

# Correlation of Maternal Serum Uric Acid Level and Feto-maternal Outcome in Hypertensive Disorder of Pregnancy: A Prospective Study

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## ABSTRACT

**Introduction:** Hypertensive disorder of pregnancy complicates around 5-10% of all pregnancies. Hyperuricemia is one of the common findings in pre-eclampsia. The uric acid level in pre-eclamptic women is increased before the onset of hypertension and proteinuria. The increase in serum uric acid is associated with an increased risk of adverse fetal outcomes like IUGR, prematurity, IUFD and increased severity of maternal hypertensive disorders like pre-eclampsia, severe pre-eclampsia, eclampsia and HELLP syndrome.

**Methods:** This was an observational, prospective cross-sectional study. One hundred and twenty women fulfilling the inclusion criteria were included in the study. Maternal uric acid was grouped into two groups i) <5.5mg/dl and ii) ≥ 5.5 mg/dl. A Pearson's Chi-Squared test was carried out to assess whether maternal serum uric acid level and maternal and fetal complications were related.

**Results:** A total of 120 women fulfilling the inclusion criteria were included in the study. Seventy-six women (63.3%) had serum uric acid level <5.5mg/dl and forty-four (36.7%) women had serum uric acid level ≥ 5.5 mg/dl. In women with serum uric acid level of 5.5 mg/dl and more; 21 fetuses had complications like IUFD, IUGR, prematurity and in those whose serum uric acid level was less than 5.5 mg/dl; 16 fetuses had complications. There was a significant association between maternal serum uric acid levels and maternal complications like pre-eclampsia, severe pre-eclampsia, eclampsia and HELLP syndrome (p=0.004).

**Conclusion:** Raised serum uric acid is associated with an increased risk of the feto-maternal outcome.

**Keywords:** HELLP Syndrome; Hypertension, Pregnancy-Induced; Uric Acid

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## INTRODUCTION

Hypertensive disorder of pregnancy complicates around 5-10% of all pregnancies. [1] In Nepal, the incidence is around 1.8-3.3%. [2,3] It is one of the leading causes of maternal and perinatal morbidity and mortality worldwide. It is a multiorgan disorder leading to renal, cardiac, hepatic and neurological complications. It also leads to adverse perinatal outcomes resulting in intrauterine growth restriction, preterm birth and intrauterine fetal demise.

Hyperuricemia is one of the common findings in pre-eclampsia. The uric acid level in pre-eclamptic women is increased before the onset of hypertension and proteinuria. [4] Uric acid is the end product of purine metabolism catalyzed by the enzyme xanthine dehydrogenase/xanthine oxidase. In preeclampsia, several factors contribute to the elevated level of uric acid: decrease glomerular filtration rate, increased tissue breakdown, acidosis and increased activity of the enzyme xanthine dehydrogenase/xanthine oxidase. [5] In early pregnancy, serum uric acid level falls, often to 3mg/dl or less due to the uricosuric effects of estrogen and from the increase in renal blood flow. During the third trimester, the serum uric acid level may reach up to 4-5mg/dl. [6]

The association between serum uric acid and its severity in hypertensive disorder in pregnancy was first reported in 1917. Since then, several studies have been done to correlate its severity with the feto-maternal outcome. [7,8,9] Rajalaxmi et al have reported a threshold value of the uric acid level of 5.5mg/dl in women with preeclampsia with the adverse feto-maternal outcome. Around 68% of women with serum uric acid more than 5.5mg/dl were associated with preterm delivery and birth weight less than 2.5kg. [10] Other studies have reported the threshold value of 6mg/dl (530.4umol/l) and 5.6 mg/dl (521.4umol/L) at 38 weeks of gestation in women with hypertensive disorders of pregnancy. [11,12] It is associated with

increased incidence of preterm birth, low APGAR scores low birth weight, IUGR and increased risk of fetal morbidity and mortality. [8,13,14]

In our context, several studies have been done on pregnancy-induced hypertension in terms of diagnosis, the fetomaternal outcome in relation to gestational age, the severity of the disease, and proteinuria. However, only a few studies have been done in relation to uric acid concentration and fetomaternal outcome. Therefore, this study was conducted to determine the relationship between maternal serum uric acid levels and fetomaternal complications in women with hypertensive disorders of pregnancy.

## METHODS

This was an observational, prospective cross-sectional study that was conducted in the department of Obstetrics and Gynaecology, Manipal Teaching hospital, Pokhara. The study was conducted after ethical approval. All the women beyond 20 completed weeks booked and unbooked admitted in our hospital with the diagnosis of hypertensive disorder of pregnancy, willing to participate in the study were included in the study. According to ACOG Practice Bulletin (2018), it will be classified as [15]

1. Gestational hypertension: BP  $\geq$ 140/90 mm Hg with no proteinuria
2. Pre-eclampsia: BP  $\geq$ 140/90 mm Hg associated with proteinuria (300mg or more in 24 i.e.hours, protein/creatinine ratio of 0.3 or dipstick reading of 2+) or associated thrombocytopenia (platelets  $\leq$ 100x10<sup>9</sup>/L), pulmonary oedema or Impaired liver function
3. Eclampsia: associated with fits.
4. Chronic hypertension with superimposed preeclampsia

Blood samples were taken for uric acid along with another routine test including creatinine, blood glucose, liver function test and a complete blood cell count. The level of uric acid was noted and divided into two groups:

Group A (<5.5 mg/dl) and Group B ( $\geq 5.5$ mg/dl). Women who were seen in OPD and were under domiciliary management were followed up till delivery. Known cases of chronic hypertension, multiple pregnancies, high-risk pregnancies like diabetes, heart disease and other medical problems, gross congenital anomalies of fetus detected in an antenatal scan, those not willing to participate in the study and who were lost to follow-up were excluded from the study. The delivery was conducted according to the hospital protocol. The serum uric acid level at the time of delivery was taken for the study and it was correlated with the maternal and fetal outcomes. Complications like antepartum haemorrhage, postpartum haemorrhage, eclampsia, HELLP syndrome, DIC and fetal outcome (birth weight, APGAR Score at 5 minutes, IUFD, NND) and NICU admission with indications were recorded. The cases were followed till discharge.

The sample size was calculated using the following formula:  $N = Z^2 \cdot p(1-p) / d^2$  where, N= desired sample size, Z= reliability quotient (1.96 for 95% reliability), p= Global prevalence of hypertensive disorders of pregnancy is 5-10%.<sup>1</sup> So, for this study, the prevalence was taken as 7.5%, d= margin of error. The sample size was calculated as 106 and adding 10% for dropouts, the estimated sample size was taken as 120.

All data were noted in the proforma. Data entry and analysis were, done using the latest SPSS software version 21 and A Pearson's Chi-Squared test Fischer's exact test was used and was depicted in tables, diagrams and charts as required.

## RESULTS

A total of 120 women fulfilling the inclusion criteria were included in the study. Overall, the mean age was  $25 \pm 4.72$  years with an age range of 20 to 40 years. Most of the ladies were second gravida (n=54, 45%). Most of the women (25%, n=30) were between 37 to 38 completed weeks. Two (1.67%) were less

than 28 completed weeks and two (1.67%) were postdated more than 40 completed weeks. Seventy-six women (63.3%) had serum uric acid levels <5.5mg/dl and forty-four (36.7%) women had serum uric acid levels  $\geq 5.5$  mg/dl. Out of 120 women, 94 (78.3%) had a cesarean section, 25 (20.8%) had a vaginal delivery and 1 (0.83%) had instrumental delivery for poor maternal effort in the second stage of labour. (Table 1)

**Table 1: Mode of delivery**

Serum Uric acid level	Cesarean section	Vaginal delivery	Instrumental delivery	Total
<5.5mg/dl	56	20	1	77
$\geq 5.5$ mg/dl	38	5	0	43
Total	94	25	1	120

A Pearson's Chi-Squared test was carried out to assess whether maternal serum uric acid level and maternal and fetal complications were related. Maternal uric acid was grouped into two groups

i) <5.5mg/dl and ii)  $\geq 5.5$  mg/dl.

In women with serum uric acid levels of 5.5 mg/dl and more, 21 fetuses had complications like IUFD, IUGR, prematurity and those whose serum uric acid level was less than 5.5 mg/dl, 16 fetuses had complications. (Table 2)

**Table 2: Fetal complications in relation to maternal serum uric acid level**

Complications	<5.5 mg/dl	$\geq 5.5$ mg/dl	Total
None	60	23	83
IUFD	4	4	8
IUGR	8	7	15
Prematurity	4	10	14
Total	76	44	120

(p=0.002)

IUFD: Intrauterine Fetal Death;

IUGR: Intrauterine Growth Retardation

There was a significant association between maternal serum uric acid levels and maternal complications like pre-eclampsia, severe pre-eclampsia, eclampsia and HELLP syndrome ( $p=0.004$ ). (Table 3)

***Table 3: Maternal complications in relation to serum uric acid level***

Complications	<5.5 mg/dl	≥5.5 mg/dl	Total
Chronic Hypertension	12	4	16
Gestational Hypertension	52	21	73
Pre-eclampsia	3	7	10
Severe pre-eclampsia	6	6	12
Eclampsia	1	4	5
HELLP	2	2	4
Total	76	44	120

$p=0.004$

HELLP:Hemolysis, Elevated liver enzymes, and Low platelets

## DISCUSSION

The present study was done to assess the fetal and maternal outcomes in relation to maternal serum uric acid levels in hypertensive pregnant women. Various studies have shown that there is an increased incidence of fetal complications like IUGR, IUFD, and preterm birth in the hypertensive disorder of pregnancy. Studies have also shown that with the increase in maternal uric acid level, fetal and maternal complications also increases.[7,8]

Several studies have shown that with the increase in maternal serum uric acid level, there is an increased risk of fetal complications. In this study, there were 8 cases of IUGR, 4 cases of IUFD and 4 cases of prematurity in women with serum uric acid levels < 5.5mg/dl, whereas there were 7 IUGR, 4 IUFD and 10 prematurity cases in women with serum uric acid level ≥ 5.5mg/dl. Different studies have also shown prematurity and low birth weight associated with hyperuricemia. Kondareddy and Prathap in their study, also have shown

that IUGR, stillbirth, and prematurity was increased with elevated uric acid level.[8] Similarly, a study done by Singh et al. has also shown that prematurity, low birth weight, and low APGAR score was more in women with serum uric acid level >5.5 mg/dl as compared to those with <5.5mg/dl.[16] In the study done by Hussain et al., the association between high maternal serum uric acid levels in pre-eclamptic women and adverse fetal outcomes like low birth weight, and stillbirth was observed.[17]

This study has shown that there is a relationship between hyperuricemia and maternal complication ( $p=0.002$ ). There were 3 pre-eclampsia, 6 severe pre-eclampsia, 1 eclampsia and 2 were HELLP syndrome in women with uric acid levels <5.5 mg/dl, whereas in women with uric acid ≥ 5.5 mg/dl, there were 7 pre-eclampsia, 6 severe pre-eclampsia, 4 eclampsia and 2 cases of HELLP syndrome. However, there was no case of abruptio. This is consistent with the study done by Meena R et al, which showed that hyperuricemia in patients with hypertensive disorders during pregnancy was a strong risk factor for several maternal complications. [18] In the study done by Kumar and Singh, it was observed that a high uric acid level was associated with increased severity of the disease and adverse maternal outcomes. [7] Similarly, Kondareddy and Prathap have also shown that an increase in uric acid level is associated with increasing severity of pregnancy-induced hypertension like eclampsia, abruptio and HELLP syndrome. [8] Similarly, other studies have also shown a strong relationship between increased levels of uric acid and the severity of hypertensive disorder during pregnancy.[19,20]

## CONCLUSION

The present study showed that the increase in maternal serum uric acid level is associated with the increased risk of the feto-maternal outcome, such as IUGR, prematurity, IUFD and maternal complications like pre-eclampsia,



severe pre-eclampsia, eclampsia and HELLP syndrome. However, the study included only a small portion of the population.

## CONFLICT OF INTEREST

None

## SOURCES OF FUNDING

None

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