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Original Research Article

Study of estimation of serum LDH and uric acid in preeclampsia and it's clinical correlation

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ABSTRACT

Background: Preeclampsia occurs in 2-8% of pregnancies and a leading cause of maternal and perinatal mortality and morbidity. The objective of this study was to compare serum lactate dehydrogenase (LDH) and uric acid levels in normotensive pregnant women and in women with preeclampsia and to correlate the maternal and perinatal outcomes and severity of the disease with serum LDH and uric acid levels
Methods: A prospective case control study conducted during the period of 18 months involving 100 normotensive pregnant women and an equal no. of patients with preeclampsia admitted under OBG department, Vani Vilas Hospital and Bowring and Lady Curzon hospital, which are affiliated to BMCRI, Bangalore. They were followed up till delivery and early post-partum period. Serum LDH and uric acid levels were sent and maternal and foetal outcomes studied.
Results: There was statistically significant increase in levels of serum LDH and uric acid among cases compared to control group. Higher levels were also associated with significant maternal and foetal complications.
Conclusions: We conclude from this study that the serum LDH and Uric acid are the inexpensive and reliable markers to predict severity and maternal and foetal outcomes in patients with preeclampsia.

Keywords: Preeclampsia, Serum LDH, Uric acid

INTRODUCTION

Preeclampsia is a clinical syndrome characterised by hypertension and proteinuria. Preeclampsia occurs in 2-8% of pregnancies and a leading cause of maternal and perinatal mortality and morbidity.[1] The incidence is still higher in India of around 8-10%.[2] As per the world health report the maternal mortality during pregnancy and puerperium is around 12%. In developing countries, 17% of direct obstetric deaths are as a result of hyprtension.[3] The disorder is probably multifactorial, although most cases of preeclampsia are characterised by maternal uterine vascular remodelling by placental trophoblast cells. The most common models of the different reports available on animal models that have been used to study different aspects of preeclampsia are placental oxygen dysregulation, abnormal trophoblast invasion, inappropriate maternal vascular damage and maternal and foetal immune interactions.[4]

Lactate dehydrogenise (LDH) is mainly an intracellular enzyme. It is responsible for inter conversion of pyruvate and lactate in the cells. Its levels are several times greater inside the cells than in the plasma. So its levels are increased in the scenario of increased cell leakiness, hemolysis and cell death. Preeclampsia is a multisystem disorder and leads to a lot of cellular death. So, serum LDH levels can be used to assess the extent of cellular death and thereby the severity of disease.[5] Hence Serum LDH Levels can be further used as help in making decision, regarding the management strategies to improve the maternal and foetal outcome.

Uric acid (UA) is an end product of purine metabolism. It is filtrated through the glomeruli and almost completely reabsorbed in the proximal convoluted tubules (PCT) by both active and passive carrier mediated processes. It is also actively secreted into the tubules. 85% of total excreted UA is derived by tubular secretion. Hyperuricemia is found to be one of the earliest laboratory manifestations of preeclampsia.

It is likely to be resulted from reduced UA clearance from reduced glomerular filtration rate (GFR) and reduced tubular secretion. Its increased levels suggest serious impending damage to kidney functions.[6]

Aims and objectives

Aim and Objective were to compare serum LDH and uric acid levels in normal pregnant women and in women with preeclampsia and to correlate the maternal and perinatal outcomes and severity of the disease with serum LDH and uric acid levels.

METHODS

Study design

Comparative case control study.

Study period

November 2016 to May 2018.

Place of study

Vani Vilas Hospital and Bowring and Lady Curzon Hospital which are affiliated to BMCRI, Bangalore.

Sample size

100 from each group selected using random table sampling.

Inclusion criteria

All pregnant women ≥20 weeks of gestation were enrolled in this study and divided into following groups: healthy normotensive pregnant women- controls, patients of preeclampsia and eclampsia- cases. Cases are divided into two groups: non-severe preeclampsia and severe preeclampsia.[7]

Exclusion criteria

These included pregnant women with: essential hypertension or hypertension <20 weeks gestation, pre-existing diabetes mellitus, renal disease, liver disorder, thyroid disorder, alcoholic, epilepsy and urinary tract infection

Methodology

After obtaining approval from Institutional Ethical Committee and informed written consent, patients who satisfy inclusion and exclusion criteria were examined and plain blood samples were collected for estimation of serum LDH and UA levels using fully automated biochemical analyser. They were followed up till early postpartum period and babies till early neonatal period for maternal and foetal outcome.

Data analysis

Data was entered into Microsoft excel data sheet and was analyzed using Statistical package for social sciences (SPSS) 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test or Fischer's exact test (for 2×2 tables only) was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test or Mann Whitney U test was used as test of significance to identify the mean difference between two quantitative variables and qualitative variables respectively. P value less than 0.05 was considered statistically significant.

RESULTS

Mean LDH among cases was 533.19±707.79 (340) and among controls was 240.59±55.52 (226). Mean UA among cases and controls was 6.01±1.69 (5.8) and 3.88±0.81 (3.9) respectively. There was significant difference in incidence of eclampsia, HELLP syndrome and abruption between two groups.

Table 1: Comparison of LDH between two groups.

			Group		Total
			Cases	Controls	
LDH	<600 IU/L	Count	82	100	182
		%	82.0	100.0	91.0
	600 to 800 IU/L	Count	10	0	10
		%	10.0	0.0	5.0
	>800 IU/L	Count	8	0	8
		%	8.0	0.0	4.0

Continued.

		Group		Total
		Cases	Controls	
Total	Count	100	100	200
	%	100.0	100.0	100.0
Mean ± SD (Median)		533.19 ± 707.79 (340)	240.59 ± 55.52 (226)	p<0.001*

χ 2 =19.78, df =2, p <0.001*. Mean LDH among cases was 533.19±707.79 (340) and among controls was 240.59±55.52 (226).

Table 2: Comparison of Uric acid between two groups.

			Group		Total
			Cases	Controls	
Uric acid	<6	Count	54	100	154
		%	54.0	100.0	77.0
	>6	Count	46	0	46
		%	46.0	0.0	23.0
Total		Count	100	100	200
		%	100.0	100.0	100.0
Mean ± SD (Median)			6.01 ±1.69 (5.8)	3.88 ± 0.81 (3.9)	p<0.001*

χ 2 =59.74, df =1, p <0.001*. Mean UA among cases and controls was 6.01±1.69 (5.8) and 3.88±0.81 (3.9) respectively.

Table 3: Comparison of perinatal morbidity between two groups.

		Group				p value
		Cases		Controls		
		Count	%	Count	%	
LBW	No	66	66.0	87	87.0	<0.001*
	Yes	34	34.0	13	13.0	
IUGR	No	71	71.0	98	98.0	<0.001*
	Yes	29	29.0	2	2.0	
RD	No	89	89.0	96	96.0	0.06
	Yes	11	11.0	4	4.0	
Preterm	No	82	82.0	95	95.0	0.004*
	Yes	18	18.0	5	5.0	
Sepsis	No	92	92.0	96	96.0	0.234
	Yes	8	8.0	4	4.0	
NICU Admission	No	81	81.0	91	91.0	0.042*
	Yes	19	19.0	9	9.0	

Table 4: Maternal morbidity comparison between two groups.

		Group				p value
		Cases		Controls		
		Count	%	Count	%	
Eclampsia	No	92	92.0	100	100.0	0.004*
	Yes	8	8.0	0	0.0	
HELLP	No	94	94.0	100	100.0	0.013*
	Yes	6	6.0	0	0.0	
CNS Involvement	No	98	98.0	100	100.0	0.155
	Yes	2	2.0	0	0.0	
Febrile Illness	No	96	96.0	99	99.0	0.174
	Yes	4	4.0	1	1.0	
PPH	No	97	97.0	99	99.0	0.312
	Yes	3	3.0	1	1.0	
Abruption	No	95	95.0	100	100.0	0.024*
	Yes	5	5.0	0	0.0	

There was significant difference in incidence of eclampsia, HELLP syndrome and abruption between two groups.

Table 5: LDH and Uric acid levels comparison between NSPE and SPE.

Group statistics						
	Group	**N**	**Mean**	**SD**	**Median**	**P value**
LDH	NSPE	50	316.70	153.86	261.00	0.002*#
	SPE	50	749.36	954.36	437.50	
Uric acid	NSPE	50	5.248	1.493	4.80	<0.001*
	SPE	50	6.810	1.609	6.75	

Table 6: Association between LDH and perinatal morbidity and mortality among cases.

		LDH						P value
		<600		**600 to 800**		**>800**		
		Count	**%**	**Count**	**%**	**Count**	**%**	
LBW	No	58	70.7	6	60.0	2	25.0	0.031*
	Yes	24	29.3	4	40.0	6	75.0	
IUGR	No	62	75.6	5	50.0	4	50.0	0.095
	Yes	20	24.4	5	50.0	4	50.0	
RD	No	73	89.0	9	90.0	7	87.5	0.986
	Yes	9	11.0	1	10.0	1	12.5	
Preterm	No	69	84.1	8	80.0	5	62.5	0.310
	Yes	13	15.9	2	20.0	3	37.5	
Sepsis	No	77	93.9	8	80.0	7	87.5	0.275
	Yes	5	6.1	2	20.0	1	12.5	
NICU Admission	No	69	84.1	7	70.0	5	62.5	0.213
	Yes	13	15.9	3	30.0	3	37.5	
Perinatal Mortality	No	77	93.9	8	80.0	8	100.0	0.192
	Yes	5	6.1	2	20.0	0	0.0	

There was significant association between LBW and LDH levels.

Table 7: Association between uric acid and perinatal morbidity and mortality among cases.

		Uric acid				P value
		<6		**>6**		
		Count	**%**	**Count**	**%**	
LBW	No	42	77.8	24	52.2	0.007*
	Yes	12	22.2	22	47.8	
IUGR	No	42	77.8	29	63.0	0.106
	Yes	12	22.2	17	37.0	
RD	No	49	90.7	40	87.0	0.547
	Yes	5	9.3	6	13.0	
Preterm	No	49	90.7	33	71.7	0.014*
	Yes	5	9.3	13	28.3	
Sepsis	No	50	92.6	42	91.3	0.813
	Yes	4	7.4	4	8.7	
NICU Admission	No	46	85.2	35	76.1	0.248
	Yes	8	14.8	11	23.9	
Perinatal Mortality	No	52	96.3	41	89.1	0.162
	Yes	2	3.7	5	10.9	

There was significant association between uric acid levels with LBW and preterm.

Table 8: Association between LDH and maternal morbidity among cases.

		LDH						P value
		<600		600 to 800		>800		
		Count	%	Count	%	Count	%	
Eclampsia	No	77	93.9	10	100.0	5	62.5	0.005*
	Yes	5	6.1	0	0.0	3	37.5	
HELLP	No	82	100.0	8	80.0	4	50.0	<0.001*
	Yes	0	0.0	2	20.0	4	50.0	
CNS Involvement	No	81	98.8	10	100.0	7	87.5	0.084
	Yes	1	1.2	0	0.0	1	12.5	
Febrile Illness	No	80	97.6	10	100.0	6	75.0	0.006*
	Yes	2	2.4	0	0.0	2	25.0	
PPH	No	80	97.6	10	100.0	7	87.5	0.237
	Yes	2	2.4	0	0.0	1	12.5	
Abruption	No	78	95.1	9	90.0	8	100.0	0.622
	Yes	4	4.9	1	10.0	0	0.0	

There was significant association between eclampsia, HELLP syndrome and LDH levels.

Table 9: Association between uric acid and maternal morbidity among cases.

		Uric acid				P value
		<6		>6		
		Count	%	Count	%	
Eclampsia	No	53	98.1	39	84.8	0.014*
	Yes	1	1.9	7	15.2	
HELLP	No	53	98.1	41	89.1	0.058
	Yes	1	1.9	5	10.9	
CNS Involvement	No	54	100.0	44	95.7	0.122
	Yes	0	0.0	2	4.3	
Febrile Illness	No	52	96.3	44	95.7	0.870
	Yes	2	3.7	2	4.3	
PPH	No	54	100.0	43	93.5	0.057
	Yes	0	0.0	3	6.5	
Abruption	No	54	100.0	41	89.1	0.013*
	Yes	0	0.0	5	10.9	

There was significant association between uric acid and eclampsia and abruption.

Mean LDH among NSPE group was 316.70±153.86 and median LDH was 261.00 and in SPE group, mean LDH was 749.36±954.36 and median LDH was 437.50. There was significant difference in median LDH levels between NSPE and SPE groups. Mean UA in NSPE group was 5.248±1.493 mg/dl and in SPE group was 6.810±1.609 mg/dl. There was significant difference in mean UA levels between two groups.

DISCUSSION

Hypertensive disorders of pregnancy which frequently manifest as preeclampsia continues to exert an enormous toll in developing countries like India and also in western society. Despite progress in its prevention, detection and treatment, it continues to be the leading cause of maternal death. Research over last decade proved the role of oxidative stress and inflammation in pathophysiology of preeclampsia. Oxidative stress, xanthine oxidase activity and inflammation are important contributors. Various traditional and newer biomarkers were suggested for diagnosis and prognosis of preeclampsia.

In view of this, the present study has been taken up to assess clinical utility of some of the promising biochemical markers like serum LDH and uric acid.

In the present study, the mean maternal age among cases was 23.54±3.23 years and among controls was 23.33±3.16 years which is comparable to Umasatyasri et al study, 24.5±3.46 and 23.46±3.29 years among cases and controls respectively.[8]

The mean gestational age in the present study 37.8±1.8 weeks among cases is comparable to Umasatyasri et al study (37.6±2.76 weeks and 36.7±2.96 weeks among those with LDH less than 600 and between 600-800).[8]

Most of the patients in the present study were primipara (67% among cases and 64% among controls) which is comparable to Yadav et al (54% and 48% respectively).[9]

Mean systolic blood pressure (BP) among cases and controls was 155.98±13.32 mmhg and 117.94±9.87 mmhg respectively which is comparable to Sonagra et al study, 157±8.77 mmhg and 113±5.34 mmhg respectively among cases and controls.[10]

Mean diastolic BP among cases and controls was 103.46±2.05mmhg and 74.52±5.19mmhg respectively which is comparable to Gandhi et al (96.24±6.65 mmhg and 70.13±5.21mmhg respectively).[11]

Mean serum LDH levels among cases and controls was 533.19±707 IU/L and 240.59±55.5 IU/L respectively which is comparable to Umasatyasri et al study which showed serum LDH levels of 646.95±401.64 IU/L among severe preeclampsia group, 400.45±145.21 among mild preeclampsia group and 278.3±119.2 IU/L among normotensives.[8] Mean serum LDH levels among severe preeclampsia group was higher compared to non-severe preeclampsia indicating that there was significant rise in the LDH levels with increasing severity of the disease. Also comparable to Qublan et al study.[12] They concluded that serum LDH can be a useful marker for the prediction of adverse outcomes of pregnancy in severe preeclampsia.

In the present study there was significant association between LBW and LDH levels. Among those with LDH <600, 29.3% had LBW, those with LDH 600 to 800, 40% had LBW and those with LDH with >800, 75% had LBW. With increase in LDH levels there was increase in incidence of LBW among cases.

In the present study, there was significant association between eclampsia, HELLP syndrome and LDH levels. Those with LDH <600, 6.1% had eclampsia. Those with LDH levels 600 to 800, 20% had HELLP. Those with LDH>800, 37.5% had eclampsia and 50% had HELLP.

Mean uric acid levels among cases and controls was 6.01±1.69 mg/dl and 3.88±0.81 mg/dl in the present study which is statistically significant and comparable to Gandhi et al study of 5.94 mg/dl and 4.63 mg/dl respectively.[11]

In the present study, there was significant association between uric acid and eclampsia and abruption. Those with uric acid levels<6, 1.9% had eclampsia and none had abruption and those with UA>6, 15.2% had eclampsia and 10.9% had abruption. This indicates that the levels of uric acid can be used as a marker for prediction of maternal complication and for prevention of these complications by early intervention.

In the present study, there was significant association between UA levels with LBW and preterm i.e. among those with uric acid levels<6, 22.2% had LBW, 9.3% had preterm. Among those with uric acid levels >6, 47.8% had LBW and 28.3% had preterm.

Limitation of this study is that the sample size is not large enough to make generalization of results and baseline values of serum LDH and uric acid were not available for cases as it was measured after diagnosing preeclampsia.

CONCLUSION

In this study, mean serum LDH and Uric acid levels were significantly higher among cases compared to control group, their levels were higher among those with severe preeclampsia compared to non-severe preeclamsia and their increasing levels were associated with higher maternal and perinatal morbidity. So we conclude from this study that the serum LDH and Uric acid are the inexpensive and reliable markers to predict severity and maternal and foetal outcomes in patients with preeclampsia.

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