Original Article

DOI: 10.7860/JCDR/2020/45496.13964

# Maternal Serum Uric Acid Levels and Adverse Pregnancy Outcomes in Women with Hypertensive Disorders of Pregnancy

Obstetrics and Gynaecology Section

ARUNA MALLANGOUDA BIRADAR[1], SHREEDEVI SOMSHEKAR KORI[2], SANGAMESH S MATHAPATI[3], SUBHASH R MUDANUR[4], NEELAMMA G PATIL[5], SHIVAKUMAR S PUJERI[6]



## ABSTRACT

**Introduction:** Hypertensive Disorders of Pregnancy (HDP) are the major cause of maternal morbidity and mortality worldwide. The maximum burden of maternal mortality and morbidity is due to HDP and its related complications which is further followed by obstetric haemorrhage, pre-existing medical diseases, infections and abortions.

**Aim:** To study the association between the serum uric acid level in hypertensive pregnant women and their association with maternal and foetal morbidity and mortality.

**Materials and Methods:** It was a prospective observational study conducted at BLDE (Deemed to be) University, Shri BM Patil Medical College Hospital and Research Centre, Vijayapura, Karnataka, India from January to June 2019. A total of 165 pregnant women with HDP were included (44 (27%) had Gestational Hypertension (GH); 86 (52%), Pre-eclampsia (PE) and 35 (21%) eclampsia) in each group in the study and they were subjected for obstetric history, examination and laboratory evaluation. The laboratory evaluation included complete blood count, liver function test, renal function test, serum uric acid level and urine albumin, sugars and microscopy. The maternal and foetal outcomes were measured, which included mode of delivery, Neonatal Intensive Care Unit (NICU) admission, neonatal outcomes in terms of preterm or term delivery, intrauterine death, fresh still born, neonatal deaths.

**Results:** A total of 165 cases with HDP were enrolled in the study. Mean serum uric acid level in GH, PE and eclampsia group was 5.13±1.32, 5.34±1.4, 6.05±1.67, respectively. A total of 118 participants presented at term and 47 were preterm (11 in GH, 20 in PE and 16 in eclampsia group). About 103 (62.42%) had vaginal delivery and 62 (31.51%) underwent caesarean section (14 in GH, 28 in PE and 20 in eclampsia group). All the perinatal deaths occurred were in women with PE (n=5) and eclampsia (n=2) and was not statistically analysed.

**Conclusion:** Present study shows that increased levels of maternal serum uric acid levels were associated with PE and eclampsia compared to GH patients and were associated with adverse foetal outcomes and increase in the instrumental and operative interventions.

**Keywords:** Eclampsia, Gestational hypertension, Maternal and foetal morbidity, Pre-eclampsia

## INTRODUCTION

Worldwide around 287,000 women die annually during pregnancy and childbirth and India accounts for approximately 19% (56000) of these total deaths [1]. HDP and their associated complications account for the maximum burden of maternal mortality and morbidity followed by obstetric haemorrhage, pre-existing medical diseases, infections and abortions all over the world [2,3]. HDP affects approximately 3-10% of all pregnancies and contributes significantly to maternal and perinatal mortality and morbidity [4]. HDP ranks second most common next to Anaemia in developing countries, complicating around 7-10% of all pregnancies in some form of hypertension [5,6]. The pregnancy may bring hypertensive changes in previously normotensive women and may exaggerate the hypertension who were known hypertensive prior to pregnancy [7]. There are several studies done worldwide to the know relation between uric acid level in normal and hypertensive pregnancy, and in relation with early diagnosis of PE, and the severity of PE and associated perinatal outcome [8,9]. Serum uric acid concentration varies throughout normal gestation [10]. Some propose that uric acid level can be useful in predicting adverse maternal and foetal outcome [11], while others suggest that increased uric acid level is a poor predictor of maternal and foetal outcome [12,13].

According to the National High Blood Pressure Education Programme (NHBPEP) working group; the spectrum of HDP mainly consists of GH, PE and eclampsia [14]. The maternal complications like PE and eclampsia are viewed as “diseases of theories”and its etiology is not known and there is multisystem involvement [15]. According to recent figures, the estimated global incidence of PE is 3-10% with about 6% incidence rate in primigravida women [4]. The incidence in developing countries ranges between 1.8-16.7% with an increasing trend [16]. Early foetus delivery is the only curative treatment for PE to halt the progression of the pathophysiology, which is responsible for 15% of preterm births in developed countries [17]. In women with PE, elevated uric acid level has been determined as a better predictor of maternal or fetal outcomes than blood pressure [9].

There is a lack of such type of study in this geographical area, so this study aimed to assess the relationship between serum uric acid and pregnancy with hypertensive disorders with maternal and perinatal consequences. The null hypothesis taken is that the serum uric acid level is not different among the study groups.

## MATERIALS AND METHODS

It was a prospective observational study done at BLDE (Deemed to be) University, Shri BM Patil Medical College Hospital and Research Centre, Vijayapura, Karnataka, India. Study duration was from January 2019 to June 2019, study was carried out after obtaining the Institutional Ethics Clearance. (BLDE(DU)/IEC/306/2018-19).

All the pregnant women with gestational age >28 weeks diagnosed with HDP according to the National Institute for Health and Care Excellence (NICE) Antenatal Care guidance and willing to participate in the study and gave informed consent were included in the study.

**Inclusion criteria:** A total of 1297 women admitted to labour ward of which 165 fulfilled the inclusion criteria, hence were included in the study.

**Exclusion criteria:** The pregnant women with other medical disorders like type 2 diabetes, chronic hypertension, pre-existing renal diseases, liver disease, cardiovascular disease, thyroid and known cases of hyperuricaemia were excluded from the study.

Each and every case were subjected to detailed physical examination and all the details were recorded. Blood pressure was measured according to the NICE Antenatal Care guidance. This includes use of the correct-sized cuff, initial inflation of the cuff 20-30 mmHg above the palpable systolic Blood Pressure (BP), deflation at a rate of 2 mmHg per second, recording BP to the nearest 2 mmHg and use of Korotkoff phase V to indicate diastolic BP [18]. Simultaneously, 2 mL of venous blood sample was drawn from the patient's antecubital vein in supine position, prior to commencement of any treatment, into properly labelled tubes for measurement of serum uric acid levels. Uric acid levels were measured in laboratory by enzymatic colour test using Uricase and Peroxidase enzymes [17]. The normal value used for reference range of >4.5 mg/dL was considered positive [19].

The study population was divided into three groups; Group 1 included antenatal women with GH, Group 2 included women with PE and Group 3 included women with eclampsia features according to the NICE guidelines [20]. The maternal and foetal outcomes were measured, which includes mode of delivery, NICU admission, neonatal outcomes in terms of preterm or term delivery, intrauterine death, fresh still born and neonatal deaths.

## STATISTICAL ANALYSIS

The data were analysed by using Statistical Package for the Social Sciences (SPSS)-20 version and later compelled. Variables were presented in number and percentage (%) and continuous variables were presented as mean±SD. Quantitative variables were compared using, Analysis of Variance (ANOVA) test and Chi-square test. The p-value <0.05 was considered to be statistically significant.

## RESULTS

A total of 1297 women delivered during the study period of which 165 (13%) cases had HDP. The mean age of the participants were 25.16±3.47 in GH group, 23.76±3.65 in PE group and 22.66±2.47 in eclampsia group. Among 165 HDP women enrolled in the study, 44 (27%) had GH; 86 (52%), PE and 35 (21%) eclampsia. About 77 were primigravida and 88 were multigravida among 165. Among 165 HDP women, 103 had vaginal delivery (24 instrumental deliveries) and 62 underwent Lower Segment Caesarean Section (LSCS) (29 elective and 33 emergency).

Among total 165 HDP women 47 babies were preterm (<37 weeks), of which maximum cases were in the PE and eclampsia group [Table/Fig-1]. The relation between the serum uric acid level and mode of delivery was statistically significant as high maternal serum uric acid levels were associated with increased instrumental deliveries and caesarean section [Table/Fig-2]. The mean serum uric acid level was 5.13±1.32; 5.34±1.4; 6.05±1.67 in GH, PE and eclampsia group, respectively. This shows a high degree of association of maternal serum uric acid levels with eclampsia group [Table/Fig-3]. Out of 165 babies born, 75 (45.5%) had NICU admissions. Maximum perinatal deaths in present study were in PE followed by GH and eclampsia group [Table/Fig-1].

| Variables | GH (44) | | Pre-Eclampsia (86) | | Eclampsia (35) | | p-value |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | |
| **Gestational age (weeks)** | | | | | | | |
| <37 | 11 | 25.0% | 20 | 23.3% | 16 | 45.7% | 0.038* |
| >37 | 33 | 75.0% | 66 | 76.7% | 19 | 54.3% | |
| **Type of delivery** | | | | | | | |
| Normal | 23 | 52.3% | 46 | 53.5% | 10 | 28.6% | 0.066 |
| Forceps | 4 | 9.1% | 7 | 8.1% | 3 | 8.6% | |
| Vacuum | 3 | 6.8% | 5 | 5.8% | 2 | 5.7% | |
| Elective | 11 | 25.0% | 10 | 11.6% | 8 | 22.9% | |
| Emergency | 3 | 6.8% | 18 | 20.9% | 12 | 34.3% | |
| **Outcome** | | | | | | | |
| Neonatal death | 1 | 2.3% | 4 | 4.7% | 1 | 2.9% | 0.518 |
| FSB** | 0 | 0.0% | 0 | 0.0% | 1 | 2.9% | |
| IUD*** | 0 | 0.0% | 1 | 1.2% | 0 | 0.0% | |
| Live | 43 | 97.7% | 81 | 94.2% | 33 | 94.3% | |
| Total | 44 | 100% | 86 | 100% | 35 | 100% | |

**[Table/Fig-1]:** Gestational age; mode of delivery and perinatal outcome in different HDP.
*Significant at 5% level of significance (p<0.05); **Fresh still born; *** Intrauterine death; Chi-sqaure test

| Uric acid level | Normal | Forceps | Vaccum | Elective | Emergency | p-value |
|---|---|---|---|---|---|---|
| Mean±SD | 5.01±1.34 | 6.09±1.2 | 5.24±1.5 | 5.96±1.62 | 5.77±1.47 | 0.004* |
| Range | 2.1-8.0 | 4.5-9.0 | 2.7-7.1 | 3.6-9.8 | 3.4-9.0 | |

**[Table/Fig-2]:** Association of serum uric acid level with the mode of delivery.
*Significant at 5% level of significance (p<0.05); ANOVA; SD: Standard deviation

| | | GH | Pre-eclampsia | Eclampsia | p-value |
|---|---|---|---|---|---|
| Uric acid level | Mean±SD | 5.13±1.32 | 5.34±1.4 | 6.05±1.67 | 0.015* |
| | Range | 2.7-7.4 | 2.1-9.6 | 3.1-9.8 | |
| | 95% CI | 4.7-5.5 | 5.0-5.6 | 5.5-6.6 | |

**[Table/Fig-3]:** Association of serum uric acid level in different HDP.
*Significant at 5% level of significance (p<0.05); ANOVA; SD: Standard deviation; CI: Confidence interval; GH: Gestational Hypertension

## DISCUSSION

In present study most of the participants were multigravida (53.3%). In a study by Toshniwal S and Lamba AR most of the participants were primigravida (80%) [21], similarly in a study by Kamath R et al., the participants were mostly primigravida [22]. In present study, most of the participants delivered at term, which was a similar finding to a study done by Kumar N et al., wherein 54% of the participants delivered at term [23]. In a study by Vyakaranam S et al., 50% had term delivery [24]. In a study by Kamath R et al., 60% of participants had term delivery [22]. In present study, the higher rates of NICU admissions and early neonatal death were associated with the increased levels of maternal serum uric acid levels in PE and eclampsia groups with an associated increase in an instrumental and operative delivery.

| Studies | GHTN (mg/dL) | Pre-eclampsia (mg/dL) | Severe Pre-eclampsia (mg/dL) | Eclampsia (mg/dL) |
|---|---|---|---|---|
| Present | 5.13±1.32 | 5.34±1.4 | - | 6.05±1.67 |
| Vyakaranam S et al., [24] | 4.27±1.0 | 6.26±1.19 | - | - |
| Toshniwal S and Lamba AR [21] | 6.89 | 7.60 | 8.33 | - |
| Kumar N et al., [23] | 5.47±1.93 | 6.72±2.51 | | 8.71±2.97 |
| Kamath R et al., [22] | | 4.03 | 5.57 | 6.47 |

**[Table/Fig-4]:** Uric acid levels in various studies [21-24].
GHTN: Gestational Hypertension

The highest levels of uric acid were in eclampsia group (6.05±1.67) compared to PE (5.34±1.4) and GH group (5.13±1.32) in present study. The findings observed in other studies are comparable to the present study as depicted in [Table/Fig-4] [21-24].

In present study, the maximum cases of LSCS were done in eclampsia group (57%) similar to Kumar N et al., in which 53% of the patients underwent LSCS [23], whereas in a study by Vyakaranam S et al., where only PE and GH patients were involved, 86% of the pre-eclamptic patients underwent caesarean section, where as 63% of GH underwent LSCS [24]. Hence, increased maternal serum uric acid can be used as one of the predictors for assessing the severity of HDP and its associated maternal and perinatal morbidity and mortality.

### Limitation(s)

The limitation of present study was in terms of less sample size, it was a single arm observational study. Other parameters could have been analysed and the serum uric acid level should have been monitored in postpartum period.

## CONCLUSION(S)

Increased levels of maternal serum uric acid levels were associated with PE and eclampsia compared to GH patients and is associated with adverse foetal outcomes and increase in the instrumental and operative interventions. It can also be used to plan management of the disease and prevent the complications.

## REFERENCES


[1] Trends In Maternal Mortality: 1990 To 2010. WHO, UNICEF, UNFPA And The World Bank Estimates. Available at http://Whqlibdoc.Who.Int/Publications/2012/9789241503631_Eng.Pdf, (Accessed on July 12, 2012).

[2] Park K. Preventive Medicine In Obstetrics, Paediatrics and Geriatrics, In: K. Park (Ed), Park S Textbook of Preventive and Social Medicine, 21st Ed, M/S BanarasidasBhanot Publishers, 2011, Pp. 514-17.

[3] Bridwell M, Handzel E, Hynes M, Louis RJ, Fitter D, Hogue C, et al. Hypertensive disorders in pregnancy and maternal and neonatal outcomes in Haiti: The importance of surveillance and data collection. BMC Pregnancy Childbirth. 2019;19(1):208.

[4] Jeybalan A. Epidemiology of pre-eclampsia: Impact of obesity. Nutr Rev. 2013;71 Suppl 1(01):S18-25. doi:10.1111/hure.12055.

[5] Tejal P, Astha D. Relationship of serum uric acid level to maternal and perinatal outcome in patients with hypertensive disorders of pregnancy. Gujarat Med J. 2014;69(2):45-47.

[6] Braunthal S, Brateanu A. Hypertension in pregnancy: Pathophysiology and treatment. SAGE Open Med. 2019;7:2050312119843700.

[7] Nagar T, Sharma D, Choudhary M, Khoiwal S, Nagar RP, Pandita A. The role of uterine and umbilical arterial doppler in high-risk pregnancy: A prospective observational study from India. Clin Med Insights Reprod Health. 2015;9:01-05.

[8] Le TM, Nguyen LH, Phan NL, Le DD, Nguyen HVQ, Truong VQ, et al. Maternal serum uric acid concentration and pregnancy outcomes in women with pre-eclampsia/eclampsia. Int J Gynaecol Obstet. 2019;144(1):21-26. doi:10.1002/ijgo.12697Le.

[9] Asgharnia M, Mirblouk F, Kazemi S, Pourmarzi D, MahdipourKeivani M, DalilHeirati SF. Maternal serum uric acid level and maternal and neonatal complications in preeclamptic women: A cross-sectional study. Int J Reprod Biomed (Yazd). 2017;15(9):583-88.

[10] Akahori Y, Masuyama H, Hiramatsu Y. The correlation of maternal uric acid concentration with small-for-gestational-age fetuses in normotensive pregnant women. Gynecol Obstet Invest. 2012;73(2):162-67. doi:10.1159/000332391.

[11] Livingston JR, Payne B, Brown M, Roberts JM, Côté A-M, Magee LA, et al. Uric acid as a predictor of adverse maternal and perinatal outcome in women hospitalized with pre-eclampsia. J Obstet Gynecol Can. 2014;36(10):870-77.

[12] Macdonald-Wallis C, Lawlor DA, Fraser A, May M, Nelson SM, Tilling K. Blood pressure change in normotensive, gestational hypertensive, preeclamptic, and essential hypertensive pregnancies. Hypertension. 2012;59(6):1241-48.

[13] Sahu S, Daniel M, Abraham R, Vedavalli R, Senthilvel V. Study of uric acid and nitric oxide concentrations in pre-eclampsia and normal pregnancy. Int J Biol Med Res. 2011;2(1):390-93.

[14] Yu H, He Y, Mao Z, Dong W, Fu X, Lei X. Hypertensive disorders during pregnancy and elevated blood pressure in the offspring: A systematical review and meta-analysis protocol. Medicine. 2019;98(20).

[15] Fekete K, Berti C, Cetin I, Hermoso M, Koletzko BV, Decsi T. Perinatal folate supply: Relevance in health outcome parameters. Maternal & Child Nutrition. 2010;6:23-38.

[16] Belay AS, Wudad T. Prevalence and associated factors of pre-eclampsia among pregnant women attending anti-natal care at Mettu Karl referal hospital, Ethiopia: Cross-sectional study. Clinical Hypertension. 2019;25(1):14.

[17] Islam M, Ahmed I, Anik MI, Ferdous M, Khan MS. Developing paper based diagnostic technique to detect uric acid in urine. Frontiers in Chemistry. 2018;6:496.

[18] Phipps EA, Thadhani R, Benzing T, Karumanchi SA. Pre-eclampsia: Pathogenesis, novel diagnostics and therapies. Nature Reviews Nephrology. 2019:1.

[19] Amini E, Sheikh M, Hantoushzadeh S, Shariat M, Abdollahi A, Kashanian M. Maternal hyperuricemia in normotensive singleton pregnancy, a prenatal finding with continuous perinatal and postnatal effects, a prospective cohort study. BMC Pregnancy and Childbirth. 2014;14(1):104.

[20] Surveillance report (exceptional review) 2017- Antenatal care for uncomplicated pregnancies (2008) NICE guideline CG62. London: National Institute for Health and Care Excellence (UK); 2017.

[21] Toshniwal S, Lamba AR. Serum uric acid as marker of severity of pre-eclampsia. Int J Reprod Contraception Obstetrics Gynecology. 2017;6(11):4915-17.

[22] Kamath R, Nayak R, Shantharam M. Serum Uric acid level in pre-eclampsia and its correlation to maternal and fetal outcome. Int Jour of Biomed Res [Internet]. 2014 [cited 2020 Jul.8];5(1):22-24.

[23] Kumar N, Singh AK, Maini B. Impact of maternal serum uric acid on perinatal outcome in women with hypertensive disorders of pregnancy: A prospective study. Pregnancy Hypertens. 2017;10:220-25. doi:10.1016/j.preghy.2017.10.002.

[24] Vyakaranam S, Bhongir AV, Patlolla D, Chintapally R. Study of serum uric acid and creatinine in hypertensive disorders of pregnancy. Int J Med Sci Public Health. 2015;4(10):1424-28.



**PARTICULARS OF CONTRIBUTORS:**

1. Associate Professor, Department of Obstetrics and Gynaecology, Shri. B.M. Patil Medical College, Vijayapura, Karnataka, India.
2. Assistant Professor, Department of Obstetrics and Gynaecology, Shri. B.M. Patil Medical College, Vijayapura, Karnataka, India.
3. Assistant Professor, Department of Obstetrics and Gynaecology, Shri. B.M. Patil Medical College, Vijayapura, Karnataka, India.
4. Professor, Department of Obstetrics and Gynaecology, Shri. B.M. Patil Medical College, Vijayapura, Karnataka, India.
5. Professor, Department of Obstetrics and Gynaecology, Shri. B.M. Patil Medical College, Vijayapura, Karnataka, India.
6. Senior Resident, Department of Obstetrics and Gynaecology, Shri. B.M. Patil Medical College, Vijayapura, Karnataka, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Shreedevi Somshekar Kori,
BLDE (Deemed to be) University, Shri. B.M. Patil Medical College,
Vijayapura-586103, Karnataka, India.
E-mail: shreedevi.kori@bldedu.ac.in



**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: Jun 16, 2020
- Manual Googling: Jul 14, 2020
- iThenticate Software: Jul 31, 2020 (22%)

**ETYMOLOGY:** Author Origin

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jun 16, 2020**
Date of Peer Review: **Jul 04, 2020**
Date of Acceptance: **Jul 14, 2020**
Date of Publishing: **Aug 01, 2020**