e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(8); 1094-1098

Original Research Article

Estimation of C-reactive Protein (CRP), Serum Uric Acid (UA) and LDH in Women with Preeclampsia

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Received: 30-05-2023 / Revised: 30-06-2023 / Accepted: 30-07-2023

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Conflict of interest: Nil

Abstract:

Background: Several markers have been proposed for pre-eclampsia using different systems. The level of CRP reflects the extent of endothelial cell damage. One of the causes of preeclampsia's onset or progression is endothelial cell damage. Serum LDH levels can be used to gauge the severity of the condition during pre-eclampsia due to the degree of cellular death. The circulating xanthine oxidase activity and oxidative stress generation are reflected in the serum uric acid levels. The purpose of this study was to determine the relationship between blood LDH, uric acid, and C-reactive protein and the severity of pre-eclampsia.

Methods: Preeclamptic and eclamptic prenatal patients (n=150) in the study group and normotensive pregnant women (n=50) in the control group had their serum levels of CRP, LDH, and uric acid measured. For statistical analysis, chi-square tests and student t-tests were employed.

Results: In comparison to the control group, where the mean CRP value was 1.20±4.37 mg/L, the study group mean CRP value was 24.80±24.70 mg/L (p = 0.001). When compared to the control group, the study group mean serum uric acid level was considerably higher (6.16±3.39 mg/dl) (p=0.001) than the control group (3.09±0.53 mg/dl). Additionally, the mean LDH in the study group was substantially greater than the control group (p=0.001), 698.95±624.08 U/L versus 301.24±124.59 U/L.

Conclusion: Monitoring of CRP, LDH, and uric acid can aid in determining the severity and course of the disease as well as aid in avoiding difficulties for the mother. An indirect risk factor for placental vasculopathy, which precedes clinical preeclampsia, is an elevated serum CRP level in preeclampsia.

Keywords: C- Reactive Protein (CRP), Hypertension, LDH, Preeclampsia, Pregnancy, Uric Acid.

Introduction

Proteinuria, ischemia end-organ damage, and hypertension are the hallmarks of preeclampsia (PE).[1] Preeclampsia with signs of chronic hypertension is referred to as preeclampsia superimposed on chronic hypertension. Eclampsia is the term used to describe women who experience seizures due to preeclampsia.[2] Several markers have been proposed for preeclampsia with involvement of multiple systems, including 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.[3-5]

The level of CRP reflects the extent of endothelial cell damage. One of the causes of preeclampsia's onset or progression is endothelial cell damage.[6] The CRP assay is easy, rapid, and reasonably priced. CRP is easily quantifiable and not overly invasive; the assay just needs a small blood sample. CRP has a 19-hour half-life, and as preeclampsia resolves, it leaves the bloodstream pretty quickly.[7] These factors led us to the conclusion that CRP is an accurate biomarker of the severity of preeclampsia.

In preeclampsia, there is a lot of cellular death. Therefore, serum LDH levels can be used to determine the degree of cellular death and, consequently, the severity of the disease.[8] When oxygen is not present or when there is hypoxia, lactate dehydrogenase converts pyruvate, the end product of glycolysis, to lactate with the simultaneous interconversion of NADH and NAD+. It also catalyzes the opposite reaction during the Cori cycle in the liver. The feedback inhibition of the enzyme lowers the

rate of pyruvate to lactate conversion at high lactate concentrations.8

The circulating xanthine oxidase activity and oxidative stress generation are reflected in the serum uric acid levels. Studies have shown that hyperuricemia and the emergence of preeclampsia go hand in hand.[9,10] However, it's not quite apparent how uric acid contributes to preeclampsia. Uric acid and preeclampsia have been linked independently in certain studies, although other research has demonstrated predictive and diagnostic importance.[11,12]

Therefore, the purpose of the study was to determine whether the levels of blood LDH, uric acid, and C-reactive protein were correlated with the severity of pre-eclampsia.

Material and Methods

From October 2020 to September 2021, the current prospective study was carried out at the Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, in the department of Obstetrics and Gynecology with association of department Biochemistry and Microbiology. 200 expectant mothers who met the inclusion requirements were enrolled in the study. Gestational age greater than 20 weeks, primi/multigravida, prenatal patients aged 18 to 40, and all antenatal patients with hypertension or normotension who did not meet the exclusion criteria made up the inclusion criteria. Patients with known renal disease, diabetes, hepatic dysfunction, alcoholism, dyslipidemia, RH negative blood group, cardiac and infectious diseases, pre-existing hypertension prior to pregnancy or receiving any type of antihypertensive treatment, multiple pregnancies, PROM (premature rupture of membranes), and any infectious disease with symptoms were excluded from the study. All subjects were separated into 2 groups after meeting inclusion and exclusion criteria and providing informed consent. The study group consisted of preeclamptic and eclamptic prenatal patients (n=150), and the control group consisted of normotensive pregnant women (n=50).

A 5ml blood sample was drawn by venipuncture into an unadorned vacutainer under all aseptic conditions. CRP, LDH, and uric acid serum levels were estimated using serum.

The concept of latex agglutination served as the foundation for the semiquantitative CRP test. Serum LDH was calculated using a kit approach and a semi-automatic analyzer. A fully automated biochemistry analyzer (EM-360) was used to estimate uric acid using a kit approach.

IBM SPSS version 20 software was used to compile and statistically analyze the data. Data were presented as mean, standard deviation, and percentage. When appropriate and required, the student t-test, chi-square test, and Pearson's correlation coefficient were applied. When the estimated p-value is less than 0.05 and less than 0.001, the statistical test is deemed significant and highly significant, respectively.

Results

The mean age of the subjects in the study group was 25.75±4.54 years, while it was 25.30±4.01 years in the control group. This difference was statistically insignificant. Most of the subjects in both groups were between the ages of 21 and 25. In the study group, 8.67% of participants and 6% in the control group were under the age of 21.

Table 1: Age-wise Distribution of subjects

Age group (years)	Study Group n(%)	Control Group n(%)	Total n(%)
18-20	13(8.67%)	3(6.0%)	16(8.0%)
21-25	71(47.33%)	28(56.0%)	99(49.50%)
26-30	44(29.33%)	11(22.0%)	55(27.50%)
≥31	22(14.67%)	8(16.0%)	30(15.0%)
Total	150(100.0%)	50(100.0%)	200(100.0%)

38% of the individuals had non-severe preeclampsia, and 31.33% had severe preeclampsia, it was found. In 30.67% of patients, eclampsia was seen (table 2).

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

Variables	No. of patients	Percentage
Non-Severe Preeclampsia	57	38.0%
Severe Preeclampsia	47	31.33%
Eclampsia	46	30.67%
Total	150	100.0%

Table 3 reveals that CRP levels were greater than 6 mg/L in 97.83% of the participants who developed eclampsia. Subjects with CRP levels more than 6 mg/L were found in 93.62% of those with severe preeclampsia and 75.44% of those with non-severe preeclampsia. CRP levels were <6 mg/L in 92% of control group participants, nevertheless. High significance was discovered for this difference (p=0.001).

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

Group	<6 mg/L n(%)	>6 mg/L n(%)	X^2	p-value
Control (50)	46(92.0%)	4(8.0%)	37.34	0.001(HS)
Non-severe preeclampsia (57)	14(24.56%)	43(75.44%)	51.73	0.001(HS)
Severe Preeclampsia (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(68.0%)	25.20	0.001(HS)

Serum uric acid levels were between 2.4 to 5.7 mg/dl in 96% of patients in the control group and 91.23% of subjects in the non-severe pre-eclampsia group. Both 74.47% of participants with severe pre-eclampsia and 84.78% of subjects with eclampsia had serum uric acid levels >5.7 mg/dl. Table 4 shows that this difference was judged to be very significant (p=0.001).

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

Group (N)	<2.4 mg/dl n(%)	2.4-5.7 mg/dl n(%)	>5.7 mg/dl n(%)	X^2	p-value
Control (50)	2(4.0%)	48(96.0%)	0	27.35	0.001(HS)
Non-severe preeclampsia (57)	1(1.75%)	52(91.23%)	4(7.02%)	33.32	0.001(HS)
Severe Preeclampsia (47)	0	12(25.53%)	35(74.47%)	41.89	0.001(HS)
Eclampsia (46)	0	7(15.22%)	39(84.78%)	38.58	0.001(HS)
Total (200)	3(1.50%)	119(59.50%)	78(39.0%)	83.83	0.001(HS)

According to Table 5, 91.30% of the subjects with eclampsia had LDH levels that were higher than 800 U/L. In cases of severe pre-eclampsia, 34.04% of individuals had LDH levels greater than 800 U/L while another 34.04% had levels between 600 and 800 U/L. 80.70% of the individuals in the non-severe pre-eclampsia group had LDH levels below 600U/L. But 94% of participants in the control groups had LDH concentrations below 600 IU/L. High significance was discovered for this difference (p=0.001).

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

Group (N)	<600 U/L n(%)	600-800 U/L n(%)	>800 U/L n(%)	X^2	p-value
Control (50)	47(94.0%)	3(6.0%)	0	33.84	0.001(HS)
Non-severe preeclampsia (57)	46(80.70%)	11(19.30%)	0	50.76	0.001(HS)
Severe Preeclampsia (47)	15(31.91%)	16(34.04%)	16(34.04%)	9.25	0.003(S)
Eclampsia (46)	0	4(8.70%)	42(91.30%)	34.27	0.001(HS)
Total (200)	108(54.0%)	34(17.0%)	58(29.0%)	15.08	0.001(HS)

It was found that the mean CRP in the study group was 24.80± 24.70 mg/L, which was significantly higher than the mean CRP in the control group, which was 1.20±4.37 mg/L (p = 0.001). When compared to the control group, the study group mean serum uric acid level was higher (6.16±3.39 mg/dl) and this difference was statistically significant (p=0.001). LDH was measured on average at 698.95±624.08 U/L in the study group and 301.24±124.59 U/L in the control group. This difference was statistically significant.

Table 6: Comparison between mean value of CRP, Serum uric acid and serum LDH levels in study group and control group

	Group	No.	Mean	SD	SE	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		
Serum 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		

Discussion

Preeclampsia, a common symptom of hypertensive disorders of pregnancy, continues to take a terrible toll on both western culture and emerging nations like India. It remains the primary cause of maternal death despite advancements in prevention, identification, and treatment. Over the past ten years, research has established the importance of inflammation and oxidative stress in the pathogenesis of preeclampsia. The goal of our study was to compare the levels of C-reactive protein, serum uric

acid, and serum LDH in preeclampsia patients to those in healthy pregnant women.

Preeclampsia is thought to affect 5- 14% of all pregnancies worldwide.13,14 Preeclampsia is thought to occur between 2% and 6% of the time in healthy, nulliparous women in the United States.[15-17]

One of the main reasons pregnant women are admitted to the intensive care unit is preeclampsia and eclampsia.18

Preeclampsia and eclampsia are directly responsible for 10%–15% of all maternal fatalities.19 Preeclampsia is seven times more common in underdeveloped nations (2.8% of live births) than in industrialized ones (0.4%), according to the WHO. In India, 8–10% of pregnancies result in preeclampsia.[20]

In the study group, the average age of the participants was 25.75±4.54 years, while it was 25.30±4.01 years in the control group.

Most of the subjects in both groups were between the ages of 21 and 25. The mean age (in years) of the patients in a research by Mehta M et al.[21] was 5.74±4.70 while that of the controls was 24.96±4.42 ($P > 0.05$), which was statistically insignificant. In a study by Sharmin S et al.22, the mean age between the study group (24.58±4.05 years) and the control group (23.92±3.72 years) did not differ significantly.

Preeclamptic patients have greater serum CRP levels than typical pregnant women. These findings are in line with a prior study by Kumru S et al.[23], who found that preeclamptic women had higher plasma CRP levels than their matched controls and that there was a significant association between CRP levels and the severity of pre-eclampsia ($r= + 0.9$, $p=0.05$).

In our study, we found that uric acid levels in 84.78% of eclampsia patients and 74.47% of patients with severe preeclampsia are higher than the upper limit of the normal range (>5.7 mg/dl). This result is consistent with research by Gandhi M et al., Punthumapol C et al., Josephine PL, and others [23-26]. Near term, maternal blood uric acid levels rise to prepregnancy levels after initially declining throughout pregnancy. A surge in foetal uric acid synthesis or a decline in uric acid clearance may be responsible for the rise in uric acid throughout the third trimester. In women with preeclampsia, elevated blood uric acid levels caused by reduced renal urate excretion are typically observed. In addition to the decreased clearance, preeclampsia hyperuricemia may be brought on by an increase in uric acid synthesis brought on by trophoblast degeneration, cytokine release, and ischemia. Inflammation, endothelial damage, and dysfunction caused by uric acid can result in oxidation. Uric acid may therefore contribute to the spread of preeclampsia, which is characterized by extensive endothelial dysfunction and inflammation.

In the current investigation, we discovered that blood LDH levels were >800U/L in 91.30% of participants with eclampsia and 34.04% of subjects with severe preeclampsia. Gandhi M. et al.[26] conducted a study that produced similar findings. In comparison to normotensive women, they discovered that women with hypertension had significantly higher serum levels of LDH and uric acid. The results were consistent with research by Umasatyasari Y et al. [27] and Bera S et al. [28] Serum LDH can be utilized as a marker for the prediction of negative pregnancy outcomes in cases of severe preeclampsia, according to Quablan H et al [29].

Conclusion

Preeclampsia is a multisystemic pregnancy disease. The preeclamptic pregnant women at risk for antepartum problems and unfavorable pregnancy outcomes had higher levels of CRP, serum uric acid, and LDH. Therefore, we would be able to determine the severity and course of the disease process by serially monitoring these affordable biomarkers. In these situations, early pregnancy termination would avoid difficulties for the mother. Preeclampsia is associated with elevated serum CRP levels, which is an indirect risk factor for placental vasculopathy that precedes clinical preeclampsia.

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