	n	%	Mean±SD
$20\text{-}27^{+6}$	03	5.7	26.63±0.77
$28\text{-}36^{+6}$	30	57.6	32.87±2.58
≥ 37	19	36.5	38.64±1.00

Table 4:Systolic BP(SBP)

BP(mm Hg)	n	%	Mean±SD
140-159	31	59.6	142.25±4.25
≥ 160	21	40.3	170±13.41

Table 5: Diastolic BP(DBP)

BP(mm Hg)	n	%	Mean±SD
90-109	44	84.6	92.70±13.84
≥ 110	08	15.3	116.25±7.44

Table 6: LDH levels

U/L	n	%	Mean±SD
< 600	39	75	385.79±120.86
600-800	09	17.3	687.44±71.13
≥ 800	04	7.6	2469.25±1774.2

Table 7: UA levels

mg%	n	%	Mean±SD
< 6	27	51.9	4.38±0.86
≥ 6	25	48.1	7.70±1.37

Table 8: Comparison of SBP with elevated LDH and UA levels

BP [mm Hg] (n)	LDH (U/L)		UA (mg%)	
	≥ 600 %		≥ 6 %	
140-159(31)	6	19.3	13	41.9
≥ 160 (21)	7	33.3	12	57.1

Table 9:Comparison of DBP with elevated LDH and UA levels

BP[mm Hg](n)	LDH(U/L) ≥ 600%		UA(mg%) ≥ 6%	
90-109(44)	6	13.6	18	40.9
≥ 110(8)	7	87.5	7	87.5

Table 10: Maternal complications

Complications	n	%
Eclampsia	07	13.4
Abruption	01	1.9
Thrombocytopenia	04	7.4
DIC	0	-
Pulmonary edema	03	5.7
Blood transfusion	05	9.6
Fundoscopy:	18	34.6
GI	13	-
GII	02	-
GIII	02	-
Retinal detachment	01	-
Imminent s/s	17	32.6
Headache	15	-
Visual disturbances	05	-
Vomiting	07	-
Epigastric pain	04	-
Oliguria	02	-
PPH	0	-
PRES	06	11.5
ICU admission	08	15.3

PPH

Postpartum hemorrhage, PRES:Posterior reversible encephalopathy syndrome, ICU: Intensive care unit.

Gestational age at delivery was more than 37 weeks in 19(36.5%) women and 28-36^{+6} weeks in 30(57.6%) women and less than 27^{+6} weeks in 3(5.7%) women given in table 2.33(63.4%) women underwent LSCS and normal vaginal delivery in 18(34.6%) women and instrumental delivery in 1(1.9%) women. 45(86.5%) live births and 7(13.4%) intrauterine deaths. Birth weight distribution given in table 11. Out of 45 live births, 6(11.5%) have IUGR and 25(55.5%) require NICU admission.

Table 11: Birth weights

BW(kg)	n	%	Mean±SD
< 2.5	34	65.3	1.41±*0.49*
≥ *2.5 – 3.5*	18	34.6	2.99±*0.32*
≥3.5	0	-	-

Table 12:Neonatal complications

Complications	n	%
Preterm delivery	33	63.4
LBW	34	65.3
IUGR	06	11.5
NICU admission	25	55.5
IUFD	07	13.4

LBW

Low birth weight, IUGR: intrauterine growth restriction, NICU: Neonatal ICU, IUFD: Intrauterine fetal demise.

The complications observed in the study were more in women with LDH levels > 600U/L and serum uric acid levels ≥ *6*mg%. Out of 13 women with increased LDH levels, eclampsia in 5(71.4%), PRES in 3(50%), thrombocytopenia in 3(75%), blood transfusion in 4(80%), pulmonary edema in 1(33.3%), retinal detachment in 1(100%), imminent symptoms in 10(58.8%), ICU admission in 6(75%) women were seen. Out of 25 women with increased serum UA levels, eclampsia in 3(42.8%), PRES in 3(50%), thrombocytopenia in 4(100%), blood transfusion in 4(80%), pulmonary edema in 3(100%) retinal detachment in 1(100%), imminent symptoms in 9(52.9%), ICU admission in 6(75%) women were seen. Preterm delivery and IUGR in 33.3% each, LBW in 32.3%, NICU admission in 24% and IUFD in 71.4% were reported in women with elevated LDH levels. In women with elevated serum UA, preterm delivery was reported in 63.6%, IUGR in 50%, LBW in 61.7%, NICU admission in 72% and IUFD in 52.9% women. Number of women with complications in each group is given in table 13 and the mode of delivery in women with elevated levels of LDH and UA is given in table 14.

Out of 52 women, both the markers were elevated in 7(13.4%) women, out of which thrombocytopenia and eclampsia was reported in 3 women each, 1 had pulmonary edema, 4 required blood transfusion and ICU admission, retinal detachment and PRES in 1 each. 5 women underwent LSCS. All the 7 women had preterm delivery with low birth weight, out of which 4 babies were admitted in NICU and 3 were IUFD.

Table 13:Complications in each group according to levels of LDH and UA

Complications	n	LDH(U/L) ≥600 %		UA(mg%) ≥ 6%	
Eclampsia	07	05	71.4	03	42.8
PRES	06	03	50	03	50
Thrombocytopenia	04	03	75	04	100
Pulmonary edema	03	01	33.3	03	100
Blood transfusion	05	04	80	04	80
Retinal detachment	01	01	100	01	100
Imminent symptoms	17	10	58.8	09	52.9
ICU admission	08	06	75	06	75
Preterm delivery	33	11	33.3	21	63.6
LBW	34	11	32.3	21	61.7
IUGR	06	02	33.3	03	50
NICU admission	25	06	24	18	72
IUFD	07	05	71.4	04	52.9

Table 14:Mode of delivery in women with elevated levels of LDH and UA

Mode of delivery	n	LDH(U/L) ≥600 %		UA(mg%) ≥ 6 %	
Caesarean section	33	06	18.1	17	51.5
Instrumental delivery	01	01	100	0	-
NVD	18	06	33.3	08	44.4

NVD: Normal vaginal delivery

Discussion

Pre-eclampsia is one of the common medical complications during pregnancy. Without any intervention, preeclampsia can progress to eclampsia, which is characterized by convulsions[8]. In cases of severe preeclampsia, symptoms like headache, visual disturbances, oliguria, pulmonary edema, vomiting, epigastric/right upper quadrant pain, hemolysis, thrombocytopenia, renal failure, impaired liver functions, abruptio placenta, DIC can be present[9]. These complications may land the women in high definition unit (HDU) or ICU. Serum biomarkers like LDH and serum UA have been reported to be significantly associated with preeclampsia [5]. So in our study, LDH and UA has been evaluated as a biochemical marker for prognosis of preeclampsia.In our study, the majority were young. This was also observed in studies done by Jaiswar et al.[10] and Kamath et al.[11]. The mean systolic BP(mm Hg) was 142.25 ± 4.25 and 170 ± 13.41 and diastolic BP(mm Hg) was 92.70 ± 13.84 and 116.25 ± 7.44 in mild and severe preeclampsia women respectively, which was found to be similar in the study done by Qublan HS et al.[12] which has mean Systolic BP (mmHg) 143±15.8 and 169.9±20.9 and Diastolic BP (mmHg) 92±9.7 and 107±12.7 in mild and severe preeclampsia groups, respectively.Out of 52 women, 7(13.4%) progressed to eclampsia, 1(1.9%) had abruption, thrombocytopenia in 4(7.6%), 3(5.7%) had pulmonary edema, 5(9.6%) required blood transfusion, 8(15.3%) required ICU admission, 18(34.6%) had fundoscopy changes,17(32.6%) had imminent symptoms and 6(11.5%) were diagnosed as PRES.In our study, LDH levels were significantly elevated with disease severity. The majority of the complications were seen in women with elevated LDH(> 600U/L). These findings are in accordance with the studies done by Jaiswaret al.[10] and Vinitha PM et al.[13]. In another study by Demir et al.[14] LDH level was significantly higher in complicated cases of preeclampsia. Another study by Qublan HS et al.[12] reported that LDH is a biochemical marker for predicting adverse outcomes in severe preeclamptic patients. Results of our study were similar to these two studies.In our study, the serum UA levels were significantly higher in severe preeclampsia. This is in accordance with study done by Kamath et al.[11] andLiggy Andrew et al.[15]. Estimation of UA is important in identifying the risk of renal involvement and fetal compromise. Many authors believed that UA is one of the earliest and consistent parameters that occurs in preeclampsia and have been cited as a better predictor of fetalrisk.The above studies compared women with preeclampsia with normotensive pregnant as controls, whereas in our study, only women who met the criteria of hypertensive disorder of pregnancy were included.The decision on mode of delivery is a concern with the live fetus as the time for induction to delivery interval may vary, which can result in worsening of maternal and neonatal outcome; which may explain the high section rate(63.4%) in our study and similar to section rate(58.6%) in the study by Qublan HS et al.[12]. In our study, the mean gestational age at delivery was less in patients with increased LDH and UA levels which was also found in a study done by Jaiswaret al.[10] and Kamath et al.[11]. This indicates an increase in preterm, LBW and IUGR deliveries and NICU admissions in patients with higher LDH and UA levels. Qublan HS et al.[12] found IUGR in 33.9%, which was similar to our study(33.3%) in elevated LDH women. LBW(61.7%) in elevated UA was similar to the study by Kamath et al.[11] which was 68%. In our study, IUFD are more in women with increased LDH and UA, which was found similar to the study done by Vinitha PM et al.[13] and AU Hosna et al.[16] respectively.

Conclusion

Preeclampsia is a multi-system disorder leading to severe maternal and fetal complications. As ours is a small study group, we cannot conclude which biomarker is better, but both UA and LDH may be reliable in preeclampsia and its prognosis as per our study findings. Monitoring UA and LDH levels during the antenatal period may help in early intervention and help prevent complications and reduce maternal and fetal morbidity and mortality due to preeclampsia.

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