

# Maternal and Fetal Outcome among Women having Pre Eclampsia with Hyperuricemia

SHAMAMA RAHIM<sup>1</sup>, SHAZIA MAHMOOD AWAN<sup>2</sup>, FAIZA KHANUM<sup>3</sup>, ERUM PERVAIZ<sup>4</sup>, SAIRA SAEED<sup>5</sup>, NEELUM ZAHIR<sup>6</sup>

<sup>1</sup>Medical Officer, Gynae & Obs Department, Hayatabad Medical Complex Peshawar

<sup>2</sup>Assistant Professor Gynae & Obs Department, CMH Quetta

<sup>3</sup>Classified Gynaecologist, Gynae & Obs Department, CMH Quetta

<sup>4</sup>Assistant Professor, Gynae & Obs Department, CMH Quetta

<sup>5</sup>Professor, Gynae & Obs Department, CMH Kharian

<sup>6</sup>Medical Officer, Gynae & Obs, Saidu Group of Teaching Hospital, Swat

Correspondence to: Dr Shazia Mahmood Awan, Assistant Professor Gynae & Obs department, CMH Quetta.

## ABSTRACT

**Objective:** To find out the frequency of some common maternal and fetal outcomes among women having pre eclampsia with hyperuricemia.

**Study design:** Cross sectional study.

**Place and duration of study:** Department of Obstetrics and Gynaecology, Hayatabad Medical Complex, Peshawar from April 2019 to Oct 2019.

**Patients and methods:** A total of 161 women with singleton pregnancy irrespective of gravity and parity, in age group ranging from 20-35 years having pre eclampsia with hyperuricemia were included in consecutive manner. All patients signed informed written consent for study and its outcome. Detailed history taking and examination were performed and standard lab investigations were sent. All patients were followed up till 40<sup>th</sup> day of delivery for maternal (caesarean section, eclampsia and maternal death) and fetal outcome [intrauterine fetal death, (small for gestational age) SGA and APGAR score]. Data was analyzed using SPSS version 20.

**Results:** Maternal complications in patients of pre eclampsia with hyperuricemia were eclampsia 15.5%, caesarean section 18% and death 19.3%. Fetal complications included SGA 11.8%, intrauterine death 16.8% and APGAR score at 5 minutes 24.2%. The mean age and standard deviation of sample were 28.4 + 4.8 years, mean gravidity (2.7±1.1), mean parity (2.4±0.9) and mean BMI (24.37±2.4 kg/m<sup>2</sup>).

**Conclusion:** Hyperuricemia in pre-eclampsia is a poor prognostic factor with increased maternal and fetal deaths, worsening of pre eclampsia to eclampsia and low APGAR scores of fetus.

**Key words:** Pre eclampsia, hyperuricemia, maternal death, caesarean section, small for gestational age, APGAR score.

## INTRODUCTION

Hypertensive disorders in pregnancy are very common which constitute upto 10% of pregnancies, out of which 3% - 5% are complicated by pre eclampsia.<sup>1</sup>

Pre eclampsia is defined as new onset hypertension (> 140mmHg systolic or > 90mmHg diastolic) after 20 weeks of gestation with protein urea and evidence of maternal organ and uteroplacental dysfunction.<sup>2</sup> It is a multisystem disease with unknown etiology. Pre eclampsia is associated with increased maternal and fetal morbidity which includes placental absorption, eclampsia, disseminated intravascular co-agulation, increased operative intervention and maternal death.<sup>3</sup>

Adverse fetal effects include intrauterine growth restriction (IUGR) or SGA, pre-term birth, low APGAR scores at birth and fetal death.<sup>4</sup> Risk of pre eclampsia is increased in patients with history of chronic hypertension, previous history of pregnancy induced hypertension, nulliparity, age > 40 years, family history of hypertension and when body mass index (BMI) is > 35kg/m<sup>2</sup>.<sup>5</sup>

International Society of Hypertension in Pregnancy (ISSHP) recommends that all patients with pre eclampsia should be investigated by measuring haemoglobin (Hb), platelet count, liver enzymes, serum creatinine and serum uric acid to determine the degree of maternal organ dysfunction and to assess the severity of pre eclampsia.<sup>6</sup> Some studies have also suggested that estimation of circulating angiogenic factors like PlGF. Till now there is no valid, reliable cost effective test for easy detection of pre eclampsia but serum uric acid is one of reliable test in some studies.<sup>2</sup> Uric acid is the final product of purine metabolism in the body. The upper limit of normal reference range for men is 7mg/dl (0.42mmol/L) and for females is 6mg/dl (0.36mmol/L).<sup>7</sup> Increased serum uric acid levels are called hyperuricemia. Hyperuricemia is the first and earliest laboratory presentation in pre eclampsia due to decreased glomerular filtration, increased tubular reabsorption and reduced secretion.<sup>2</sup> Studies show that serum uric acid can be a poor predictor of onset of pre eclampsia but it is a very strong predictor of poor maternal and fetal outcomes.<sup>8</sup> Hyperuricemia is associated with poor obstetric outcomes like increased chances of

emergency caesarean section, development of eclampsia and maternal morbidity. It is also associated with preterm labor, small for gestational age fetus, low APGAR scores and fetal death.<sup>9</sup>

Keeping in view the prevalence of pre eclampsia in this study we aimed to investigate the relationship between the levels of uric acid with maternal and fetal complications in women with pre eclampsia. Knowing the effects of uric acid on the severity of pre eclampsia and maternal and neonatal complications can help easy diagnosis, optimization and treatment. Results can be used for early decision making and prevention from maternal and neonatal complications.

## MATERIALS AND METHODS

This cross sectional study was conducted at department of Obstetrics and Gynaecology, Hayatabad Medical Complex Peshawar from April 2019 to Oct 2019. Total of 161 patients were included in this study. All pregnant women with age range of 20-35 years with singleton pregnancy and having pre eclampsia (PE) with hyperuricemia were included in study admitted through OPD and emergency. Women were included irrespective of gravidity and parity and they were counseled about purpose of study and informed written consent was signed. Women with pre-existing medical disorders, multiple pregnancy and congenitally anomalous fetuses were excluded.

All women were subjected to detailed history and examination. Their age, BMI, gravidity and parity were noted. Standard lab investigations were performed. Patients with raised serum uric acid levels were included and were followed up till 40<sup>th</sup> day post-partum. Patients were followed to determine common maternal and fetal death, intrauterine fetal death, SGA and low APGAR score at birth.

All data was analyzed by SPSS version 20.0. Descriptive statistics like frequencies and percentages were used to describe the qualitative variables. Mean and SD ratio were calculated for numerical variables like age, BMI, gravidity, parity and serum uric acid level. Chi square test with p value of <0.5 kept as significant to see the effect modification.

## RESULTS

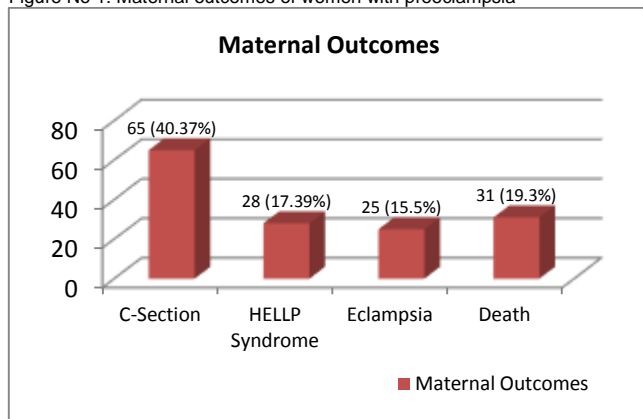
A total of 161 women presenting with pre-eclampsia and having hyperuricemia were included in study in consecutive manner and followed up for maternal and fetal outcome. The mean age and standard deviation of the sample was 28.4±4.8 years. The mean gravidity was 2.6±1.1 and mean parity was 2.4±0.9. The body mass index of the study sample was 24.3±2.4 kg/m<sup>2</sup>. Mean gestational age was 34.45±4.68 weeks. The mean serum uric acid level of the whole sample was 6.0±0.5 mg/dl. (Table No 1)

Table No 1: Baseline Details of all the patients

Variable	Mean	SD
Mean Age	28.4	4.8
Gestational Age	34.45	4.68
Gravidity	2.6	1.1
Parity	2.4	0.9
Serum Uric Acid Level (mg/dl)	6	0.5

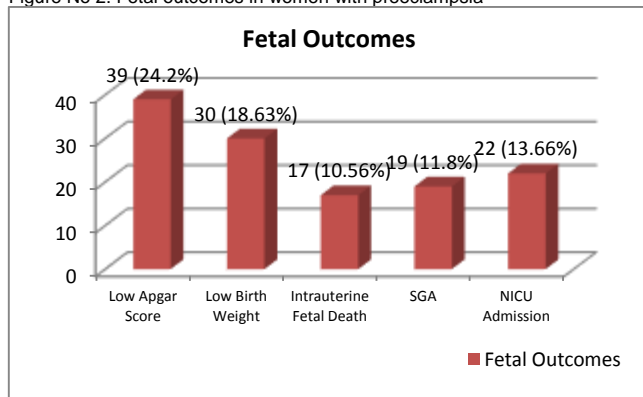
According to maternal complications, we found that 65 (40.37%) patients had cesarean sections, 28 (17.39%) had HELLP syndrome, 25 (15.5%) patients had eclampsia, and maternal death was found in 31 (19.3%) patients. (Figure 1)

Figure No 1: Maternal outcomes of women with preeclampsia



According to the fetal outcomes, we found that intrauterine fetal death was found in 17 (10.56%) patients, SGA found in 19 (11.8%), Low Apgar score found in 39 (24.2%), low birth weight found in 30 (18.63%) and NICU admission found in 22 (13.66%) patients. (Figure 2)

Figure No 2: Fetal outcomes in women with preeclampsia



## DISCUSSION

An association between raised level of serum uric acid and pre eclampsia has been acknowledged in 1800's.<sup>10</sup> Uric acid has been reported as a key factor in pathogenesis of pre eclampsia.

Increased levels of serum uric acid increase the severity of disease and is predictive of poor maternal and fetal outcomes.<sup>11</sup>

The same is proved in our study that raised serum uric acid level is poor predictor of maternal and fetal outcome. Increased levels of serum uric acid increase the severity of the disease and maternal and fetal outcomes have poor prognosis.<sup>11</sup> Endothelial dysfunction and placental ischemia are key factors in pathogenesis of pre eclampsia. Excessive cellular activity due to process of placental ischemia leads to excessive production of uric acid, which subsequently serves as a biomarker of the disease. Studies show that abnormal levels of serum uric acid can be detected before the appearance of proteinuria.<sup>12</sup> Uric acid is the end product of purine metabolism. Mazzali et al. demonstrated an elevation in serum uric acid levels followed by increase in blood pressure levels.<sup>13</sup> Reduction in blood pressure was noted with reduced levels of serum uric acid. In a recent metaanalysis it is shown that estimation of concentration of uric acid is clinically useful in prediction of adverse outcomes of pre eclampsia.<sup>12</sup> Study of Enarun et al. suggests that threshold concentration of serum uric acid for prediction of SGA fetus is 6.35 mg/dl. Another study by Nair A et al. showed that mean serum uric acid concentration to predict adverse fetal outcome is 6.37 mg/dl.<sup>14</sup> In another study maternal serum uric acid is a predictor of preterm birth and low birth weight.<sup>15</sup>

One study of Jim B et al. showed that pre eclampsia with hyperuricemia is associated with poor maternal outcomes like eclampsia and maternal death.<sup>16</sup>

In developing countries pre eclampsia is a leading cause of maternal mortality causing an estimated > 50,000 deaths per year.<sup>17</sup> While in developed countries it is a common cause of maternal morbidity and intensive care unit admissions. Although some studies also reported that uricemia is not a consistent predictor of pre eclampsia.<sup>18</sup>

One study showed that 52.9% of pre eclamptic patients had caesarean section and 19.6% had preterm labour. This study also showed that pre eclamptic patients with hyperuricemia had 66 times more likely to have APGAR scores less than 7, and also had 3 times less birth weight and had more neonatal intensive care units (NICU) admissions. This study also showed that 53% of patients had very severe pre eclampsia or eclampsia.<sup>19</sup>

Pre eclamptic patients with raised serum uric acid level have high maternal mortality rate and morbidity.<sup>20</sup> In 2016 a prospective, cross sectional comparative study of 200 patients, with 100 patients in each group also showed that serum uric acid level more than 6 mg/dl in patients with pre eclampsia is an important biomarker for presence of adverse maternal and fetal outcomes.<sup>21</sup>

Our data suggests that presence of hyperuricemia, identifies as population of hypertensive pregnant women at increased risk of maternal and fetal complications.

## CONCLUSION

Hyperuricemia is an important complication of pregnancy and pre eclampsia has worse maternal and fetal outcome. We recommend more studies particularly analytical studies on larger sample size to identify effects of hyperuricemia on maternal hepatic dysfunction and it's cerebral effects.

## REFERENCES

- Rachael F, Jamie K, Adam J, Lewandowski. Pre eclampsia: risk factors, diagnosis, management, and the cardio vascular Impact on the offspring. J Clin Med. 2019 Oct; 8 (10): 1625.
- Asgharnia M, Mirblouk F, Falemah Dalil S. Maternal serum uric acid level and maternal and neonatal complications in pre eclamptic women: A cross sectional study. Int J Reprod Biomed. 2017 Sep; 15 (9): 583-588.
- Modazli R, Yuksel MA, Imamoglu M, Tuten A, Oncul M, Aydin B, Demirayak G. Comparison of Clinical and Perinatal Outcomes in Early and late-onset Pre eclampsia. Arch. Gynaecol. Obstet. 2014; 290: 53-57.
- Rezk M, Gamal A, Emara M. Maternal and Fetal Outcome in deNovo Pre eclampsia in Comparison to Superimposed Pre eclampsia: A

- Two-Year Observational Study. *Hypertens. Pregnancy.* 2015; 34:137-144.
5. Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, Hall DR, Warren CE. Hypertensive Disorders of Pregnancy: ISSHP Classification, Diagnosis, and Management Recommendations for International Practice. *Hypertension.* 2018; 72:21-43.
  6. Kumar N, Singh AK. Maternal Serum Uric acid as a Predictor of Severity of Hypertensive Disorders of Pregnancy: A Prospective Cohort Study. *Med Gen.* 2019; 15 (2): 154-160.
  7. Livingston JR PB, Brown M, Roberts JM, Cote AM. Uric acid as a predictor of adverse maternal and perinatal outcomes in women hospitalized with pre eclampsia. *J Obstet Gynaecol Can.* 2014; 36: 870-877.
  8. Elmas AY, Simsak T. The relationship between Hypertension and plasma allantoin, uric acid, xanthine oxidase activity and nitrite and their predictive capacity in severe pre eclampsia. *J Obstet Gynaecol.* 2016; 36:34-38.
  9. Soura MS, Makedou K, Theodoridis T, Kourtis A, Zepiridis L. The Involvement of uric acid in the pathogenesis of pre eclampsia. *Curr Hypertens Rev.* 2015; 11: 110-115.
  10. Zangana JW, Hamadaman AI. Serum uric acid as a predictor of perinatal outcome in women with pre eclampsia. *Int J Med Research & Health Sci.* 2018; 7 (3): 168-174.
  11. Khaliq P et al. Role of Uric acid in pre eclampsia: Is Uric Acid a Causative Factor or a sign of Pre eclampsia? *Curr Hyper Tens Rep.* 2018 Jul 10; 20 (9): 80.
  12. Enaruna ON, Idemudia OJ, Aikoriogiel. Serum lipid profile and uric acid levels in pre eclampsia in University of Benim Teaching Hospital. *Niger Med J.* 2014 Sep-Oct; 55 (5): 423-427.
  13. Ryu A, Cho JN, Young Lee E. Predictive value of serum uric acid levels for adverse perinatal outcomes of pre eclampsia. *Medicine (Baltimore).* 2019 May; 98 (18): e15462.
  14. Nair A, Savitha C. Estimation of serum uric acid as an indicator of severity of pre eclampsia and perinatal outcome. *J Obstet Gynaecol India* 2017; 67:109-18.
  15. Vyakaranam S, Bhongir AU, Pallolla D, et al. Study of serum uric acid and creatinine in hypertensive disorder of pregnancy. *Int J Med Sci Public Health* 2015; 4: 1424-8.
  16. Jim B, Karumanchi SA. Pre eclampsia: Pathogenesis, Prevention and long term complications. *Semin Nephrol.* 2017;37: 386-397.
  17. World Health Organization. World Health Report: Make Every Mother and Child Count. World Health Organization. Geneva, Switzerland, 2005.
  18. Martin AC and Brown MA. Could uric acid have a pathogenic role in pre eclampsia? *Nature Reviews Nephrology*, 2010; vol. 6 (12): 744-48.
  19. Ugwuanyi RU, Chiege MI, Agwu FE, Eleje GU, Martin N. Association between Serum Uric Acid levels and Perinatal Outcome in Women with Pre eclampsia. *Obstet Gynaecol Int.* vol 2021.
  20. Patel T, Dudhat A. Relationship of serum uric acid levels to maternal and perinatal outcome in patients with hypertensive disorders of pregnancy. *GMJ.* 2014; 69 (2): 45-47.
  21. Santillan AA, Garduna JC, Lean Ponce MA. Uric Acid in pregnancy: New Concepts. *Contrib Nephrol.* 2018; 192: 110-115.