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"Serum Uric Acid and C-Reactive Protein in Preeclampsia"

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Abstract:
Objective: *Estimation Of Serum Uric Acid (UA) And C-Reactive Protein (CRP) In Preeclamptic Patients And To Find Out Association Between These Biomarkers And Preeclampsia And Also The Role Of These Biomarkers As Predictors Of The Disease.*
Study-Design & Setting: *A Case-Control Study Was Carried-Out In The Deptt. Of Biochemistry In Collaboration With Deptt.Of Obst.& Gynae., Regional Institute Of Medical Sciences(RIMS),Imphal (Manipur),India, From October 2011upto June 2013.*
Methods: *Data Collected From 52 Preeclamptic Patients And 52 Normal Pregnant Women In 3rd Trimester Admitted In Antenatal Ward And Labour Room, Deptt. Of Obst.& Gynae.,RIMS Hospital.The Blood Samples Were Collected From The Patients And Analyzed For Serum UA And CRP Level.*
Results: *The Serum Uric Acid And CRP Levels Were Found Significantly Higher In Preeclamptic Cases Than In Normal Controls. Mean± SD Of Uric Acid And CRP Levels Were 5.46±1.84 Mg% And 8.14±6.3 Mg/L Respectively In The Study Group (Cases) Compared With 3.65±1.09 Mg% And 6.28±4.66 Mg/L In Controls. A Significant Positive Correlation Was Found Between Serum Uric Acid And CRP, And Between UA And BP. Thus, The Study Showed A Strong Association Between Increased Uric Acid, Blood Pressure And CRP Levels In Preeclamptic Patients.*
Conclusion: *Serum UA And CRP May Be Feasible To Be Used As Biomarkers For Identifying Women At Risk Of Preeclampsia.*
Key Words: *CRP, Preeclampsia, Uric Acid.*

I. Introduction

Hypertension Is One Of The Common Complications During Pregnancy And Contributes Significantly To Maternal And Perinatal Morbidity And Mortality. Pre-Eclampsia Is A Type Of Hypertensive Disorder Complicating Pregnancy. It Is A Multisystem Disorder Of Unknown Etiology Characterized By Development Of Hypertension To The Extent Of 140/90 Mmhg Or More With Proteinuria After The 20th Week In A Previously Normotensive And Non-Proteinuric Patient.[1]

The Global Incidence Of Preeclampsia Has Been Estimated At 5- 14% Of All Pregnancies.[2, 3] The Incidence Of Preeclampsia In The United States Is Estimated To Range From 2% To 6% In Healthy, Nulliparous Women.[4, 5, 6] Overall, 10%–15% Of Maternal Deaths Are Directly Associated With Pre-Eclampsia And Eclampsia.[7] WHO Estimates The Incidence Of Preeclampsia To Be Seven Times Higher In Developing Countries (2.8% Of Live Births) Than In Developed Countries (0.4%)[8] In India The Incidence Of Preeclampsia Is Reported To Be 8-10% Of The Pregnancies.[9] The Incidence In Primigravidae Is About 10% And In Multigravidae About 5%.[1].

Its Pathophysiology Is Poorly Understood But Numerous Maternal, Paternal And Fetal Factors Have Been Implicated In Its Development. The Factors Currently Considered To Be The Most Important, Include The Followings [10]:

1) Maternal Immunologic Intolerance.
2) Abnormal Placental Implantation.
3) Genetic, Nutritional And Environmental Factors.
4) Cardiovascular And Inflammatory Changes.

Among All These Factors, Though 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.[11]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.[10,11]

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.[12] 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.[12,13] C-Reactive Protein (CRP) Is A Sensitive Marker Of Systemic Inflammation And Is Primarily Synthesized In Hepatocytes In Response To Infection And Tissue Injury,[14] Which Is Stimulated By The Release Of Proinflammatory 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.

The Present Study Was Conducted To Estimate The Serum Uric Acid Level And Serum CRP Level In Preeclamptic Indigeneous Manipuri Women And To Find Out Any Correlation Between These Parameters And The Disease.

II. Materials And Methods

A Case Control Study Was Conducted To Evaluate The Level Of Serum Uric Acid And Serum CRP Levels In Preeclamptic Patients (Cases) And Normal Pregnant Women (Controls) In 3rd Trimester Admitted In The Antenatal Ward And Labour Room In The Deptt. Of Obstetrics And Gynaecology. It Was Done In The Department Of Biochemistry In Collaboration With The Department Of Obstetrics And Gynaecology, Regional Institute Of Medical Sciences, Imphal,

From October 2011 Upto June 2013. Approval of Institutional Ethics Committee was taken for the study. The Diagnosis Of Preeclampsia Was Based On The Definition OfAmerican College Of Obstetrics And Gynaecology[15]: I) Systolic Blood Pressure Greater Than 140 Mmhg Or A Rise Of At Least 30 Mmhg, Ii) Diastolic Blood Pressure Greater Than 90 Mmhg Or A Rise Of At Least 15 Mmhg (Measured On Two Occasions At Least 6 Hours Apart) And Iii) Proteinuria Of 300 Mg Or More In 24 Hours Urine Collection Or Protein Concentration Of 1 Gm/L (On Two Occasions Of At Least 6 Hours Apart), Or $\geq 2^+$ In Mild Preeclampsia And $>3^+$ In Severe Preeclampsia By Dipstick Method.

Those Patients Whose 24 Hours Urine Sample Examination Revealed Single Plus (+) By Dipstick Method Were Categorised As Normal Patients, Those Who Revealed Two Plus (++) Or Three Plus (+++) Were Categorised As Mild Preeclampsia, And Those Who Revealed More Than Three Plus (+++) Were Categorised As Severe Preeclampsia.

All The Subjects Had Been Divided Into Two Groups: **Group-1(Case Group Or Study Group):** Fifty Two Diagnosed Preeclamptic Patients In Third Trimester Of Pregnancy (29-40 Weeks).

Group-2 (Control Group): Fifty Two Normal Pregnant Women Of Comparable Gestational Age.

All The Cases And Controls In The Study Were Subjected To Detailed History Regarding Age, Parity, Gravida, Height, Pre-Pregnancy Weight, And Weight At The Time Of Blood Collection Was Noted Down. Maternal Occupation, Literacy, Husband's Occupation Along With Literacy, Religion, Race, Socioeconomic Status, Family History Of Preeclampsia, Past Obstetric History, Past Medical History, Smoking, Medical Disorders Like Hypertension And Diabetes Of First Degree Relatives, Physical Activity During Pregnancy Were Taken. Systemic Examination With Special Reference To Oedema, Blood Pressure And Gestational Age Was Carried Out. And Routine Antenatal Investigations Were Recorded In The Proforma Specially Designed For The Study.

Patients Who Were Overweight Based On Bmi, Severe Anaemic (< 6 Gm %), Suffering From Any Other Known Systemic Or Endocrine Disorder, Usg Proven Congenital Abnormality Or Malformation Of The Foetus, Unwilling To Give Consent And Who Are In Labour Pain And/Or Having Premature Rupture Of Membrane (Prom) Were Excluded From The Study.

Five Ml Of Venous Blood Was Drawn From Anterior Cubital Vein After An Overnight Fast. The Sample Was Centrifuged For 10 Minutes And Analysed For Total Serum Uric Acid And Crp In The Department Of Biochemistry, Rims. Total Serum Crp Estimation Was Carried Out By High Sensitivity C-Reactive Protein (Hscrp) Elisa Kit, Obtained From: Biomerica Co, U.S.A. Through A Germany Based Authorized Representative Whose Catalog No. Is 7033. Serum Uric Acid Was Measured By Enzymatic Colorimetric Test For Uric Acid Using Lipid Clearing Factor (Lcf) By Pap-Method/Uricase Method,[16,17] By Using Kits Marketed By Human Gesellschaft Fur Biochemica And Diagnostica Mbh Through Its Indian Branch Supply.

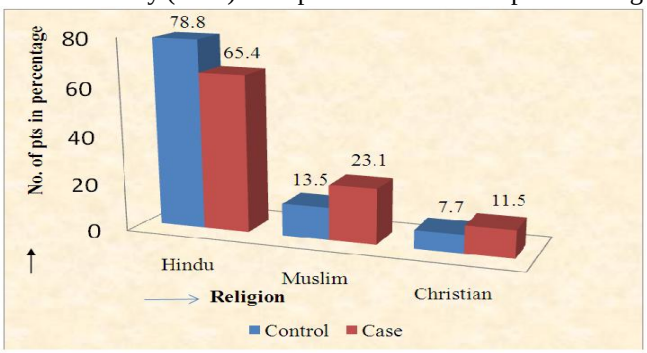
III. Statistical Analysis

After Thorough Checking And Scrutinizing, The Data Were Processed Through Computer With Statistical Software Using SPSS-16 Version. Statistical Formulae Like Chi-Square (χ^2) - Test, Independent

Sample T-Test, Pearson's Correlation Coefficient "R", Degree Of Freedom (Df) Were Used Wherever Found Suitable And Necessary, And Accordingly Interpretations Were Made.

IV. Results And Observations

Fig.I. Distribution Of Study (Case) Group And Control Group According To Religion.



X2 = 2.36, Df = 2, P = 0.30.

Fig. I Shows The Distribution Of Preeclamptic Women And Normal Pregnant Women Among The Various Religious Groups. The Majority Of Women In The Control Group Are Hindus I.E. 41 Nos (78.8%) Whereas The Number Of Muslims And Christians Patients Are 7 And 4 Comprising Of 13.5% And 7.7% Respectively. In The Study Group Hindus Are 34 In Numbers Which Comprises 65.4% Whereas The Number Of Muslims And Christians Are 12 And 6, Comprising 23.1% And 11.5% Respectively. It Is Found That No Significant Difference (P= 0.30) Was Observed Between Different Ethnic Groups.

Table 1. Distribution Of Study Group And Control Group According To Socioeconomic Status.*

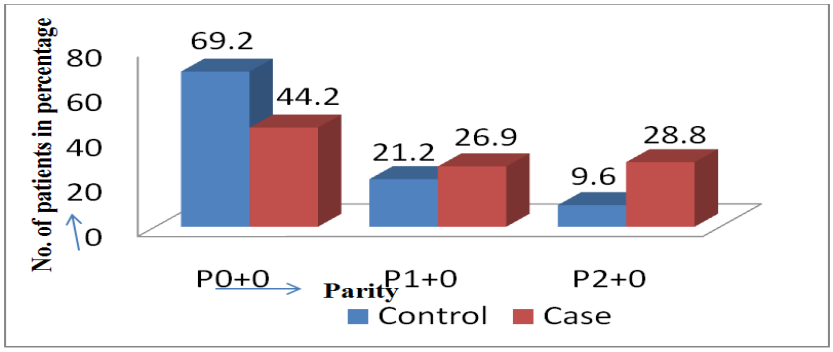
Socioeconomic Status* (Score)	Control Group	Study Group	Total
	Number (%)	Number (%)	Number (%)
Lowest (< 5)	0	0	0
Lower (5-10)	20 (38.5)	38 (73.1)	58 (55.8)
Lower Middle (11-15)	30 (57.7)	13 (25.0)	43 (41.3)
Upper Middle (16-25)	2 (3.8)	1 (1.9)	3 (2.9)
Upper / High (26-29)	0	0	0
Total	52 (100)	52 (100)	104 (100)

X^2 = 12.640, Df = 2, P = 0.002.

*Kuppuswamy's Socioeconomic Status Scale (2012).[18]

Table 1 Shows That Majority Of The Women In The Study Group Belong To Lower Socioeconomic Group (73.1%) Followed By Women Belonging To Lower Middle (25.0%) And Upper Middle Class (1.9%) Respectively. But In The Control Group Maximum Number Of Women Belongs To Lower Middle Class (57.7%) Followed By Lower (38.5%) And Upper Middle (3.8%) Socioeconomic Status Respectively. This Difference Between The Study Group And Control Group Is Statistically Significant (P = 0.002).

Fig. II. Distribution Of Study (Case) Group And Control Group According To Parity.



X^2 = 8.224, Df = 2, P = 0.01.

Fig. Ii Shows The Distribution Of Controls And Study Groups According To Parity. It Is Seen That Maximum Number Of Cases Occurs In Nulliparous (P_{0+0}). It Is Found That 69.2% In Control Group And 44.2% In Study Group Are Nulliparous. And 21.2% And 26.9% In Control Group And Study Group Respectively Are In Parity One. And 9.6% And 28.8% In Control And Study Group Respectively Are In Parity Two. But Significant Value Of X^2 = 8.224, And P = 0.01, Suggests That Parity Is Matched Between The Groups.

Table 2. Distribution Of Study Group And Control Group According To Age-Group.

Age (Years)	Control Group		Study Group		Total	Df	P-Value
	Number (%)	Mean±SD (Years)	Number (%)	Mean±SD (Years)			
18-25	27 (51.9)	25.96±3.89	12 (23.1)	29.42±5.10	39(37.5)	2	0.001
26-30	20 (38.5)		18 (34.6)		38(36.5)		
31-35	5 (9.6)		22 (42.3)		27(26.0)		
Total	52 (100)		52 (100)		104		

X^2= 16.5, Df = 2, P = 0.001.

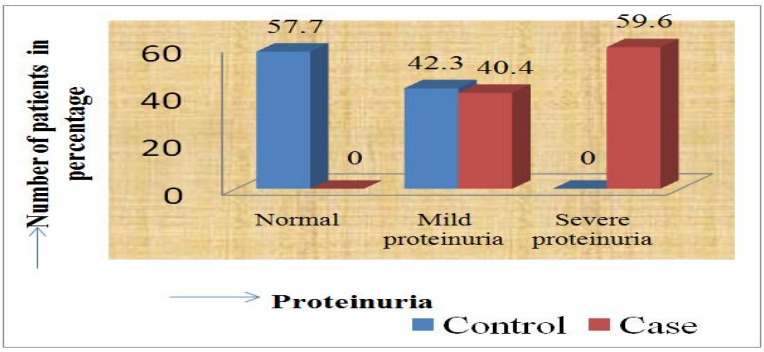
It Is Evident From The Table 2 That Maximum Number Of Cases Belong To Age Group Of 31-35 Years (42.3%) And Maximum Number Of Control Group Belong To Age Group Of 18-25 Years (51.9%). The Difference Is Highly Significant (P = 0.001) At 5% Probability Level. It Is Also Observed That Mean Value Of Age In Control Group Is 25.96±3.89 (Years) Whereas In Study Group It Is 29.42±5.10 (Years), Which Is Also Statistically Significant.

Table 3. Distribution Of Study Group And Control Group According To Mean±SD Of Weight And Haemoglobin.

Parameter	Control Group		Study Group		T-Value	Df	P-Value
	Number Of Cases	Mean± SD	Number Of Cases	Mean± SD			
Weight (Kg)	52	55.87±1.23	52	57.23±2.15	3.960	51	0.001
Hb (Gm%)	52	11.44±1.39	52	11.32±1.21	0.456	51	0.644

Table 3 Shows The Distribution Of Study Group And Control Group According To Mean ± Sd Of Weight And Haemoglobin. It Is Observed That Mean Weight Of Women In The Study Group (57.23 ± 2.15 Kg) Is More Compared With That Of Control Group (55.87 ± 1.23 Kg), And This Difference Is Statistically Significant (P = 0.001). The Hb Concentration Is More In The Controls (11.44 ± 1.39 Gm %) Compared With Cases (11.32 ± 1.21 Gm %). But This Difference Is Not Statistically Significant (P = 0.644).

Fig.III. Comparison Of Proteinuria In Study (Case) Group And Control Group.



$X^2 = 48.32$, $P = 0.001$.

Fig. Iii Shows That In Study Group Maximum Number Of Patients Have Severe Proteinuria I.E. >+++ (59.6%), And In Control Group Maximum Number Of Patients Have Proteinuria Of + (57.7%) Which Is Considered As Physiologically Normal. But In Both Study And Control Groups Mild Proteinuria I.E. ++ Or Is Observed In 40.4% And 42.3% Patients Respectively. There Is A Significant Difference Of Proteinuria Between Study Group And Control Group (P=0.001).

Table 4. Comparison Of Mean ± Sd Of Blood Pressure (Mmhg) Level Between The Study Group And Control Group.

Parameter	Control group			Study group			t-value	df	p-value
	No. of patients	Mean ± SD (mmHg)	Median (mmHg)	No. of patients	Mean ±SD (mmHg)	Median (mmHg)			
Systolic BP	52	119.19 ± 10.36	120	52	163.04 ± 24.26	153	11.98	102	0.001
Diastolic BP	52	77.42 ± 7.37	80	52	104.19 ± 15.32	100	11.35	102	0.001

Table 4 shows the comparison of mean ± SD (mmHg) of blood pressure between the study groups and controls. It is seen that the mean ± SD of systolic as well as diastolic blood pressure levels in preeclamptic women (163.04 ± 24.26 mmHg, 104.19 ± 15.32mmHg) are much higher than that of normal pregnant women (119.19 ± 10.36 mmHg, 77.42 ± 7.37 mmHg). This difference is found to be very highly significant (p = 0.001).

Table 5. Distribution of frequency of uric acid and CRP at different levels in study group and control group.

Name of parameter	Range of parameter	**Study group**	**Control group**	**Total**	**Grand total**
		Number (%)	Number (%)	Number (%)	
Uric acid (mg%)	< 2.4	0	0	0	104
	2.4-5.7	32 (61.5)	49 (94.2)	81 (77.9)	
	> 5.7	20 (38.5)	3(5.8)	23 (22.1)	
CRP (mg/L)	< 0.068	0	0	0	104
	0.068-8.2	29 (55.8)	38 (73.1)	67 (64.4)	
	> 8.2	23 (44.2)	14(26.9)	37 (35.6)	

In Table 5, it is observed that uric acid level is within normal range in 61.5% of study group (preeclamptic group) and 94.2% patients of control group, whereas it is above the upper limit of normal range (i.e. >5.7 mg%) in 38.5% of study group and 5.8% patients in control group. On the other hand, CRP level is within normal range in 55.8% patients of study group and 73.1% patients of control group. Whereas it is above the upper limit of normal range (i.e. >8.2 mg/L) in 44.2% patients of study group and 26.9% patients of control group. It is also found that not a single patient is there below the lower limits of both the uric acid level and CRP level in both of study group and control group.

Table 6. Relationship/comparison between mean value of serum uric acid level and CRP level in study group and control group.

Parameters	Group	Mean±SD	Median	t-test	df	p-value
Serum uric acid (mg%)	Study group	5.46±1.84	5.03	6.112	102	0.001
	Control	3.65±1.09	3.45			
Serum CRP level (mg/L)	Study group	8.14±6.3	7.30	1.68	102	0.09
	Control	6.28±4.66	5.00			

Table 6 shows the comparison of mean values of serum uric acid level and CRP level between the study and control groups. It is observed that mean value of serum uric acid level in study group is 5.46 ± 1.84 mg% which is quite higher than that of control group i.e. 3.65± 1.09 mg% and this difference is statistically significant (p =0.001). On the other, the mean value of serum CRP level in study group is higher (8.14±6.3 mg/L) than that of control group (6.28±4.66 mg/L) but this difference is not statistically significant (p= 0.09). The mean values of both serum uric acid and CRP levels in study group were very much near to their respective upper limits of normal ranges. But, the mean values of serum uric acid and CRP levels always remain higher in study group than that of control group.

Table 7. Correlation matrix of Serum Uric Acid level, Blood pressure and CRP level.

	Serum uric acid (mg %)	SBP(mmHg)	DBP(mmHg)	Serum CRP (mg/L)
Serum uric acid	1	0.445*	0.495*	0.282*
SBP	0.445*	1	0.896*	0.161
DBP	0.495*	0.896*	1	0.166
Serum CRP	0.282*	0.161	0.166	1

*Correlation is significant at the 0.01 level.

In order to study the correlation among the parameters viz. serum uric acid, blood pressure and serum CRP - Pearson's correlation coefficient "r" is advocated and findings are shown in Table 7. The analysis is based on the case group only. Table 6 highlights that there is a strong positive correlation between serum uric acid and blood pressure (systolic and diastolic) which is highly significant. A significant positive correlation is also observed between serum uric acid and serum CRP level.

V. Discussion

The study shows that majority of patients belong to Hindus. It may be due to the reason that the study was conducted in Hindu dominated area. The preeclampsia is more prevalent in the primigravidae (P_{0+0}) (**Fig.1I**) and in the older age group where the mean age ± SD in years is 29.42±5.10 (**Table 2**). Women in the lower socioeconomical status have the highest frequency of preeclampsia (73.1%) followed by lower middle class (25.0%) and least patients in upper middle socioeconomic class (1.9%) as shown in **Table 1**. This pattern is statistically significant (p= 0.002) when compared with control group.. Our study findings are almost similar to the study of **Punam D et al [19]** where they showed maximum number of preeclamptic women belonged to lower socioeconomic status (56%) followed by middle class(23%) and higher status(21%) which was statistically significant . The body weight of preeclamptic patients (57.23±2.15 kg) are significantly higher than that of the normal pregnant women (55.87±1.23 kg) of same gestational age. This finding is in agreement with that of **Rajkovic A et al[20]** where the weights of the preeclamptic women were more than that of the normal pregnant controls. Haemoglobin level in case group is slightly lower (11.32±1.21 gm %) than control group (11.44±1.39 gm%) but it is statistically not significant(**Table 3**). The cause may be due to the variance in their dietary habits. Edema is significantly absent in majority (75%) of preeclamptic women. Edema is a common occurrence in women with normal pregnancy, and preeclampsia may occur in women with no edema. The use of edema as a defining criterion for preeclampsia is controversial, and most recent reports omit it from the definition. [21]

Maximum number of patients with severe proteinuria (59.6%) is observed in cases. Mild proteinuria is observed in 40.4% and 42.3% patients respectively in both case and control groups .This difference is statistically significant (p=0.001) (**Fig. III**). The triad of severe preeclampsia is often described as a combination of hypertension, edema and proteinuria. Proteinuria is the last sign to develop. [21,22] Although salt and water retention are common features of preeclampsia, they (salt and water) do not cause the condition and are not an essential part of it.

The mean ± SD of blood pressure (mmHg) is significantly higher in preeclampsia (systolic: 163.04±24.26; diastolic: 104.19±15.32) compared with normal controls (systolic: 119.19±10.36; diastolic: 77.42±7.37) (**Table 4**). This is comparable to the findings of **Baksu A et al**[23] and **Powers RW et al** [24].

The level of serum uric acid is significantly higher in the study group than in the controls (5.46±1.84 mg/dl versus 3.65±1.09 mg/dl) (**Table 6**). In study group, 38.5% women have uric acid level more than upper limit of normal range (>5.7 mg %) (**Table 5**). During pregnancy maternal serum uric acid levels initially falls, with a subsequent rise to prepregnancy levels near term. [25] 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. [26] Elevated serum uric acid levels due to decreased renal urate excretion are frequently found in women with preeclampsia. [27] Soluble uric acid impairs nitric oxide generation in endothelial cells inducing endothelial dysfunction. [28] Besides the reduced clearance hyperuricemia in pre-eclampsia 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. [29] It has also been reported that rise in uric acid level in preeclampsia is secondary to placental damage leading to purine catabolism and production of uric acid. Besides the increased uric acid level in our cases a positive correlation is observed between serum uric acid and serum CRP level.(**Table 7**). This is supported by the findings of **Ingec M et al**.[30] In their study, it had been reported that rise in uric acid level in preeclampsia is secondary to placental damage leading to purine catabolism and production of uric acid.

A positive correlation is found between the serum uric acid level and blood pressure (systolic and diastolic).

The level of serum CRP is higher in preeclamptic patients than the normal pregnant women (8.14±6.39 mg/L versus 6.28±4.66 mg/L). But this is not significant (Table **7**). A positive correlation is found between serum CRP level and blood pressure (systolic and diastolic) and this is also not significant. A significant positive correlation is observed between serum uric acid and serum CRP (**Table 7**).This is supported by the findings of **Ingec M et al**.[31] In their study, it had been reported that rise in uric acid level in preeclampsia is secondary to placental damage leading to purine catabolism and production of uric acid.

In preeclampsia the level of CRP is increased . Native CRP is synthesized in a soluble form by hepatocytes and then secreted into the circulation. The production of CRP is induced by proinflammatory cytokines IL-1, IL-6 and IL-17 in the liver, although extra hepatic production can contribute to systemic concentrations. Cytokines exert their biological effects on CRP by signalling through their receptors on hepatic cells and activating different kinases and phosphatases, leading to the translocation of various transcription factors on the CRP gene promoter and the production of CRP.[32] The sole determinant of the plasma concentration is the rate of synthesis. The rise in blood CRP after tissue insult or injury is rapid and robust. In preeclampsia when there is endothelial cell injury or endothelial cell dysfunction, the concentration doubles every 8 hours and peaks at 36-50 hours, although that depends on the stimulus and its severity. In response to an inflammatory insult, CRP concentration can increase above 500 mg/l and this amounts to as much as a 1000-fold or more concentration change. [33,34] but if preeclampsia is accompanied by superimposed infection then the level of CRP increases more.

It is also observed that the mean value of CRP is higher in both the study and control groups than their respective median values (7.30 mg/L, 5.00 mg/L) (**Table 6**). Though, the mean value in study group is within the normal range (0.068-8.2 mg/L), it is always higher than the mean value of the control group.

In the study group, 44.2% women have CRP level more than upper limit of normal range (>8.2 mg/L) (**Table 5**). It is also found that in few preeclamptic patients (28.84%), the CRP value is >10 mg/L and in these study group the cause of increased CRP value may be superimposed infection along with preeclampsia which was latent or undiagnosed during taking of blood sample.

VI. Conclusion

The results of this study confirm the hypothesis that hyperuricemia and increased serum CRP level are correlated with preeclampsia being indirect risk factors for placental vasculopathy predating clinical preeclampsia. Thus it can be concluded that hyperuricemia and increased serum CRP level can be used as biomarkers for identifying women at risk of preeclampsia and its complications along with adverse effects.

Several potential limitations of our study are worth mentioning. All the patients in study group were preeclamptic before the measurement of uric acid and CRP levels, so it cannot be determined whether the observed elevation in serum uric acid level or CRP level or both preceded the development of preeclampsia. Hyperuricemia and increased CRP level in preeclamptic patients need to be confirmed in a designed strategy in which uric acid and CRP level can be measured before the development of preeclampsia or early in pregnancy in order to identify and monitor the patients at risk of preeclampsia and thus to provide the best prenatal care for these women and their babies.

However, further studies are required to determine whether genetic, nutritional defects or diseases related to uric acid or CRP metabolism account for hyperuricemia or increased serum CRP level observed in pregnant women with preeclampsia.

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