

“A COMPARATIVE STUDY OF SERUM URIC ACID AND CRP LEVEL IN PREECLAMPSIA AND NORMAL PREGNANCY”

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ABSTRACT

Background – Preeclampsia (PE) is a pregnancy specific multisystem disorder in human beings, which may cause maternal and neonatal morbidity and mortality. The present study is an effort to estimate the serum uric acid level and serum CRP level in preeclamptic women and to find out any correlation between these parameters and the disease.

Methods – In this prospective study, total number of 110 subjects attending in antenatal clinic and labour room which include 55 pre-eclampsia patients as cases and 55 normotensive pregnant women as controls and both these study groups were studied in their third trimester of gestation. A standardized questionnaire was used and details pertaining to family history, medical and obstetric history was collected. Informed consent was taken from the patients. General examination and investigations were done. The patients were regularly examined and follow-up was taken till delivery.

Result – Higher level of CRP and uric acid are early marker of severe preeclampsia and it might be upregulated just before clinical disease. The correlation between preeclampsia with uric acid and CRP have been studied with in consistent result in predicting adverse maternal and fetal outcomes and these are preventable if identified at an early stage and adequately managed.

Conclusion – Serum uric acid and CRP is positively correlated with severity of preeclampsia. Identification of high-risk patients with elevated levels of serum uric acid and CRP, their close monitoring and prompt management may prevent or at least reduce the complications.

Keywords: - Pre-Eclampsia. Eclampsia, Serum Uric Acid, CRP levels, Maternal Morbidities

INTRODUCTION:

The global incidence of preeclampsia has been estimated at 5-14% of all pregnancies.[1, 2] In India the incidence of preeclampsia is reported to be 8-10% of the pregnancies.[3] While Immunologic factors have long been considered to be key players in preeclampsia, the endothelial cell dysfunction and inflammation are considered to have a crucial role in pathophysiological mechanism of preeclampsia.[4] An inflammatory response is usually accompanied by increasing concentrations of pro-inflammatory cytokines, acute-phase proteins and may involve leukocyte activation.

It has been suggested that elevated levels of CRP, in accordance with its proposed function, may reflect the inflammatory response characteristics of preeclampsia. Currently Endothelial Dysfunction is most popularly hypothesized to be a central pathophysiological feature of preeclampsia leading to altered vascular reactivity, loss of vascular integrity and activation of the coagulation cascade. [4, 5]

Uric acid (UA) is the major end-product of purine metabolism. The cause of hyperuricemia in preeclampsia has been attributed to either a decreased excretion or to an increased production of uric acid. Decreased uric acid clearance, reflected by altered tubular function has been documented, while in 1990 Fay proposed an increased breakdown of purines in the placenta as a possible explanation for the overproduction of uric acid.6 hyperuricemia is one of the most consistent and earliest detectable changes in preeclampsia and has been cited as a better predictor of fetal risk than blood pressure. [6]

C-reactive protein (CRP) is a sensitive marker of systemic inflammation and is primarily synthesized in hepatocytes in response to infection and tissue injury, which is stimulated by the release of pro-inflammatory cytokines. The value of CRP level reflects the severity of endothelial cell injury which is one of the responsible factors for developing or initiating preeclampsia.

A generalized activation of circulating leukocytes, characteristic of inflammation, has been found during PE. Moreover, increased concentrations of CRP and inflammatory cytokines have been reported in PE women. CRP is produced by the liver and the production is stimulated by the inflammatory cytokines, interleukin-6 and TNF-alpha. CRP level increases during inflammatory response to tissue injury or infection. CRP, though not pathology specific, as it increases in a number of conditions, is an objective and sensitive index of overall inflammatory activity in the body. Plasma CRP levels rise in cases of acute infection, malignancy & inflammatory diseases. It has been suggested that elevated levels of CRP, in accordance with its proposed function, may reflect the inflammatory response characteristics of preeclampsia.

Raised serum uric acid (UA) is one of the characteristic findings in preeclampsia. In clinical practice, serum UA determination is considered to be a part of the workup, in women with preeclampsia, to monitor disease severity, and aid management, of these women. [7] Hyperuricemia is a common finding in pre-eclamptic pregnancies. The elevation of uric acid in pre-eclamptic women, often precedes hypertension and proteinuria, the clinical manifestations, used to diagnose the disorder. [8] There are several potential origins, for uric acid in

preeclampsia; abnormal renal function, increased tissue breakdown, acidosis, and increased activity of the enzyme xanthine oxidase/dehydrogenase.[9]

The aim of the study is to establish baseline serum CRP and uric acid levels in both preeclampsia and normal pregnancy, assess the potential of CRP and uric acid as predictors of preeclampsia severity, and investigate their impact on maternal and perinatal outcomes in preeclampsia.

MATERIALS AND METHODOLOGY:

It is a hospital based prospective case – control study conducted from August 2020 – July 2021 conducted in the antenatal clinic in the Department of Obstetrics and Gynecology at Bokaro General Hospital. A total of 110 antenatal patients of third trimester of gestation were screened for preeclampsia after excluding pre-existing medical illness according to exclusion criteria. A standardized questionnaire was used and details pertaining to family history, medical and obstetric history was collected. Informed consent was taken from the patients. General examination had done for blood pressure, edema, and proteinuria. The investigations were included serum uric acid and CRP level. Proper proforma was maintained. The patients were regularly examined and follow-up up till delivery.

Inclusion Criteria:

Cases: Pregnant women in third trimester of gestation, who had diagnosed as having preeclampsia on the basis of Clinical history, examination, systolic blood pressure >140mmHg, diastolic blood pressure >90mmHg and proteinuria 300mg or more per 24 hour urine collection.

Controls: Apparently healthy singleton pregnant women in the third trimester of gestation.

Exclusion criteria

The exclusion criteria for this study include patients with a prior history of chronic renal disease, diabetes mellitus, cardiovascular disorders, and chronic hypertension. Additionally, patients with twin gestation and premature rupture of membranes, medical complications with superimposed preeclampsia, congenital malformations of the fetus, febrile illness, retroviral disease, or urinary tract infections, as well as those in active labor, will be excluded. Furthermore, patients who refuse to provide consent will also be excluded from participation in the study.

RESULTS

The study analyzed the age distribution in both the Case and Control Groups (Table 1). In the Case Group, most individuals (63.64%) were aged 21-25 years, followed by 16.36% aged ≤20 years, 14.55% aged 26-30 years, and 5.45% aged 31-40 years. In comparison, the Control Group had 49.09% aged 21-25 years, 41.82% aged 26-30 years, 3.64% aged ≤20 years, and 5.45% aged 31-40 years. A significant difference in age distribution between the two groups was evident ($p=0.0052$). The mean age in the Case Group was 23.84 ± 4.03 years, and in the Control Group, it was 25.25 ± 3.12 years. However, there was no significant difference in mean ages between the two groups ($p=0.1485$).

The mean gestational age (GA) in the Case Group was 36.60 ± 1.80 weeks, whereas in the Control Group, it was 35.10 ± 2.60 weeks. A statistically significant difference in mean GA between the two groups was observed ($p < 0.0001$).

Table 1. Comparison of demographic data of study participant in two groups

Age distribution (in year)	Group –I (CASE) (n=55)	Group –II (CONTROL) (n=55)	P Value
	No. of patients (%)	No. of patients (%)	
≤20 year	9 (16.36%)	2 (3.64%)	0.0052
21 – 25 years	35 (63.64%)	27 (49.09%)	
26 – 30 years	8 (14.55%)	23 (41.82%)	
31 – 40 years	3 (5.45%)	3 (5.45%)	
Average age (Yr)	23.84 ± 4.03	25.25 ± 3.12	
POG (Weeks)	36.60 ± 1.80	35.10 ± 2.60	<0.0001
Weight (Kg)	57.00 ± 3.98	56.00 ± 6.55	0.3354

POG=Period of Gestation,

In our present investigation, all 55 (100%) patients in the Control group exhibited normotensive conditions. However, within the Case group, 19 (34.55%) patients were diagnosed with Mild Preeclampsia, while 36 (65.45%) patients were diagnosed with Severe Preeclampsia. Statistical analysis revealed a significant contrast in the severity of Preeclampsia between the two groups, demonstrating a p-value of less than 0.0001 (Table 2).

Table 02: Distribution of cases between two groups

Groups	Control		Mild Preeclampsia		Severe Preeclampsia		χ^2_{cal}	P Value	Results
	No.	%	No.	%	No.	%			
Case	0	0%	19	34.55%	36	65.45%	110.00	<0.0001*	significant
Control	55	100%	0	0%	0	0%			

*P<0.05 is statistically significant using chi square test.

Table 03: Comparison of Blood Pressure between two groups

Mean ± SD (Beats per minute)	Group –I (CASE) (n=55)	Group –II (CONTROL) (n=55)	P value
SBP (mmHg)	158.70 ± 16.69	114.50 ± 5.70	<0.0001
DBP (mmHg)	103.60 ± 8.90	77.70 ± 4.40	<0.0001

A statistically significant difference was observed between the two groups in terms of the mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP). Specifically, the mean blood pressure values in the Case group patients were notably higher compared to those in the Control group, with a p-value of less than 0.0001 (Table 3).

Table no. 04: Association between Serum uric with Severity of Preeclampsia

Serum uric acid	Group –I (CASE) (n=55)				Group –II (CONTROL) (n=55)		P Value
	Mild Preecl. (n=19)		Severe Preecl. (n=36)				
	No.	%	No.	%	No.	%	
2 – 5 mg/dl	0	0%	0	0%	39	70.90%	<0.0001
5 – 7 mg/dl	12	63.16%	20	55.56%	16	29.10%	
>7 mg/dl	8	36.84%	16	44.44%	0	0%	

In the Control group, 39 (70.90%) patients exhibited serum uric acid levels within the range of 2-5 (mg/dl), while 16 (29.10%) patients had uric acid levels ranging from 5-7 (mg/dl). Among patients with Mild Preeclampsia, 12 (63.16%) had uric acid levels ranging from 5-7 (mg/dl), and 8 (36.84%) had uric acid levels exceeding 7 (mg/dl). In the Severe Preeclampsia subgroup, 20 (55.56%) patients had uric acid levels between 5-7 (mg/dl), and 16 (44.44%) patients had serum uric acid levels exceeding 7 (mg/dl). The aforementioned association between serum uric acid levels and the severity of Preeclampsia among patients in the two groups demonstrated statistically significant findings, with a p-value of less than 0.0001 (Table 4).

Table 5. Association of CRP with severity of preeclampsia

CRP	Group –I (CASE) (n=55)				Group –II (CONTROL) (n=55)		P Value
	Mild Preecl. (n=19)		Severe Preecl. (n=36)				
	No.	%	No.	%	No.	%	
< 5 mg/dl	0	0%	2	5.56%	27	49.10%	<0.0001
5 – 10 mg/dl	7	36.84%	7	19.44%	25	45.45%	
>10 mg/dl	12	63.16%	27	75%	3	5.45%	

Within the Control group, 27 (49.1%) patients exhibited C-reactive protein (CRP) levels below 5 (mg/dl), 25 (45.55%) patients displayed CRP levels ranging from 5 to 10 (mg/dl), and 3 (5.45%) patients had CRP levels exceeding 10 (mg/dl). In the subset of patients diagnosed with Mild Preeclampsia, 7 (36.84%) had CRP levels between 5 and 10 (mg/dl), while 12 (63.16%) patients presented with CRP levels surpassing 10 (mg/dl). Among those with Severe Preeclampsia, 2 (5.56%) patients exhibited CRP levels below 5 (mg/dl), 7 (19.44%) patients had CRP levels ranging from 5 to 10 (mg/dl), and 27 (75.0%) patients had CRP levels exceeding 10 (mg/dl). The aforementioned association between CRP levels and the severity of Preeclampsia within the two groups demonstrated statistically significant results, with a p-value of less than 0.0001 (Table 5).

Table 6. Comparison of mode of delivery between two groups

Mode of delivery	Group –I (CASE) (n=55)		Group –II (CONTROL) (n=55)		P Value
	N	%	N	%	
VD	24	43.64%	43	78.18%	0.001
Forceps	2	3.64%	0	0%	
LSCS	29	52.73%	12	21.82%	

Within the Case Group, 2 (3.64%) patients underwent forceps delivery, 29 (52.73%) patients underwent lower segment cesarean section (LSCS), and 24 (43.64%) patients had vaginal delivery (VD). In contrast, within the Control Group, 12 (21.82%) patients underwent LSCS, and 43 (78.18%) patients had VD. A statistically significant difference was observed in the comparison of mode of delivery between the two groups, with a p-value of less than 0.05 ($p<0.05$).

Table 7. Comparison of type of maternal complications between two groups

Maternal complications	Group –I (CASE) (n=55)		Group–II (CONTROL) (n=55)		P Value
	No. of patients	%	No. of patients	%	
Abruption	4	7.27%	1	1.82%	0.17
ARDS	2	3.64%	0	0%	0.15
ARF	3	5.45%	0	0%	0.08
Eclampsia	10	18.18%	0	0%	0.001
DIC	2	3.64%	0	0%	0.15
HELLP	6	10.91%	0	0%	0.01
pulm oedema	3	5.45%	0	0%	0.08
PPH	7	12.73%	2	3.64%	0.08
NIL	30	54.55%	52	94.54%	<0.0001

Within the Case Group, 4 (7.27%) patients experienced placental abruption, 2 (3.64%) patients suffered from acute respiratory distress syndrome (ARDS), 3 (5.45%) patients developed acute renal failure (ARF), 10 (18.18%) patients manifested eclampsia, 2 (3.64%) patients encountered disseminated intravascular coagulation (DIC), 6 (10.91%) patients were diagnosed with HELLP syndrome, 3 (5.45%) patients exhibited pulmonary edema, 3 (5.45%) patients presented with pulmonary edema, and 7 (12.7%) patients encountered postpartum hemorrhage (PPH). Conversely, within the Control Group, 1 (1.8%) patient experienced placental abruption, and 2 (3.6%) patients encountered postpartum hemorrhage (PPH). Among all the aforementioned conditions, eclampsia, HELLP syndrome, and pulmonary edema demonstrated statistically significant associations, with p-values less than 0.05 ($p<0.05$), while placental abruption, ARDS, DIC, and PPH did not display statistically significant associations, with p-values greater than 0.05 ($p>0.05$), except for eclampsia and HELLP syndrome which exhibited significant results ($p<0.05$).

DISCUSSION

In this prospective study, a total of 110 subjects participated, comprising 55 pre-eclampsia patients as cases and 55 normotensive pregnant women as controls. Both groups were evaluated during their third trimester of gestation. Among the pre-eclampsia patients, 19 (34.5%) exhibited mild symptoms, while 36 patients presented with severe manifestations. The mean gestational age (GA) in the Case Group was 36.60 ± 1.80 weeks, whereas in the Control Group, it was 35.10 ± 2.60 weeks. A statistically significant difference in mean GA between the two groups was observed ($p < 0.0001$).

In the study conducted by K. Kameshwarama et al., the mean gestational age in the cases group was reported as 32.6 ± 2.8 weeks, while in the control group it was 33.5 ± 3.9 weeks, with a p-value of 0.08, which aligns closely with the findings of the current study [10]. Furthermore, our investigation revealed a statistically significant difference in mean systolic blood pressure (SBP) between the Case Group [158.70 ± 16.69 mmHg] and the Control Group [114.50 ± 5.70 mmHg] ($p < 0.0001$). This observation is consistent with the findings of Begum G et al., who reported a mean SBP of 153.59 ± 12.42 mmHg in cases and 114.90 ± 8.7 mmHg in controls. Additionally, they found mean diastolic blood pressure (DBP) values of 101.65 ± 9.72 mmHg in cases and 74.80 ± 7.03 mmHg in controls, which also corresponds with our present study [11].

In Mild Preeclampsia, 12 (63.16%) patients exhibited uric acid levels between 5-7 (mg/dl), while 8 (36.84%) patients displayed uric acid levels exceeding 7 (mg/dl). Among those diagnosed with Severe Preeclampsia, 20 (55.56%) patients had uric acid levels ranging from 5-7 (mg/dl), and 16 (44.44%) patients had serum uric acid levels surpassing 7 (mg/dl). These findings indicate a statistically highly significant association between serum uric acid levels and the severity of Preeclampsia among patients in the two groups, with a p-value of less than 0.0001 ($p < 0.0001$). In a study conducted by Meena R et al., they reported a mean serum uric acid level of 7.13 mg/dl in mild preeclampsia and 8.45 mg/dl in severe preeclampsia, with a significantly higher level observed in severe cases compared to mild cases [12]. This observation is in concordance with the findings of the present study. Similarly, Thanna RC et al., also reported similar findings, with a mean serum uric acid level of 7.23 ± 0.83 mg/dl in mild preeclampsia and 8.39 ± 0.58 mg/dl in severe preeclampsia [13].

In the Case Group, 2 (3.64%) patients demonstrated C-reactive protein (CRP) levels below 5 (mg/dl), 14 (25.45%) patients exhibited CRP levels between 5-10 (mg/dl), and 39 (70.91%) patients displayed CRP levels exceeding 10 (mg/dl). Similarly, within the Control Group, 27 (49.10%) patients had CRP levels below 5 (mg/dl), 25 (45.45%) patients had CRP levels between 5-10 (mg/dl), and 3 (5.45%) patients exhibited CRP levels surpassing 10 (mg/dl). A statistically significant difference was observed in the comparison of CRP levels between the two groups ($p < 0.0001$). Abdel Hamid et al., reported mean serum CRP levels of 10.25 ± 7.25 mg/dl, 10.94 ± 6.32 mg/dl, and 3.45 ± 1.7 mg/dl in mild preeclampsia, severe preeclampsia, and normotensive patients, respectively, which closely resemble the findings of the present study [14].

In the Case Group, 2 (3.64%) patients underwent forceps delivery, 29 (52.73%) patients underwent lower segment cesarean section (LSCS), and 24 (43.64%) patients had vaginal delivery (VD). In the Control Group, 12 (21.82%) patients underwent LSCS, while 43 (78.18%) patients had VD. A statistically significant difference was observed in the comparison of mode of delivery between the two groups ($p < 0.05$). Ugwanyi et al., reported in their study that 52.9% of cases were delivered via LSCS compared to 19.6% of controls, and 47.1% of cases were delivered via vaginal delivery compared to 80.4% of controls, with a p-value of < 0.001 , which parallels our findings [15]. Conversely, R Meena et al., found in their study that 76% of cases underwent LSCS and 24% delivered vaginally, whereas in the control group, 89% underwent LSCS and 11% delivered vaginally. This discrepancy may be attributed to differences in sample size [12]. In the Case Group, 10 (18.2%) patients experienced eclampsia, which was statistically significant ($p = 0.0009$). Additionally, 6 (10.9%) patients presented with HELLP syndrome, which also exhibited statistical significance ($p = 0.0117$). Furthermore, 6 (10.9%) patients developed pulmonary edema, with statistical significance noted ($p = 0.0117$).

In the study conducted by R. Meena et al., it was observed that among the cases, 6 (6%) patients experienced placental abruption, 12 (12%) presented with antepartum eclampsia, 2 (2%) developed acute renal failure, and 4 (4%) encountered postpartum hemorrhage (PPH), while no complications were noted in the control group [12]. Similarly, Asgharnia M et al., reported a higher incidence of maternal complications including placental abruption, HELLP syndrome, antepartum eclampsia, acute renal failure (ARF), and postpartum hemorrhage (PPH) among preeclamptic patients compared to normotensive individuals [16].

CONCLUSION

Preeclampsia stands as one of the most prevalent medical conditions during pregnancy and remains a significant contributor to maternal and perinatal morbidity and mortality on a global scale. Early diagnosis of this condition is crucial for effective prevention. Serum uric acid (UA) and C-reactive protein (CRP) serve as cost-effective, readily accessible, and non-invasive biochemical markers. These tests can be readily administered to all patients with suspected preeclampsia. Identifying high-risk individuals displaying elevated levels of serum uric acid and CRP enables closer monitoring and timely intervention, potentially mitigating or minimizing associated complications.

Conflict of Interest – None, Disclaimer - NIL

REFERENCES

1. Villar J, Betran A, Gulmezoglu M. Epidemiological basis for the planning of maternal health services. WHO/RHR. 2001; 111:298-298.
2. Khedun S, Moodley J, Naicker T, Maharaj B. Drug management of hypertensive disorders of pregnancy, Pharmacology & therapeutics. 1997; 74(2):221-258.
3. Pushparaj JL, Subramanyam G. Preeclampsia, dyslipidemia, atherogenesis, lipid profile, placental ischemia, cardiovascular disease. Dyslipidemia in Preeclampsia-Risk Factor for Future Maternal Cardiovascular Diseases. 2012, (187).
4. Kharb S, Gulati N, Singh V, Singh G. Lipid Peroxidation And vitamin E Level S In Preeclampsia. Gynecologic and Obstetric Investigation, 1998; 46(4):238240.

5. Preeclampsia-overview. [Online]. 2013 [cited 2013 May 30]; www.emedicine.medscape.com/article/1476919-overview
6. Fay RA. Uric acid in pregnancy and preeclampsia : An alternative hypothesis. *Aust N Z J Obstet Gynecol* 1990;30(2):141-42.
7. White CR, Darley-Usmar V, Berrington WR, Mcadams M, Gore JZ, Thompson JA, et al. Circulating plasma xanthine oxidase contributes to vascular dysfunction in hypercholesterolemic rabbits. *Proc Natl Acad Sci U S A.* 1996;93:8745.
8. Powers RW, Bodnar LM, Ness RB, Cooper KM, Gallaher MJ, Frank MP, et al. Uric acid concentrations in early pregnancy among preeclamptic women with gestational hyperuricemia at delivery. *Am J Obstet Gynecol.* 2006;194:160.
9. Johnson RJ, Kang DH, Feig D, Kivlighn S, Kanellis J, Watanabe S, et al. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? *Hypertension.* 2003;41:1183-90.
10. Kameswaramma K. Association of C-reactive protein and uric acid with severity of preeclampsia attending to teaching hospital.
11. Begum G, Nayyar Zaman F, Dar H. ASSOCIATION OF URIC ACID WITH PREECLAMPSIA. *KJMS.* 2018 Sep;11(3):454.
12. Meena R, Pachori P, Chaudhary S. ChandraKanta. Level of serum uric acid in patients with preeclampsia compared to controls and its relation to fetomaternal outcome. *Int J Reprod Contracept Obstet Gynecol.* 2019;8:2471-4.
13. Thanna RC, Choudhary R, Pathak S, Vamne A, Nigoskar S. LEVEL OF SERUM URIC ACID IN PREECLAMPSIA. *International Journal of Clinical Biochemistry and Research.* 2015 Jun 15;2(2):120-2.
14. Abdel-Hamid MA, Zakaria AE, Alomda FA, Abd El Moneim M. Serum Calcium, Magnesium, Uric Acid and C-Reactive Protein in Preeclampsia and Normal Pregnant Women. *The Egyptian Journal of Hospital Medicine.* 2019 Oct 1;77(1):4847-54.
15. Ugwuanyi RU, Chiege IM, Agwu FE, Eleje GU, Ifediorah NM. Association between Serum Uric Acid Levels and Perinatal Outcome in Women with Preeclampsia. *Obstetrics and Gynecology International.* 2021 Apr 16;2021.
16. Asgharnia M, Mirblouk F, Kazemi S, Pourmarzi D, Keivani MM, Heirati SF. Maternal serum uric acid level and maternal and neonatal complications in preeclamptic women: A cross-sectional study. *International Journal of Reproductive BioMedicine.* 2017 Sep;15(9):583.