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Original Research Paper

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LOW PLATELET COUNT SERUM URIC ACID AND SERUM CREATININE AS A PROGNOSTIC INDICATOR IN PREGNANCY INDUCED HYPERTENSION

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ABSTRACT

Background and Objective: Preeclampsia is associated with variable maternal and perinatal complications. It has been indicated that increased serum uric acid and low platelet count play a prognostic role in preeclampsia. The present study was undertaken to evaluate severity of preeclampsia with raised S. uric acid and low platelet count and to evaluate perinatal outcome in preeclampsia with these parameters.

Methods: Study was done on women with hypertensive diseases of the pregnancy at Maharani Laxmi Bai Medical College and Hospital, Jhansi (U.P). After approval by the Ethical committee, patients were recruited in the study by obtaining written informed consent. 511 pregnant females were included in the study out of which 260 were taken as controls and 251 were taken as cases. Demographic, clinical and biochemical data at time of referral and delivery were collected for each pregnant women. Women were grouped according to diagnosis (gestational hypertension, mild preeclampsia, severe preeclampsia or eclampsia) and logistic regression analysis was used to determine relationship between serum uric acid and low platelet count with adverse outcomes.

Result: Out of 511 patients 251 were cases out of which 67 (26.69%) patient were severe preeclampsia. The mean level of uric acid in these women was significantly higher than in non severe preeclampsia. 83 (33.06%) women were diagnosed as eclampsia and were associated with significantly high serum uric acid levels, high serum creatinine levels and low platelet count and adverse perinatal outcomes like neonatal deaths and low birth weight.

Conclusion: In conclusion, our observations indicate that serum uric acid level is better indicator for the diagnosis of non severe PE even in the absence of positive USG observations. Platelet count may be a good indicator for the detection of milder form of preeclampsia. However for the severe form both serum uric acid and serum creatinine detect the severity. Additionally, continuous serial monitoring of the platelet count may indicate the progression of the disease. Serum creatinine values have positive correlation with the severity of the disease due to the ongoing renal pathology. Even though our data provide greater predictor value for platelet count, uric acid level and serum creatinine, the cutoff or threshold levels that change the progression cannot be ascertained. Additional study is required to find the critical levels.

KEYWORDS : Preeclampsia, Uric Acid Levels, Gestational Age.

INTRODUCTION

Hypertensive disorders remains among the most significant and commonest medical disorders during pregnancy and continue to be a major cause of maternal and perinatal morbidity and mortality worldwide. In developing countries they rank second only to anemia, with approximately 5-10% of all pregnancies being complicated by some form of hypertensive disease. Pregnancy may induce hypertension in women who are normotensive before pregnancy and may aggravate hypertension in those who are hypertensive before pregnancy. The International Society for the Study of Hypertension in Pregnancy (ISSHP) (Brown et al., 2001) has classified four categories as (1) pre-eclampsia and eclampsia syndrome (2) chronic hypertension – essential or secondary (3) pre-eclampsia superimposed on chronic hypertension and (4) gestational hypertension. Further, the term gestational hypertension was adopted by working group of NHBPEP (2000) to replace pregnancy induced hypertension (Brown and de Swiet 2001; Leeman and Fontaine, 2008). Thus early screening for gestational hypertension may allow vigilant antenatal surveillance and appropriate timing of fetal delivery in order to avoid serious sequelae.

Several studies have been done where these parameters are individually used to predict preeclampsia. There are several biomarkers such as vascular endothelial growth factor (VEGF) and placental growth factor (PlGF), P-selectin, cell free DNA, pregnancy-associated plasma protein A, TNF-α, β-hCG, C-reactive protein, nitric oxide, malondialdehyde and many more. Most of them are non specific and have to be used in combination with uterine artery Doppler screening.

Despite the presence of many of these different potential markers for preeclampsia, the reliability of these markers in predicting preeclampsia has been inconsistent between different studies. Furthermore, preeclampsia is a multifaceted disorder, some say it is not one but several diseases. Therefore there is a need for simple non-invasive cost effective marker to detect the pre-eclampsia or eclampsia.

It is seen that preeclampsia is associated with extensive platelet activation. Further alteration in coagulation, fibrinolysis and platelet and vascular endothelial function are believed to play an important role in pathogenesis of gestational hypertension. The fall in platelet count is most frequent abnormality and is probably due to low-grade intravascular coagulation. Mean platelet volume and platelet distribution width are significantly higher in patients with gestational hypertension compared to those with normal pregnancy. Even though numbers of studies have reported reduction in platelet count as a marker for preeclamsia or eclampsia.

Uric acid is a terminal metabolite of the degradation of nucleotides, and its blood level is in patients with preeclampsia-eclampsia. Elevated uric acid level in maternal blood, presumably due to decreased renal urate

excretion is frequently found in women with preeclampsia. Various studies have been conducted to find out the relationship between elevated uric acid level and preeclampsia. 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.

Hyperuricemia is one of the earliest and consistent observations in preeclamptic pregnancies. While elevated concentrations of circulating uric acid are not uniformly seen in every woman with pre-eclapmsia, they do appear to identify a subset of preeclamptic women who are at greater risk for maternal and fetal mortalities. So, measurement of serum uric acid concentration seems to be useful test to predict maternal complications in the management of women with preeclampsia. However, the literature is not consistent with serum uric acid levels in preecalampsia or eclampsia patients. Number of studies has revealed increase in serum uric acid levels while in several other studies showed that serum uric acid is a poor predictor of preeclampsia.

During normal pregnancy, renal blood flow and glomerual filtration rate rise appreciably. With pre eclampsia, several reversible anatomical and pathophysiological changes ensure. Of clinical importance, renal perfusion and glomerular filtration are reduced. Levels that are much less than normal non pregnant values are infrequent and are the consequence of severe disease. Most of the decrement in glomerual filtration is from higher renal afferent arteriolar resistance that may be elevated upto to five fold (Conrad, 2015, Cornelis 2011). Diminished filtration causes serum creatinine levels to rise to values seen in nonpregnant individuals that is 1mg/ml and sometimes higher (Lindheimer, 2008). Abnormal values usually begin to normalize 10 days or later after delivery (Cornelis, 2011, Spaan, 2012a).

Serum uric acid and creatinine levels are a part of work up for the pregnant women with hypertension. The elevated levels of these parameters were due to decreased urinary clearance secondary toreduced GFR and increased reabsorption. Serum uric acid is not only a marker of severity of disease but also contributes to the pathology of disorder.

AIMS AND OBJECTIVES

The study was undertaken with following Aims and objectives.

1.Association of Platelet count, Serum uric acid and Serum creatinine as a prognostic indicator in Pregnancy induced hypertension.

2.Association of Platelet count, Serum uric acid and Serum creatinine with severity of Pregnancy induced hypertension.

3.Association of Platelet count, Serum uric acid and Serum creatinine with the maternal and perinatal outcome of disease.

MATERIAL AND METHODS

Source Of Data:

Study was done on women with hypertensive diseases of the pregnancy at Maharani Laxmi Bai Medical College and Hospital, Jhansi (U.P). After approval by the Ethical committee, patients were recruited in the study by obtaining written informed consent.

Method Of Collection Of Data:

a)Study design : A clinical prospective case control study

b)Study period : April 2018 to July 2019

c)Place of study : Departmentof Obs. & Gynaecology, Maharani Laxmi Bai Medical College , Jhansi (U.P)

Inclusion Criteria For Cases:

- Age- 18-39 years
- Patient with BP >140/90 mmHg
- Presence of proteinuria
- More than 20 weeks of gestation

Inclusion Criteria For Control:

- 18-39 years age group
- Patient with BP <140/90 mmHg
- Absence of urinary protein
- More than 20 weeks of gestation

Exclusion Criteria For Cases And Control:

- Patient refusal
- Patients suffering from hemorrhagic disease
- Thromboembolic episodes
- Untreated coagulopathy or patient on any anticoagulant therapy
- History of epilepsy
- Patient on long term steroids
- Patients having any pre-existing heart or kidney disease

Study Methodology:

In the present study, 511 pregnant females were selected from those who attended antenatal clinic and those who were admitted in labor room and maternity ward of Department of Obstetrics and Gynecology of Maharani Laxmi Bai Medical College, Jhansi after taking informed written consent. Out of these recruited 511 pregnant women, 251 were cases of preeclampsia of different severity. The cases were further divided in non severe preeclampsia, severe preeclampsia (SPE) and eclampsia group. We also recruited 260 patients who were having normal pregnancy to serve as control group. The previous investigations of the patients of both groups were assessed. Platelet count, serum uric and serum creatinine was evaluated in both groups and compared.

RESULT AND DISCUSSION

In the present prospective study, 511 pregnant females were selected from those who attended antenatal clinic and those who were admitted in labor room and maternity ward of Department of Obstetrics and Gynecology of Maharani Laxmi Bai Medical College, Jhansi. Out of these recruited 511 pregnant women, 251 were cases of preeclampsia of different severity. The cases were further divided in non severe preeclampsia, severe preeclampsia (SPE) and eclampsia group. We also recruited 260 patients who were having normal pregnancy to serve as control group.

In patients in both the groups, the blood pressure measurement was undertaken and the blood test for platelet count, serum uric acid and serum creatinine was evaluated. In addition, urine was examined for albuminuria as mentioned in the methods. The birth weight of the babies born in the above groups was also recorded.

Table 1: The Data Of All The Patients (Controls And Cases) Recruited In The Study

Parameters	Cases	Control
N	**251**	**260±5.2**
Age(years)	23.2±4.5(18-39)	24.4(18-39yrs)
Gravidastatus	1.9(1-6)	2.8(1-6)
Gestationalage (weeks)	34.9±3.22(28-39)	36.5±2.95 (28-39)
Systolicpressure (mmHg)	162.5±11.3 (140-190)	116.4±8.4 (100-139)
Diastolicpressure (mmHg)	102.4±8.1 (90-130)	72.9±7.3 (60-89)

Proteininurine (number of pts)		
Niltraces	0	260
+	44	0
++	107	0
+++	32	0
	21	0
Plateletcount (lacs/μl)	0.80±0.36 (0.35-1.0lac)	1.30±0.42lacs (1.0-1.8lac)
Uricacid (mg/dL)	6.3±1.1 (5.1-8.3)	4.9±0.8 (4.0-6.2)
Serumcreatinine (mg/dL)	1.84±0.62 (0.80-3.4)	0.63±0.20 (0.40-0.80)
Deliverytype (number of pts)		
Normal	102(40.6%)	133(51.2%)
LSCS	149(59.4%)	127(48.8%)
Fetaloutcome (numberofpts)Live	208	260
Hospitalized	35	40
Dead	43	0
Fetal weight(Kg)	2.1±1.1 (1.5-2.5)	2.7±1.7 (2.1-3.2)

An asterisk (*) indicates P < 0.001 as compared to control group (Student's t test for unpaired observations)

The mean age of patients in Cases (23.2 ± 4.5) were similar to the Control group (24.4 ± 5.2) , however the maximum age in cases was lesser than control.

The gravida status in both groups found to be similar with no significant difference. But the mean gestational age of the patient at time of delivery in cases (34.9 ± 3.22) is significantly lesser than the control (36.5±2.95) patients.

The mean systolic (162.5 ± 11.3)and mean diastolic (102.4 ± 8.1mmHg) blood pressure in cases were found to be significantly higher in cases as compared to control group, systolic (116.4± 8.4) and diastolic (72.9 ± 7.3) blood pressure.

The mean platelet count (0.80±0.36 lacs/μl) in cases is significantly lesser than the control group (1.30±0.42 lacs/μl) whereas the mean uric acid level (6.3±1.1 mg/dl) in cases was significantly higher than the control (4.9±0.8 mg/dl).

The mean serum creatinine level (1.84±0.62mg/dl) in cases was significantly higher than the control (0.63±0.20mg/dl) levels.

Table 2: Distribution Of Patients In Cases And Control Groups In Various Age Groups.

Agerange(years)	Cases(numbers)	Control(numbers)
<20	18	22
21-25	159	100
26-30	56	102
31-35	18	26
36-39	-	10

Majority of patients entering the study were in the age group 21-25 years in cases and 26-30 yrs in control

Table 3: Distribution Of Number Of Patients According To Gestational Age In Cases And Control Group

Gestationalage (weeks)	Cases (numbers)	Control (numbers)
28-30	143	25
31-35	94	86
36-39	17	149

Mean gestational age in cases was lesser in cases than in controls. The distribution of gestational ages in cases was maximum in 28-30 wks duration and control was maximum in the 36-39 weeks duration.

Table 4: Maternal Related Parameters In Controls And Various Groups Recruited In Cases In The Study Are Shown.

Parameters	Control	Cases		
		Nonsevere PE	SPE	E
N	260	101	67	83
Age (years)	24.4 (19-39)	24.1 (19-36)	23.8 (19-39)	25.3 (19-36)
Gravida status	2.6 (1-8)	2.8 (1-8)	2.1 (1-6)	2.3 (1-5)
Gestational age (weeks)	36.5 (28-40)	34.1 (28-39)	33.6 (28-36)	32.9 (28-34)

As per our criterion the blood pressure in cases was significantly higher than control group. The systolic pressure was around 162 mm Hg and diastolic pressure was around 102 mm Hg. They were significantly greater than the control groups (P< 0.01, Students t test for unpaired observations).

In controls maximum numbers of cases are seen in 100-120 mm Hg range in systolic and 60-80 mm Hg range in diastolic pressures. In Cases the greater number of patients were seen in systolic 160-170mm Hg range and 90-110 in diastolic ranges.

The mean age of patients in Cases (23.2±4.50 years) were similar to the Control group (24.4±5.24 years). The age range of patients in non severe preeclampsia, severe preeclampsia (SPE) and eclampsia (E) were similar to each other.

The mean gestational age of the patient at time of delivery in cases (28-30 weeks) was significantly lesser than the control (36-39 weeks) patients. Gestational age in non severe PE, SPE and E decreased with severity and were 2.1 years, 23.8 and 25.3 years respectively.

Table 5: Table Showing Data Of Diagnostic Parameters Used In The Study.

Parameters	Control	Nonsevere PE	Cases SPE	E
N	260	101	67	83
Systolic pressure	116.4	148.4	164.3	188.2
(mmHg)	(100-139)	(140-159)	(160-180)	(160-200)
Diastolic pressure	72.9	98.8	100.7	112.4
(mmHg)	(60-89)	(90-109)	(110-130)	(100-130)
Proteinuria (nofpts)				
Nil	260	-	-	-
traces	-	30(29.7%)	-	-
+	-	71(70.3%)	10(14.9%)	3(3.6%)
++	-	-	50(74.6%)	56(67.4%)
+++	-	-	7(10.4%)	24(29.0%)

The mean systolic (162.5±11.3mm Hg)and mean diastolic (102.4±8.1 mm Hg) blood pressure in cases was found to be significantly higher in cases as compared to control group (SP- 116.4±8.4 and DP 72.9±7.3 mm Hg). In SPE and E groups the systolic and diastolic pressures were significantly higher than non severe PE.

Table 6: The Platelet Count, Serum Uric Acid And Serum Creatinine In Non Severe Pe, Spe, E Groups. Figures In Parenthesis Indicate Range.

Parameters	Control	Cases		
		Non severe	PE	E

N	260	101	67	83
Platelet count (lacs/μl)	1.30 (1.0-1.8)	0.84 (0.80-1.1)	0.72 (0.64-96)	0.41 (0.35-0.76)
Uricacid (mg/dL)	4.9 (4.0-6.2)	5.6 (5.1-6.4)	6.2 (5.6-7.3)	7.4 (6.3-8.3)
Serum creatinine (mg/dl)	0.63 (0.40-0.80)	1.02 (0.91-1.32)	1.13 (0.90-1.64)	2.37 (0.22-3.43)

The mean platelet count (0.35-1.0 lacs/μl) in cases is significantly lesser than the control group (1.0-1.8 lacs/μl). Mean platelet count in non severe PE, SPE, E groups were 0.84, 0.72, 0.41 lacs/μl, respectively. The platelet count in non severe PE and control are comparable, thus making platelet count not a very effective predicting MPE, but there was significant decrease in SPE and E groups.

The mean uric acid level (6.3 ± 1.1 mg/dl) in cases was significantly higher than the control (4.9 ± 0.8 mg/dl). The mean uric acid in non severe PE, SPE and E groups are 5.1-6.4, 5.6-7.3, 6.3-8.3 mg/dl, respectively and were significantly different from the control. The uric acid level increased significantly in a severity-dependent manner of disease. Thus, uric acid appears as a better predictor of the disease.
The mean serum creatinine level in cases (1.84±0.62) was significantly high than the control (0.63±0.20mg/dl). The mean serum creatinine level in non severe PE, SPE and E groups are 1.02,1.13 and 2.37mg/dl respectively and were significantly raised from the control group. Cases with raised creatinine levels belong to severe preeclampsia and eclampsia indicating negative correlation of increase.

Table 7: Fetal Outcome As Number Of Live Births, Neonates Admitted To Nicu And Dead Fetus In Cases And Control Groups.

Fetaloutcome	Case	Control
Livebirths	228	260
NICUadmitted	86(37%oftotal)	56(21.5%oftotal)
Dead	63(24.7%oftotal)	6(2.3%oftotal)

The mean fetal weight (2.1 ± 1.1 kg) in cases was significantly lesser than those in control group (2.61± 0.57 kg).The mean fetal weight in non severe PE, SPE, E groups are 2.48,2.40,1.82 kg, respectively. Fetal mortality in non severe PE, SPE and E was 7.9%,16.4%, 28.9% of the patients, respectively. Thus showing an increasing adverse fetal outcome with increasing severity of the disease

Table 8: Data Of Fetal Outcomes In Reference To Non Severe Pe, Spe, And E Groups Compared With Control Group. Figures In Parenthesis Indicate % And Range.

Parameters	Control	Nonsevere PE	Cases SPE	E
N	260	101	67	83
Delivery type(nofpts)				
Normal	133(51.2%)	36(24.3%)	14(13.5%)	52(20.7%)
LSCS	127(48.8%)	55(15.9%)	48(13.1%)	46(12.3%)
Fetal out come(n of pts)				
Live	254	93	56	59
NICU admitted	40	7	10	18
Dead	6	8	11	24
Fetalweight (Kg)	2.61±0.51	2.48±0.30	2.40±0.31	1.82±0.21
	(2.0-3.2)	(2.0-2.8)	(1.9-2.50)	(1.50-2.20)

Nearly 55.4% of patients in eclampsia group were subjected to cesarean section as compared to 54.4%% and 71.6% in non severe PE and SPE group. This apparent decrease in cesarean rate in Eclampsia group may be because of prematurity, intrauterine deaths and poor chances of neonatal and maternal survival post caesarean

Uric acid had strongly and negative correlation with fetal birth weight in PIH (r=-0.59, p=0.006), whereas creatinine had negative but weak correlation (r=0.03, p=0.87).

Further, our findings indicate that serum uric acid may be useful in the early detection of mild preeclampsia.

Constant high blood pressure increases the level of vasoconstrictors like thromboxane A2, angiotensin II, endothelin I and decreases the level of vasodilators like prostaglandin I2, prostaglandin E2, NO etc. As a result, there was increase in peripheral resistance and further increase of blood pressure. Our results indicate that the systolic pressure was significantly higher even in non severe PE group and was maximal in SPE rather than diastolic pressure. However, the systolic or diastolic pressures were not different from SPE group as compared to Eclamspia group. This may be due to the anticonvulsants given in these patients. It is known that anticonvulsants decrease the skeletal muscle tone and may alter the blood pressure.

Pre-eclampsia is a disease which has a significant impact on both fetal and maternal well being and accounts for a considerable cause of hospital admission in current obstetric practice. It is principally a disease of primi gravidae at the extremes of reproductive age. This age distribution is well correlated with the number of patients in the study sample, as most of them were primi gravidae between the age of 21 -25 years.

The gestational age decreased with severity of the eclampsia. The decrease was much greater in eclamsia group.

This disease which is unique to human pregnancy is a real dilemma as yet its etiology is unknown as hypertensive disease of pregnancy which has led to clinical signs such as hypertension and proteinuria, not merely diagnosing disease but defining it.

These observations indicate progressive damage/injury to the glomerulo-capillary membrane. It is reported that the endothelial dysfunction is seen in preeclampsia. The endothelial dysfunction increases capillary permeability leading to edema. The endothelial injury or inflammation in glomerular capillaries loses the repulsive negative charges and allows the albumin to be filtered easily.

Besides the hypertension and proteinurea, reduced platelet count has been reported by several workers. In this study, platelet count was significantly lower in pre-eclampsia and eclampsia group when compared to control group. Reduced platelet count was seen in severe pre-eclampsia and in eclampsia. The count in eclampsia was much greater. The reduction in platelet count is comparable to those reported by other authors.

In our study the platelet counts were similar in SPE and Eclampsia group as compared to others except with Kulkarni and Sutaria (1983). In our study the platelet count was not much higher than those reported earlier. In case of non severe PE cases the count was not different from the control group. Even in other groups the decrement is not as much. Thus the platelets do not play a major role at this mild or initial stage of disease. It may be possible due to the initial activation of platelets. However the drastic decreases in platelet in SPE and Eclamapsia patients suggest the role of platelets in the pathogenesis of the SPE or Eclampsia.

The decreased platelet count can be due to the consumptive

coagulopathy, as suggested (Arul Kumaran et al., 2005). Association with haemolysis and a low platelet count due to platelet consumption constitute the HELLP syndrome (haemolysis, elevated liver enzymes, low platelets) (Rath and Bartz, 2004, Boudhraa et al., 2010). Therefore it is likely that the platelet consumption at a greater rate in SPE and Eclampsia stages than at MPE and the platelet activation may be reason for no changes in platelet count in MPE.

It is suggested that if patients are followed continuously with each women acting as her own control, a relative reduction in platelet count may be commonly seen many weeks prior to the onset on clinical disease suggesting platelet consumption occurring in the early part of disorder (Redman et al). Therefore monitoring of platelet count maybe an indicator of the progression of the disease rather than one time evaluation of platelet count.

Degree of thrombocytopenia present was directly related to severity of the disease process. Hence a positive correlation was established between thrombocytopenia and severity of preeclampsia. Previous studies on exploring the pathophysiology of preeclampsia suggest a change in prostaglandins metabolism at placental and extra placental tissue. There is inadequate amount of maternal blood to the placenta and fetus which affects placentation and the uteroplacental vasculature developing placental ischemia. Placental ischemia is thought to activate maternal vascular endothelium leading to higher sensitivity to angiotensin II, with increased thromboxane, and endothelin. There is decrease in vasodilators like nitric oxide and prostacyclin. In addition to these factors, there is activation of the hemostatic system that further activates platelets to release other factors like 5-HT, catecholamines, endothelins and neuropeptides from α granules of the platelets. These further add up to the pathophysiology of preeclampsia like hypertension, systemic endothelial dysfunction and platelet activation. The prognostic value of platelet count in pre-eclampsia in our study correlated well after comparison with some studies.

In normal pregnancy, serum uric acid level slowly decreases until about 16 weeks of gestation, secondary to plasma volume expansion, increased renal clearance, and the uricosuria effect of estrogen. For most of the 2nd trimester, the uric acid level remains stable, and then increases during the 3rd trimester because of increase catabolism/ production. Uric acid is one of the most sensitive indicators of the disease severity in pregnancy induced hypertensive disorders and can beof great help in monitoring the cause of disease process .In preeclampsia, uric acid level has been known to be increased and to correlate with maternal and fetal morbidity, but always has been assumed to be a reflection of disease rather than a cause and it has antioxidant properties that serve to protect from oxidative stress, but it also appears to contribute directly to endothelial dysfunction by its proinflammatory effects, as well as to hypertension during preeclampsia.

In the present study, serum uric acid level in preeclampsia was significantly higher in cases as compared to controls group (Table 1; $p < 0.0001$). The observation showed significant difference between mild preeclamspia and severe preeclampsia and eclampsia. These findings suggest that uric acid can be a good marker to assess the severity of disease.

Hyperuricemia is one of the most earliest and consistent observations in preeclamptic pregnancies. While elevated concentrations of circulating uric acid are not uniformly seen in every woman with preeclapmsia, they do appear to identify a subset of preeclamptic women who are at greater risk for maternal and fetal mortalities. So, measurement of serum uric acid concentration seems to be useful test to predict maternal complications in the management of women with preeclampsia.

Literature is not consistent with serum uric acid levels in preecalampsia or eclampsia patients. Number of studies has revealed increase in serum uric acid levels while in several other studies showed that serum uric acid is a poor predictor of preeclampsia. In our study we have seen the increase in uric acid levels in an incremental manner with the severity of the eclampsia. Interestingly, the uric acid level increased significantly even in mild preeclampsia. In contrast we did not detect reduction in the platelet count Considering these points the uric acid level, a simple cost effective investigation, can detect MPE. The identification of methods to predict preeclampsia in early pregnancy assumes a great importance in the management of preeclampsia. Therefore, our observation with raised serum uric acid provides evidence for the one of the most convenient screening tests for predicting PE. Early detection thus can be useful in the management of the progress of the eclampsia.

Serum creatinnine is a marker of GFR and renal dysfunction. In our study, we observed elevated levels of serum creatinine in cases when compared with control group In our study we did not observe significant correlation between creatinine and fetal weight, indicating its limited role in predicting fetal outcome. Serum creatinine is a marker of renal GFR and renal dysfunction. In our study we observed elevated levels of serum creatinine in severe preeclampsia and eclampsia when compared with non severe PE group. In our study we also did not observe significant correlation between creatinine and fetal weight, indicating its limited role in predicting fetal outcome.

Mean serum creatinine levels were significantly elevated in non severe preeclampsia, SPE and E group are (1.02,1.13,2.37) when compared with control group (0.63).

Serum creatinine has significantly strong and negative correlation with fetal birth weight whereas creatinine had negative but weak correlation ($p=0.87$) and was not statistically significant in perinatal outcome.

Serum uric acid and creatinine are elevated in cases whereas no significant difference was observed between control. Serum uric acid had better specificity and sensitivity for PE and also correlated negatively with fetal birth weight. Serum uric and creatinine levels vary with gestational age, hence study should focus on estimating these markers in all trimesters so as to diagnose PE at an early stage.

The risk factors for adverse neonatal outcomes were severe pre-eclampsia and preterm delivery. In this study women with severe pre-eclampsia, eclampsia were at an increased risk of delivering an infant which developed an adverse outcome. This is similar to what was found by other researchers. Buchibinder and colleagues, in Ohio in the United States reported that the perinatal mortality in women with severe pre-eclampsia was 8.9% and there was a high perinatal morbidity. Jenkins and colleagues studied maternal and neonatal outcomes in women with severe pre-eclampsia before 25 weeks gestation and observed that only 10% of the neonates survived with major morbidities. Haddad and colleagues studied the maternal and perinatal outcomes during expectant management of women with severe pre-eclampsia between 24 and 33 weeks gestation. The still birth rate was 2.5% and neonatal mortality rate was 3% but with high neonatal morbidity. Perinatal mortality and morbidity were highest in women who developed severe pre-

eclampsia at an earlier gestational age and improved with increasing gestational age and where mothers were managed conservatively with prolongation of the pregnancy. Women with severe pre-eclampsia have decreased uteroplacental blood flow and ischemia which compromisesblood flow to the fetus. These increases the chances that a mother with severe pre-eclampsia will deliver a baby that will develop an adverse outcome.

In our study, women who delivered preterm were at an increased risk of adverse neonatal outcomes. This is similar to what has been found by other researchers. Khashu and colleagues studied perinatal outcomes associated with preterm birth at 33 to 36 weeks gestation and found perinatal mortality rate to be 8 times higher, neonatal mortality rate to be 5.5 times higher and, respiratory morbidity to be 4.4 times higher in the pre-term babies than in term babies. Similarly, Young and colleagues studied mortality in late preterm new born babies.

Pre-eclampsia is a progressive disorder and the only definitive management is the delivery of the fetus to minimize the maternal morbidity and mortality. However, this increases the chance of premature delivery with low odds of child survival . As noted, preterm babies are more likely to be admitted to the neonatal intensive care unit, have assisted ventilation, to be of low birth weight and small for gestational age, and to develop respiratory distress syndrome than term infants. This undoubtedly increases the cost of hospital stay. Given the resource-constraints within the health system, early detection of pre-eclampsia is critical. This can be achieved by ensuring that all maternity facilities are able to provide basic emergency obstetric care. Progression of the preeclampsia to severe form or to ecalmpsia indicates for the termination of pregnancy. The termination of pregnancy depends upon maternal and fetal factors. Thus in Eclampsia pregnancy is induced even at the preterm period either to save the mother or thefetus. Our data supports that significant decrease in the gestational age of the Eclampsia patients supports it (Table 1). Further, our data indicate that nearly 70% of the patients were subjected to vaginal delivery and only 23 % underwent LSCS. In this group 50% fetuses were dead and hence suggestive for lower rate of LSCS. In 50 % of the live fetuses, 61% of them required special NICU admissions. These results suggest preterm induction of labour supported with lower fetal weights in this group. In case of MPE or SPE groups 55% were vaginal deliveries and more than 90 % of the babies survived and 3-15 % required NICU admissions. Even the fetal weights were significantly lower. Considering these points, the management of the preeclampsic patients should be aimed to prevent further progression of the disease to eclampsic stage.

CONCLUSIONS

In conclusion, our observations indicate that serum uric acid level is better indicator for the diagnosis of non severe PE even in the absence of positive USG observations. Platelet count may be a good indicator for the detection of milder form of preeclampsia. However for the severe form both serum uric acid and serum creatinine detect the severity. Additionally, continuous serial monitoring of the platelet count may indicate the progression of the disease. Serum creatinine values have positive correlation with the severity of the disease due to the ongoing renal pathology. Even though our data provide greater predictor value for platelet count, uric acid level and serum creatinine, the cutoff or threshold levels that change the progression cannot be ascertained. Additional study is required to find the critical levels.

Our observations indicate that serum uric acid level is better indicator for the diagnosis of non severe PE in early pregnancy even in the absence of positive USG observations.

Serial measurement of platelet count is a better evaluator of prognosis in preeclampsia cases rather than one time measurement.

Monitoring of platelet count may be an indicator of the progression of the disease rather than one time evaluation of platelet count.

Thrombocytopenia and increased uric acid level taken together can be provide better index for the detection of severe preeclampsia and eclampsia group. Thus both serum uric acid and platelet count is good marker for the severity of preeclampsia.

Increased mean serum creatinine levels in severe PE and E group implicate the poor prognosis due to the ongoing glomerular damage and subsequent decrease in GFR.

Correlation between fetal birth weight with serum uric acid and creatinine in PE- serum acid has significantly strong and negative correlation ($p=0.006$) with fetal birth weight whereas creatinine had negative but weak correlation ($p=0.87$) and was statistically not significant.

Serum uric acid and creatinine are elevated in cases whereas no significant difference was observed between control. Serum uric acid had better specificity and sensitivity for PE and also correlated negatively with fetal birth weight. Serum uric and creatinine levels vary with gestational age, hence study should focus on estimating these markers in all trimesters so as to diagnose PE at an early stage.

Even though our data provide greater predictive value for platelet count, serum creatinine and uric acid level, the cutoff or threshold levels that change the progression cannot be ascertained.

Raised uric acid, thrombocytopenia and serum creatinine in combination provide greater predictability of the severity of diseases and also on adverse fetal outcome in women with preeclampsia.

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