

## SERUM URIC ACID AS A MARKER OF HYPERTENSIVE DISORDERS IN PREGNANCY: A PROSPECTIVE STUDY

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### ABSTRACT

**Background:** Pregnancy-related hypertensive disorders, a condition with numerous maternal and foetal consequences, can be avoided. By measuring serum uric acid levels, the condition can be detected early on and its progression can be stopped. In India, the prevalence of PIH varies from 5% to 15%. Fetal growth restriction, low birth weight, spontaneous or iatrogenic premature delivery, respiratory distress syndrome, and admission to neonatal intensive care are all significantly linked to preeclampsia. Preeclampsia prediction may aid in classifying women into high risk groups so that surveillance can be stepped up and preventative treatments can be started.

**Aim and Objectives:** The purpose of this research is to investigate the role that serum uric acid plays as a predictive factor in hypertensive disorders of pregnancy. The purpose of this study is to determine the function that serum uric acid plays in the determination of hypertensive problems in pregnancy. The purpose of this study is to evaluate the accuracy of blood uric acid as a potential predictive predictor of maternal and foetal problems related with hypertensive diseases of pregnancy.

**Methods:** Patients with hypertensive disorders of pregnancy who came in for antenatal checkups between 24-32 weeks and had blood pressure readings of more than or equal to 140/90 mmHg but did not have proteinuria were included in a study that was conducted in the department of obstetrics and gynaecology at the Modern government maternity hospital in Petlaburz. The inclusion and exclusion criteria were met by these patients. As part of the

standard evaluation, the level of uric acid in the serum was determined for each and every hypertensive patient. Recording was done for both the maternal and perinatal outcomes.

**Results:** In the current study, 46 (46%) of the 100 women with HDP had elevated serum uric acid levels. Of the 64 women who had pre-eclampsia, 34 (53.1%) had high serum uric acid levels. The median serum uric acid level was 6.2mg/dl, with an SD of 1.8. Numerous maternal and postnatal problems, including eclampsia, abruption of the placenta, HELLP syndrome, and foetal growth restriction, were linked to hyperuricemia in HDP patients.

**Conclusion:** Patients who have been given a diagnosis of hypertensive disorders of pregnancy and who also have hyperuricemia are at an increased risk for a variety of different maternal and perinatal complications.

**Keywords:** Hypertensive disorders of pregnancy, serum, uric acid, pregnancy

## INTRODUCTION:

One of the maternal diseases that harms both the mother and the foetus is hypertensive disorders of pregnancy. In poor nations, only anaemia comes in second place. Despite decades of intensive research, it is still unclear how pregnancy causes or worsens hypertension [1]. They continue to be some of the most important and fascinating unresolved issues in obstetrics. 5 to 10 percent of pregnancies are complicated by hypertensive problems. The fatal trifecta of hypertensive diseases, bleeding, and infection is a major factor in maternal morbidity and mortality [2-6].

Every obstetrician faces a serious management challenge with hypertension during pregnancy. Delivery is the only effective treatment for the gradual clinical course of gestational hypertension, which is characterised by constant deterioration. Both maternal and foetal outcomes may be improved by early identification and adequate care. The most serious of these illnesses is the preeclampsia syndrome, whether it occurs on its own or in conjunction with persistent hypertension. According to FOGSI and other studies, preeclampsia occurs in India between 11 and 13% of the time [7, 8]. The World Health Organization (WHO) reports that hypertensive diseases account for 16% of maternal mortality in wealthy nations. Additionally, foetal growth restriction, low birth weight, spontaneous or iatrogenic preterm delivery, respiratory distress syndrome, and admissions to neonatal intensive care are all strongly linked to hypertension. Preeclampsia is best characterised as a syndrome that only occurs during pregnancy and can impact all organ systems. Although most cases of preeclampsia are defined by aberrant maternal uterine vascular remodelling by fatally generated trophoblast cells, the condition is likely complex.

It has been determined that placental oxidative stress is the primary factor in the pathophysiology of gestational hypertension. One theory that has received significant attention to explain the etiopathogenesis of hypertensive disorders in pregnancy is placental implantation with abnormal trophoblastic invasion of uterine vessels, which results in narrowing of spiral arterioles' lumens and decreased placental blood flow, which in turn triggers the release of cytokines that cause systemic inflammation. Preeclampsia prediction may assist in classifying women into high risk groups so that surveillance can be stepped up and preventative treatments can be started. One of the most enduring and easily observable alterations in preeclampsia is hyperuricemia. A significant byproduct of purine metabolism is uric acid. Reduced uric acid clearance due to decreased glomerular filtration and increased tubular reabsorption most likely causes hyperuricemia. Due to increased plasma volume, glomerular filtration rate, and fractional excretion of uric acid, the serum uric acid concentration falls in the first and second trimesters of a typical pregnancy. The levels increase later in pregnancy, probably as a result of increased foetal production, decreased albumin binding, and a decrease in uric acid elimination [8-10].

One significant factor in the explanation of hyperuricemia in (potential) preeclamptic individuals has been renal impairment. The overproduction of uric acid caused by an enhanced purine breakdown in the ischemic placenta is a potential second explanation. Uric acid plays a significant function in oxidative stress and vascular damage. The aetiology of hypertension and decreased endothelial integrity may both be reflected by hyperuricemia. Serum uric acid's potential to predict preeclampsia, however, has been the subject of multiple research with conflicting results. This study seeks to evaluate the impact of blood uric acid in the development of substantial poor maternal/fetal outcomes following the beginning of hypertension as well as the progression of prenatal hypertension to preeclampsia [11-13].

## **MATERIALS AND METHODS**

**Study design:** A Prospective study

**Study population:** The study population consists of all primigravidas and multigravidas with singleton pregnancy who come for antenatal check up after 20 weeks i.e. 24-32 weeks with BP readings  $\geq 140/90$  mmHg with absent proteinuria.

**Study setting:** Department of Obstetrics and Gynaecology, Modern Government Maternity Hospital.

**Study period:** From November 2019 till October 2021.

**Sample size:** All the women attending the OPD in the Department of Obstetrics and Gynaecology, Modern Government Maternity Hospital who met the inclusion criteria during the period of November 2019-October 2021 were enrolled in the study.

Total number of study participants: 100

**Inclusion criteria:**

1. Pregnant women >20wks diagnosed with gestational hypertension.
2. Singleton pregnancy.

**Exclusion criteria:**

1. Women with chronic hypertension.
2. Women with other medical disorders like Diabetes mellitus, congenital heart disease, renal diseases.
3. Patients who do not give consent to participate in the study.
4. Multiple gestations.

**Sampling technique:** Data will be tabulated using Microsoft excel and analyzed statistically using SPP trial version 20.0 Chi square test, Fisher's test and other appropriate statistical tests were used for finding the association between the factors.  $p < 0.05$  was considered significant.

**Procedure:**

The Osmania Medical College Institutional Ethics Committee gave their approval to the study protocol. 100 pregnant women with singletons with gestational hypertension between 24 and 32 weeks of gestation were included in the study. An informed consent was acquired when the study's goal was stated. Age, occupation, socioeconomic level, current complaints, prior history, and obstetric history were all taken into account when compiling the patient's thorough medical history. The study subjects underwent a clinical examination as well as an antenatal check-up in accordance with standard antenatal care. Sphygmomanometer readings were taken when the patient was laying on her side, ideally the left lateral side, on a cot. A second BP reading of 140/90 mm Hg or higher was taken four hours apart. Patients were monitored for the development of pre-eclampsia and eclampsia till birth during their routine prenatal sessions. Results for the mother and the newborn were tracked.

**Study parameters:**

1. Sociodemographic characteristic details: Age, education, occupation, income, socio economic status.

2. Serum uric acid normal levels:
3. Non pregnant adult : 2.5-5.6mg/dl
4. First trimester: 2.0 - 4.2 mg/dL
5. Second trimester: 2.4 -4.9 mg/dL
6. Third trimester: 3.1 -6.3 mg /dL

## RESULTS:

Total number of subjects recruited: 100

Number of drop outs: 0

Total Number of patients for study analysis: 100

Total Number of live births: 89

Total Number of Intra uterine fetal demise: 11

### Characteristics of the study population:

The average age of study participants were 28.49 yrs with a SD of 4.19.

Number of patients with age <20 yrs: 26 (26%)

Number of patients with age 21- 25 yrs: 49(49%)

Number of patients with age above 26yrs: 25 (25%)

Maximum no. of patients belonged to the age group of 21-25 yrs: 49%

**Table 1: Relationship between serum uric acid and age**

Serum Uric Acid	Age (Years)			Total
	<20	21 – 25	26 and Above	
Normal	14	27	13	54
Increased	12	22	12	46
<b>Total</b>	26	49	25	100

**Table 2: Distribution of study population according to socioeconomic status**

Grading of socio economic status	Socio economic Class	Frequency	Percentage (%)
26-29	Upper	0	0
16-25	Upper middle	0	0
11-15	Lower middle	14	14
5-10	Upper lower	18	18

<5	Lower class	68	68
	TOTAL	100	100

According to modified kuppuswamy socio economic status classification.

Number of patients belongs to upper class: 0

Number of patients belongs to upper middle class: 0

Number of patients belongs to lower middle class: 14 (14%)

Number of patients belongs to upper lower middle class: 18 (18%)

Number of patients belongs to lower class: 68 (68%)

Majority of patients belong to lower class: 68 (68%).

**Table 3: Parity status in the study population**

Parity	No. of Subjects	Percentage
Primigravida	52	52.0%
Second Gravida	29	29.0%
Third Gravida	14	14.0%
Gravida four and above	5	5.0%
Total	100	

Number of primigravida: 52(52%)

Number of women who were second gravida: 29(29%)

Number of women who were third gravida: 14(14%)

Number of women who were Gravida 4 and more: 5(5%)

Maximum no. of patients were primigravida: 52

The average value of serum uric acid level was 6.2 mg/dL with SD 1.8. Total no of patients who had normal serum uric acid levels were 54(54%). Total no of patients who had increased serum uric acid levels were 46(46%).

Total Number of patients who developed non severe preeclampsia: 25(25%)

Total Number of patients who developed severe pre-eclampsia: 39(39%).

Total Number of patients who did not develop preeclampsia: 36 (36%)

**Table 4: Relationship between serum uric acid and hypertensive disorders of Pregnancy**

Serum Uric Acid	Pre-Eclampsia			Total
	Absent	Non Severe Preeclampsia	Severe Preeclampsia	
Normal	24	20	10	54
Increased	12	5	29	46
<b>Total</b>	36	25	39	100

Number of patients who developed preeclampsia was 64 among which 34 patients (53.1%) had elevated serum uric acid values and 30 patients had normal serum uric acid levels (46.8%).

P value: <0.001 with p value being statistically significant.

Total Number of patients who developed complications was 79 (79%) and who did not have complications were 21(21%).

**Table 5: Type of complications**

COMPLICATIONS	TOTAL NUMBER OF PATIENTS
Fetal growth restriction	28
Abruptio placenta	7
Oligohydramnios	11
Eclampsia	20
Hellp syndrome	2
IUD	11

Of the 79 patients who developed complications, 28 (28%) had fetal growth restriction, 20 (20%) developed eclampsia, 11 (11%) had oligohydramnios and 7 (7%) had abruption.

**Table 6: Relationship between Serum uric acid and eclampsia**

Serum Uric Acid	Eclampsia		Total
	Present	Absent	
Normal	2	52	54

<b>Increased</b>	18	28	46
<b>Total</b>	10	80	100
P Value	<0.001		
(Chi-Square Test)			

**Table 7: Relationship between Serum Uric Acid and Abruption**

Serum Uric Acid	Abruption Placenta		Total
	Present	Absent	
<b>Normal</b>	1	<b>53</b>	<b>54</b>
<b>Increased</b>	6	40	46
<b>Total</b>	7	93	100
P Value	0.029		
(Chi-Square Test)			

Number of patients who had increased serum uric acid and had fetal growth restriction: 20 (71.43%)

**Table 8: Relationship between serum uric acid and FGR**

Serum Uric Acid	Fetal Growth Restriction		Total
	Present	Absent	
<b>Normal</b>	8	46	54
<b>Increased</b>	20	26	46
<b>Total</b>	28	72	100
P value 0.01. (chi-square test)			

Number of patients who delivered at < 37 weeks: 42 (42%)

Number of patients who delivered between 37-40 weeks: 55 (55%)

Number of patients who delivered after 40 weeks: 3 (3%)

Majority patients delivered between 37-40 weeks of gestation: 55 (55%)

**Table 9: Relationship between serum uric acid and gestational age at delivery**

SERUM URIC ACID LEVELS	PRETERM (<37WEEKS)	TERM (>37 WEEKS)	TOTAL
NORMAL	12	42	54
INCREASED	30	16	46
TOTAL	42	58	100

Total Number of patients who had preterm delivery are 42, among which 30 patients (71%) had elevated serum uric acid levels and 12 patients (28%) had normal uric acid levels.

**Table 10: Average gestational age at delivery**

SERUM URIC ACID LEVELS	AVERAGE GA	STANDARD DEVIATION
INCREASED	34.76	2.846
NORMAL	36.97	2.205

p value 0.001

The average gestational age at delivery in weeks in the patients who had elevated serum uric acid was 34.76 with SD 2.846 and of those with normal uric acid levels is 36.97 with SD 2.205 with a p value of 0.001 which is statistically significant.

Total Number of patients who underwent elective LSCS: 9(9%)

Total Number of patients who underwent emergency LSCS: 11(11%)

Total Number of patients who had spontaneous vaginal delivery: 53(53%)

Total Number of patients who had vaginal delivery following induction of labor: 27 (27%)

Most of the patients delivered vaginally: 80(80%) among which 53 patients (53%) had spontaneous labor and 27 patients (27%) had vaginal delivery following induction of labor.

**Table 11: Relationship between serum uric acid and mode of delivery**

Serum Uric Acid	Mode of Delivery			Total
	Vaginal Delivery following Induction	Vaginal Delivery	C-Section	
Normal	9	36	9	54
Increased	18	17	11	46
Total	27	53	20	100
P Value	0.009			
(Chi-Square Test)				

Vaginal deliveries following induction were 27, of which 18 (66.67%) had increased uric acid level and 9(33.33%) had normal uric acid level. Spontaneous vaginal deliveries were 53, of which 17 (32.08%) had elevated uric acid. Level and 36 (67.92%) had normal uric acid level. 20 underwent C-section of which 11(55%) had elevated uric acid level and 9(45%) had normal uric acid level

Neonates with birth weight <1.5 kg: 23(23%)

Neonates with birth weight 1.5-2.5 kg: 58(58%)

Neonates with birth weight >2.6 kg: 19 (19%)

Most of the neonates were of birth weight 1.5 -2.5 kg: 58.

**Table 12: Relationship between serum uric acid levels and birth weight of babies**

Serum uric Acid levels	Birth weight			Total
	<1.5 kgs	1.5-2.5 kgs	2.6 kgs and above	
Increased	19	25	2	46
Normal	4	33	17	54
Total	23	58	19	100
P value <0.001 (Chi-square test)				

Total no. of patients who had babies of birth weight <1.5 kg were 23, among whom 19 (82.61%) patients had increased serum uric acid levels. Total no. of patients who had babies with birth weight between 1.5 - 2.5 kg were 58, among whom 25(43.1%) had elevated uric acid levels.

**Table 13: Average birth weight of neonates**

Serum Uric Acid	Birth Weight (Kg)		
	N	Mean	Std. Deviation
Normal	54	2.34	0.579
Increased	46	1.65	0.574

Average birth weight of babies of patients who had elevated serum uric acid was 1.65 kg with SD of 0.574 where as the average birth weight of babies of patients with normal serum uric acid levels was 2.34kgs with SD 0.579, with a p value of 0.001 which was statistically significant. Total number of IUD: 11 Out of 89 neonates, 29(29%) required NICU admissions and 60 neonates (60%) did not require NICU admission.

**Table 14: Relationship between serum uric acid and NICU admissions**

Serum Uric Acid	NICU Admission		Total
	Present	Absent	
Normal	17	37	54
Increased	12	34	46

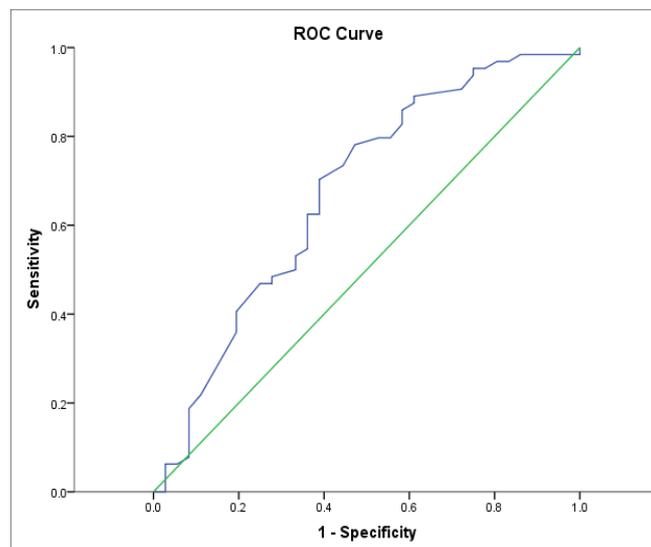
<b>Total</b>	29	71	100
P Value	0.554		
(Chi-Square Test)			

Total no. of neonates who had NICU admission were 29, among whom 12 neonates (41.38%) were born to mothers with increased serum uric acid levels. p value 0.554 was statistically insignificant .

**Table 15: Relationship between serum uric acid levels and IUD**

Serum Uric Acid	IUD		Total
	Present	Absent	
<b>Normal</b>	1	53	54
<b>Increased</b>	10	36	46
<b>Total</b>	11	89	100
P Value	0.002		
(Chi-Square Test)			

Total no. of IUD were 11 among which 10 had elevated serum uric acid levels (90.91%) and 1 had normal uric acid level (9.09%)



**Figure 1:** Area under the curve was 67.3% with threshold value of serum uric acid of 5.5mg/dl for the sensitivity of 70.3% and specificity of 61.1%.

## DISCUSSION

Preeclampsia and other hypertensive diseases of pregnancy continue to take a terrible toll in both developed nations like India and western nations. It remains the primary cause of maternal death despite advancements in prevention, identification, and treatment. Important

factors include inflammation, xanthine oxidase activity, and oxidative stress. The diagnosis and prognosis of preeclampsia have been suggested using a variety of biochemical markers. The goal of the current study is to evaluate the clinical value of one of the biochemical indicators, uric acid, in pregnancy-related hypertensive diseases. There were 100 patients in total in this study group who were primigravidas and multigravidas with gestational ages of at least 20 weeks and who had blood pressure readings of at least 140/90 and no proteinuria. The majority of the patients in the current study were between the ages of 21 and 25. Participants in the study had an average age of 23.81 years, with a standard deviation of 3.95 years. According to a study by Yuquan Wu et al., the study participants' average age was 24.3 years, with a standard deviation of 5.8 years. In a similar vein, Gianni Bellomo et al. discovered that the participants in their study had a mean age of 25.4 years with an SD of 4.1. According to a study by Nosakhare O Enaruna et al, the majority of the patients in their study group were between the ages of 20 and 29 years old, and the mean age was 23.09 years with an SD of 5.5 [14, 15].

The majority of the patients in our study group, as determined by the modified Kuppuswamy classification, belonged to the lower (68%) class. 52% of the patients in the current study were primigravidas. In a study by Mary Esien Kooffreh, the majority of the patients were primigravidas, and similar findings were made. Similar findings were made in a study by Yuquan Wu et al., which found that primigravida patients made up the majority of the hypertensive patients. In the current investigation, an average serum uric acid level of 6.23mg/dl with SD of 1.87 was discovered. Similar findings from a study conducted by Yuquan Wu et al. showed that the average serum uric acid level was 4.89 mg/dl with SD of 0.90. Average blood uric acid levels were higher, at 5.6 mg/dl, according to A C Urato et al [16, 17].

**TABLE 16: comparison of average serum uric acid level with respect to other studies**

Current study	6.23 with SD 1.87
Yuquan wu et al	4.89 with SD 0.90
Padma et al	6.13 with SD 1.8
Taefi et al	5.8 with SD 2.0

**Preeclampsia:** Total no. of patients who developed preclampsia were 64%. A study done by Gianni Bellomo et al found that 44.7 % of patients who had elevated BP readings with absent proteinuria developed preclampsia. Yuquan Wu et al showed that out of the total patients

with an initial presentation of gestational hypertension 67% progressed to preeclampsia which is slightly higher compared to our study.

**TABLE 17: Comparison of preeclampsia with respect to other studies**

Current study	<b>64%</b>
Yuquan Wu et al	<b>67%</b>
Gianni Bellomo et al	<b>44.7%</b>

In the current study the onset of hypertension in majority patients were after 36 weeks (53.33%). A study done by Joel R Livingston et al also showed that the gestational age at the onset of hypertension in majority of patients as at 35 weeks which was earlier compared to our study. Total no. of patients who had complications was 79 in our study group, among which fetal growth restriction was common.

**Time of delivery:** In the current study 58% patients delivered after 37 weeks. The average gestational age at the time of delivery was 36.9 weeks with SD of 2.2. According to study done by Yuquan Wu, they found out the average gestational age at the time of delivery was 36.4 weeks with SD 3.5. In a study done by Joel R Livingston the average gestational age at the time of delivery was 37 weeks. According to study done by TL-A Hawkins et al <sup>81</sup> the average gestational age at the time of delivery was 36.4 weeks.

**TABLE 18: Comparison of gestational age at the time of delivery**

Current study	36.9 weeks
Yuquan Wu <sup>80</sup>	36.4 weeks
Livingston	37 weeks
Hawkins et al	36.4 weeks

In the current study, 53% had spontaneous vaginal delivery and 27% patients delivered following induction of labor. The percentage of patients who underwent LSCS was 20%. In study done by Gianni Bellomo et al cesarean section rate was 39% which was more compared to our study results.

**Average birth weight:** In our study the average birth weight of the neonates was 2.34 kg with SD 0.57 and 89.47% of neonates were more than 2.6 kgs. In a study done by Gianni Bellomo et al the average birth weight of the neonates was 3060 gms with SD 0.740.

**NICU Admissions:** In our study 29 babies' required NICU admission among which 12(41.38%) had elevated serum uric acid levels with a p value of 0.554.

In our study among 100 patients who had elevated BP recordings, 64 patients developed preeclampsia. p value was statistically significant. Sensitivity of serum uric acid as a marker of Hypertensive disorders of pregnancy was 70.30% and specificity 61.1%.

**ROC Curve:** According to the ROC curve, the greatest sensitivity was 70.30% and the maximum specificity was 61.1% with a threshold value of 5.5 mg/dl for blood uric acid. Gianni Bellomo's study revealed that for a cutoff of 5.2 mg/dL, the areas under the receiver operating characteristic curve for sensitivity and specificity were 87.7% and 93.3%, respectively. With a cutoff value of serum uric acid >4.9 mg/dl, Sapna Vyakaranam's study also discovered that serum uric acid had a sensitivity of 86.7% and a specificity of 83.9%. The best cut-off value in a study by Yuquan Wu et al. was serum uric acid of 4.7 mg/dl, with sensitivity 73% and specificity 58%. When the relationship between serum uric acid and gestational age at delivery was compared in our study, patients with elevated serum uric acid levels had an average gestational age of 34.7 weeks with an SD of 2.846 and patients with normal serum uric acid levels had an average gestational age of 36.97 weeks. Statistics showed that the p value of 0.00193 was significant. Out of 100 patients, 42 (42%) had premature deliveries, and 30 (71.43%) of those had high serum uric acid levels. This might be the result of difficulties during pregnancy, which would have caused iatrogenic preterm.

**Eclampsia:** In our study, 20 patients developed Eclampsia among which 8 (90%) had elevated serum uric acid levels and 2 (10%) had normal uric acid levels. p value was statistically significant  $p < 0.001$ .

**Mode of delivery:** There was statistically significant association between serum uric acid and mode of delivery. 80% patients had vaginal delivery and 20% patients had caesarean section for various indications.

**FGR:** In our study, 28 patients had FGR among which 20 patients had elevated serum uric acid levels. Hence p value was statistically significant between serum uric acid and FGR. In a study done by Gianni Bellomo et al there was significant correlation between serum uric acid and incidence of SGA with p value 0.02.

**Oligohydramnios:** In our study serum uric acid levels had no significant correlation with oligohydramnios with p value 0.497.

**Abruption:** There was correlation between serum uric acid and abruption placenta with p value 0.029. Hence those patients (36%) who did not develop preeclampsia can be correctly termed at the end of the study as patients with

**Neonatal outcome:** In our study there was statistically significant correlation between serum uric acid and average birth weight of the baby with p value < 0.001 and no significant correlation between serum uric acid and NICU admissions with p-value 0.554 which could be explained because of antenatal complications i.e FGR [18].

## CONCLUSION

According to studies, 5–10% of pregnancies in India are complicated by hypertensive disorders, which is responsible for 8–10% of maternal deaths. Patients with hypertension problems require constant observation. It is essential to have laboratory tests that can foretell a disease's severity at an early stage. The risk of renal involvement and foetal impairment can be determined by estimating serum uric acid levels. Women with high blood pressure should be monitored more closely since early hyperuricemia diagnosis increases the risk of problems for both the mother and the foetus. Hyperuricemia and preeclampsia severity are positively correlated with unfavourable maternal and foetal outcomes. According to my research, adverse problems for the mother and the foetus are linked to serum uric acid levels of >6.2 mg/dl. A steady rise in its level should be interpreted as a call for quick action to enhance the course of the pregnancy. In order to detect preeclampsia issues at an early stage, a greater level of serum uric acid can be a highly valuable diagnostic.

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