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RESEARCH ARTICLE

Estimation of C-reactive protein (CRP), serum uric acid (UA) and LDH in women with preeclampsia

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ABSTRACT

Background: For pre-eclampsia with the involvement of various systems, several markers have been proposed. The value of CRP indicates the severity of endothelial cell injury. Endothelial cell injury is one of the responsible factors for developing or initiating preeclampsia. During pre-eclampsia due to the extent of cellular death, the severity of the disease can be assessed by serum LDH levels. Serum uric acid levels reflect the circulating xanthine oxidase activity and oxidative stress production. **Objectives:** The objective of this study was to find out the correlation of C-reactive protein, serum uric acid and serum LDH with the severity of pre-eclampsia. **Methodology:** Serum levels of CRP, LDH and uric acid were estimated among the study group included of preeclamptic & eclamptic antenatal patients (n=150) and the control group included normotensive antenatal women (n=50). Student t-tests and chi-square tests were used for statistical analysis. **Results:** The mean value of CRP in the study group was 24.80 ±24.70 mg/L which was significantly higher than the control group i.e. 1.20± 4.37 mg/L (p =0.001). The mean value of serum uric acid level in the study group was significantly higher (6.16±3.39 mg/dl) than in the control group (3.09±0.53 mg/dl) (p= 0.001). The mean value of LDH in the study group was also significantly higher 698.95±624.08 U/L than 301.24±124.59 U/L in the control group (p= 0.001). **Conclusion:** Monitoring of CRP, LDH and uric acid can help diagnose the severity, and progression of the disease process and help prevent maternal complications. Increased serum CRP level is correlated with preeclampsia being an indirect risk factor for placental vasculopathy predating clinical preeclampsia.

Keywords: C- reactive protein (CRP), hypertension, LDH, preeclampsia, pregnancy, uric acid.

Preeclampsia (PE), is characterized by hypertension, proteinuria and ischemic end-organ damage.[1] Chronic hypertension with evidence of preeclampsia, is classified as chronic hypertension with superimposed preeclampsia. The occurrence of seizures in women with preeclampsia is characterized as eclampsia.[2] For preeclampsia with involvement of various systems, several markers have been proposed, like markers for renal and liver function – urea, creatinine, uric acid, aspartate and alanine transaminases, vascular function (prostacyclin, thromboxane, fibronectin, homocysteine, nitric acid, cytokines), coagulation and fibrinolytic systems (tissue plasminogen activators, platelets, fibrinogen, antithrombin III, Von Willebrand factor), oxidative stress and lipids (lipid peroxides, antioxidants, lipoproteins), and placental function (human chorionic gonadotropin, corticotrophin-releasing hormone, placental growth factor, α-fetoprotein, inhibin, activin, and uteroplacental flow (velocity waveform).[3-5]

The value of CRP indicates the severity of endothelial cell injury. Endothelial cell injury is one of the responsible factors for developing or initiating preeclampsia.[6] The CRP assay is simple, quick and affordable. CRP is easily measurable and not too invasive, requiring a simple blood draw for the assay. The half-life of CRP is 19 hours and it is

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cleared from the bloodstream fairly quickly as preeclampsia resolves.[7] For these reasons, we saw that CRP is a good biomarker of the severity of preeclampsia.

There is a lot of cellular death in preeclampsia. So, the extent of cellular death and thereby the severity of the disease can be assessed by serum LDH levels.[8] Lactate dehydrogenase converts pyruvate, the final product of glycolysis, to lactate with concomitant interconversion of NADH and NAD+ when oxygen is absent or in hypoxia, and it catalyses the reverse reaction during the Cori cycle in the liver. At high concentrations of lactate, the rate of conversion of pyruvate to lactate is decreased due to the feedback inhibition of the enzyme.[8]

Serum uric acid levels reflect the circulating xanthine oxidase activity and oxidative stress production. There are studies which demonstrate that the development of preeclampsia is associated with hyperuricemia.[9,10] But yet, the role of uric acid in preeclampsia is less clear. Some studies reported an independent association between uric acid and preeclampsia, but others found prognostic and also diagnostic significance.[11,12]

Thus the study was conducted to find out the correlation of C-reactive protein, serum uric acid and serum LDH with the severity of pre-eclampsia.

Material and methods

The present prospective study was conducted in the department of obstetrics and gynaecology in association with the department of biochemistry and department of microbiology, Govt. Medical College, Rajindra Hospital, Patiala, Punjab during the period 2018-2019 after obtaining ethical clearance from the institutional ethical committee.

200 pregnant women were included in the study after fulfilling inclusion criteria. Inclusion criteria consisted of gestational age > 20 weeks, prime/multigravida, antenatal patients of age 18 – 40 years and all antenatal patients' normotensive as well as hypertensive, which do not fall under exclusion criteria. Exclusion criteria comprised patients with known renal disease, diabetes, hepatic dysfunction, alcoholism, dyslipidaemia, RH negative blood group, cardiac and infectious diseases; pre-existing hypertension before pregnancy or on any type of antihypertensive treatment; multiple pregnancies, PROM (premature rupture of membranes) and any symptomatic infectious disease. After fulfilling inclusion and exclusion criteria and taking informed consent, all the subjects were divided into 2 groups, the study group included preeclamptic & eclamptic antenatal patients (n=150) and the control group included normotensive antenatal women (n=50).

Under all aseptic conditions, a 5ml blood sample was taken by venipuncture in a plain vacutainer. Serum was used for estimation of serum levels of CRP, LDH and uric acid.

The semiquantitative CRP test was based on the principle of latex agglutination. Estimation of serum LDH was done by kit method via semi-auto analyser. Estimation of uric acid was done by kit method via a fully automated biochemistry analyser (EM-360).

The data obtained were compiled and analysed statistically using IBM SPSS version 22 software. Data were expressed in terms of mean±SD and percentage. Student t-test, chi-square test, and Pearson's correlation coefficient were used whenever found suitable and necessary. The statistical test is considered significant when the calculated p-value is less than 0.05 and considered highly significant when the p-value is less than 0.001.

Results

Table 1 shows that the mean age of subjects in the study group was 25.75±4.54 years and in the control group 25.30±4.01 years, which was statistically non-significant. The majority of subjects in both groups were in the age group of 21 to 25 years. 8.67% of subjects in the study group and 6% in the control group were below 21 years of age.

Table 1: Age-wise distribution of subjects

Age group	Study group		Control group		Total	
(Years)	N	%	N	%	N	%
18-20	13	8.67	03	6	16	8
21-25	71	47.33	28	56	99	49.50
26-30	44	29.33	11	22	55	27.50
≥31	22	14.67	08	16	30	15
Total	150	100	50	100	200	100
Mean±SD	25.75±4.54		25.30±4.01		25.63±4.41	
Median	25.00		25.00		25.00	
Range	18-40		18-34		18-40	
t-test				0.620		
p value				0.536		

It was observed that 38% of subjects had non-severe pre-eclampsia and 31.33% had severe pre-eclampsia. Eclampsia was seen in 30.67% of patients (table 2).

Table 2: Distribution of subjects in study group according to severity of preeclampsia

Variables	N	%
Non-Severe PE	57	38
Severe PE	47	31.33
Eclampsia	46	30.67
Total	150	100

Table 3 shows, that 97.83% of the subjects with eclampsia had CRP levels > 6mg/L. In severe preeclampsia group 93.62% subjects and 75.44% subjects in non-severe pre-eclampsia group had CRP levels > 6mg/L. However 92% subjects in control groups had CRP levels < 6mg/L. This difference was found to be highly significant (p=0.001).

Table 3: Comparison of CRP levels in control and study group

Group	≤6 mg/L		>6 mg/L		X2	P value
	N	%	N	%		
Control (50)	46	92	4	8	37.34	0.001 (HS)
Non-severe PE (57)	14	24.56	43	75.44	51.73	0.001 (HS)
Severe PE (47)	3	6.38	44	93.62	31.75	0.001 (HS)
Eclampsia (46)	1	2.17	45	97.83	10.99	0.001 (HS)
Total (200)	64	32	136	68	25.20	0.001 (HS)

96% of subjects in the control group & 91.23% of subjects in the non-severe pre-eclampsia group had serum uric acid in the range of 2.4-5.7 mg/dl. Serum uric acid level >5.7 mg/dl was observed in 74.47% of subjects with severe pre-eclampsia and 84.78% of subjects with eclampsia. This difference was found to be highly significant (p=0.001) (table 4).

Table 4: Comparison of serum uric acid levels in control and study group

Group (No. of patients)	<2.4 (mg/dl)		2.4 - 5.7 (mg/dl)		>5.7 (mg/dl)		X2	P value
	N	%	N	%	N	%		
Control (50)	2	4	48	96	0	0	27.35	0.001 (HS)
Non-severe PE (57)	1	1.75	52	91.23	4	7.02	33.32	0.001 (HS)
Severe PE (47)	0	0	12	25.53	35	74.47	41.89	0.001 (HS)
Eclampsia (46)	0	0	7	15.22	39	84.78	38.58	0.001 (HS)
Total (200)	3	1.50	119	59.50	78	39	83.83	0.001 (HS)

Table 5 shows that 91.30% of the subjects with eclampsia had higher LDH levels >800 U/L. In severe pre-eclampsia, 34.04% of subjects had LDH levels >800 U/L and another 34.04% of subjects had LDH levels in the range of 600 - 800 U/L. In the non-severe pre-eclampsia group, 80.70% of subjects had LDH levels <600U/L. However, 94% of subjects in the control groups had LDH levels <600 IU/L. This difference was found to be highly significant (p=0.001).

Table 5: Comparison of LDH levels in control and study group

Group (No. of patients)	<600 U/L		600-800 U/L		>800 U/L		X2	P value
	N	%	N	%	N	%		
Control (50)	47	94	3	6	0	0	33.84	0.001 (HS)
Non-Severe PE (57)	46	80.70	11	19.30	0	0	50.76	0.001 (HS)
Severe PE (47)	15	31.91	16	34.04	16	34.04	9.25	0.003 (S)
Eclampsia (46)	0	0	4	8.70	42	91.30	34.27	0.001 (HS)
Total (200)	108	54	34	17	58	29	15.08	0.001 (HS)

It was observed that the mean value of CRP in the study group was 24.80 ±24.70 mg/L which was quite higher than that of the control group i.e. 1.20± 4.37 mg/L and this difference was statistically significant (p =0.001). The mean value of serum uric acid level in the study group is higher (6.16±3.39 mg/dl) than that of the control group (3.09±0.53 mg/dl) & this difference was statistically significant (p= 0.001). The mean value of LDH in the study group was 698.95±624.08 U/L and 301.24±124.59 U/L in the control group & this difference was statistically significant (p= 0.001) (table 6).

Table 6: Comparison between mean value of CRP, S. uric acid and S. LDH level in study group and control group

Group	Group	N	Mean	SD	Std.error mean	t-test	P value
CRP (mg/L)	Study group	150	24.80	24.70	2.02	6.71	0.001
	Control group	50	1.20	4.37	0.62		
S. uric acid (mg/dl)	Study group	150	6.16	3.39	0.28	6.383	0.001
	Control group	50	3.09	0.53	0.07		
LDH (U/L)	Study group	150	698.95	624.08	50.96	4.47	0.001
	Control group	50	301.24	124.59	17.62		

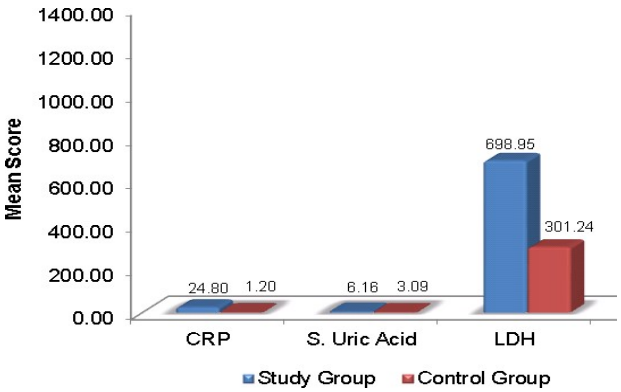

Figure 1: Comparison between mean value of CRP, S. Uric acid and S. LDH level in study group and control group

Discussion

Hypertensive disorders of pregnancy frequently manifested 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 the last decade proved the role of oxidative stress and inflammation in the pathophysiology of preeclampsia. Our study was conducted to determine the level of C- reactive protein, serum uric acid and serum LDH in preeclampsia women along with its relation with normal pregnant women.

Globally the incidence of preeclampsia has been estimated at 5- 14% of all pregnancies.[13,14] In the United States the incidence of preeclampsia in healthy nulliparous women, is estimated to range from 2% to 6%.[15-17] Preeclampsia & eclampsia, are one of the leading causes of the admission of pregnant women to the intensive care unit.[18] Overall 10%–15% of maternal deaths are directly caused by preeclampsia and eclampsia.[19] According to WHO the incidence of preeclampsia is seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%). The incidence of preeclampsia in India is 8-10% of pregnancies.[20]

The mean age of subjects enrolled in the study group was 25.75±4.54 years and in the control group 25.30±4.01 years. The majority of subjects in both groups were in the age group of 21 to 25 years. In a study conducted by Mehta M et al,[21] the mean age (in years) of cases was 5.74 ± 4.70 and that of controls was 24.96 ± 4.42 (P > 0.05) and was statistically non-significant. In a study conducted by Sharmin S et al,[22] the mean age showed no significant difference between the study (24.58±4.05 years) and control (23.92±3.72 years).

The level of serum CRP is higher in preeclamptic patients than the normal pregnant women. These results are in agreement with the previous report of Kumru S et al[23] who had recorded an elevation of plasma CRP among preeclamptic women when compared to their matched controls and a positive significant correlation (r= + 0.9, p=0.05) between CRP levels and pre-eclampsia severity.

In our study, we observed that 84.78% of subjects with eclampsia and 74.47% of subjects with severe preeclampsia have uric acid levels more than the upper limit of the normal range (>5.7 mg/dl). This finding is in accordance with the study done by Punthumapol C et al,[24] Josephine PL,[25] Gandhi M et al.[26] During pregnancy maternal serum uric acid levels initially fall, with a subsequent rise to prepregnancy levels near term. The third trimester rise in uric acid may be related to an increase in foetal uric acid production or a decrease in uric acid clearance. Elevated serum uric acid levels due to decreased renal urate excretion are frequently found in women with preeclampsia. Besides the reduced clearance hyperuricemia in preeclampsia may be due to increased uric acid production caused by trophoblast breakdown, cytokine release and ischemia. Uric acid can promote endothelial dysfunction, damage and inflammation, which leads to oxidation. So, preeclampsia, which is characterized by widespread endothelial dysfunction and inflammation, might be propagated by uric acid.

In the present study, we found that 91.30% of subjects with eclampsia and 34.04% of subjects with severe preeclampsia have serum LDH >800U/L. Similar results were seen in a study by Gandhi M et al [26]. They found a significant increase in serum LDH and serum uric acid levels in women with hypertension in comparison with normotensive women. The finding was in accordance with a study done by Umasatyasari Y et al[27] and Bera S et al.[28] Quablan H et al[29] concluded serum LDH can be used as a marker for the prediction of adverse outcomes of pregnancy in severe preeclampsia.

Conclusion

Preeclampsia is a multisystem disorder of pregnancy. The pregnant women with preeclampsia associated with elevated CRP, serum uric acid and LDH levels were at a greater risk for antepartum complications and adverse pregnancy outcomes. Hence by serial monitoring of these inexpensive biomarkers, we would be able to know the severity and progression of the disease process. Prompt termination of pregnancy in such cases would prevent maternal complications. Increased serum CRP levels are correlated with preeclampsia being an indirect risk factor for placental vasculopathy predating clinical preeclampsia.

Conflict of interest: None. **Disclaimer:** Nil.

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