

Hyperuricemia as a Risk Factor for Preterm Delivery in Women with Pre-Eclampsia

FAREEHA USMAN¹, SAEQAH MANZOOR², SUMAIRA MAQSOOD³, AFZAL ARIF⁴, ABIDA HIJAZI⁵, SUMAIRA MANZOOR⁶

¹Senior Registrar, Department of Obstetrics & Gynaecology, Bahawalpur Medical & Dental Hospital, Bahawalpur

^{2,3,6}Women Medical Officers, Department of Obstetrics & Gynaecology, Sadiq Abbasi Hospital, Bahawalpur

⁴Senior Medical Officer, Department of Anaesthesia, Bahawal Victoria Hospital, Bahawalpur

⁵Senior Women Medical Officer, Civil Hospital, Bahawalpur

Correspondence to: Fareeha Usman, Email: fareehausmanbwp@gmail.com, Cell: 0333-0681433

ABSTRACT

Objective: To determine hyperuricemia as a risk factor for preterm delivery in women with pre-eclampsia.

Study Type: Case control study.

Duration and Place of Study: Department of Gynaecology and Obstetrics, Sadiq Abbasi Hospital Bahawalpur from 1st July to 31st December 2019.

Material and Methods: One hundred cases of pre-eclamptic and hyperuricemic women admitted for delivery through out-patient and emergency departments were divided in two groups, 50 cases in each group.

Results: 70% women had hyperuricemia and pre-eclampsia deliver preterm and 34% women who had hyperuricemia and preeclampsia deliver at term.

Conclusion: High serum uric acid concentration increased the chances of preterm delivery in pre-eclamptic women.

Keywords: Hyperuricemia, Pre-eclampsia, Gestational hypertension, Uric acid, Pre-term delivery

INTRODUCTION

Pre-eclampsia is a common hypertensive disorder of pregnancy affecting 3-14% of pregnancies world wide.¹ It is characterized by development of hypertension with proteinuria after 20 weeks of gestation.²

Pre-eclampsia is associated with increased maternal perinatal mortality and morbidity.² Complications of hypertension are the 3rd leading cause of pregnancy related death.³ It accounts for 15% of preterm deliveries per year and five-fold increase risk of fetal death worldwide.⁴

Serum uric acid is raised in 75% of pre-eclamptic women.⁴ It is one of the earliest detectable change in pre-eclampsia.⁵ Severity of pre-eclampsia increases with increase in concentration of serum uric acid.⁶ Some assuring, uric acid in pre-eclamptic women can identify patients at higher risk for medically indicated preterm delivery.⁷

In pre-eclampsia hyperuricemia is linked with higher chances of small for gestational age infants, smaller and preterm birth, weight centiles.⁴ Among pre-eclamptic women who deliver preterm 56.3% found to have raised uric acid level, and among pre-eclamptic women who deliver at term 7.24% have raised uric acid level.⁸ Hyperuricemia causes seven fold increase risk of preterm delivery in preeclampsia, for every one unit increase in uric acid level, odds of preterm delivery increases 2.3 times. Most of early deliveries are induced to prevent more severe maternal illness.⁴

There are several proposed mechanisms for elevation of serum uric acid, such as abnormal renal clearance increased tissue breakdown and acidosis. Raised serum uric acid level promotes inflammation, oxidative stress and endothelial dysfunction, which causes placental dysfunction and have potential impact on maternal vascular health, results in increase risk of preterm delivery and adverse fetomaternal outcomes in pre-eclampsia.⁹

The importance of my study is to identify high risk pre-eclamptic women with raised serum uric acid levels, so that proper management strategies for these patients could be developed earlier, and preterm deliveries could be prevented.

MATERIALS AND METHODS

It was a case control study led at Department of Obstetrics & Gynecology, Sadiq Abbasi Hospital Bahawalpur from 1st July to 31st December 2019. A total of 100 cases were taken, 50 cases in each group. Age 18-35 years, primigravida, single pregnancy (on ultrasound) and diagnosed case of pre-eclampsia were included. Smoking, diagnosed case of gout (on history), diagnosed case of chronic renal diseases (on history), vaginal and urinary tract

infections (on HVS and MSU cultures), ruptured membranes (on clinical examination), fetal malformations and polyhydroamnios (on ultrasound) and anaemia (Hb <9g/ml) were excluded. Name, age and gestational age were recorded. They were divided in two groups; cases are pre-eclamptic and preterm (<37 weeks gestation on ultrasound) and controls are pre-eclamptic at term (>37 weeks gestation on ultrasound).

Blood samples of mothers were drawn with the help of syringe before delivery and will be sent to laboratory of Sir Ganga Ram Hospital, Lahore. Report was analyzed to assess the presence or absence of hyperuricemia. Data was entered and analyzed by SPSS-21. Odds ratio was calculated to assess the strength of association between hyperuricemia and preterm delivery OR >2 considered as significant.

RESULTS

The mean age was 27.32±3.16 years in group A while in group B, it was 29.24±4.15 years and 20 (40%) patients between 18-26 years in group A while 13 (26%) patients between 18-26 years in group B. 30 (60%) patients between 27-35 years in group A and 37 (74%) patients in group B. Most of the patients in both group were 67 (67%) in the age range between 27-35 years. The difference was statistically not significant between two groups (Table 1).

Group A had 33.0±2.60 weeks as a mean gestational age where as 38.02±1.33 week was the mean gestational age of group-B. Out of 50,23 (46%) patients were in gestational age group between 27-33 weeks in group A while only 6 (12%) patient was in gestational age group between 27-33 weeks in group B. 27 (54%) patients were between 34-40 weeks in group A and, 44 (88%) patients in group B. Most of patients in both group were 71 (71%) in gestational age range between 27-40 weeks (Table 2).

The mean uric acid of patients in group A was 6.08±1.89 mg/dl between 2.8-5.0 mg/dl. From 5.1-8.0 mg/dl uric acid 12 (24%) patients in group A and 26 (52%) were in group B. Nine (18%) patients were in group A, while 6 (12%) patient were in group B. Most of the patients in both group were 50 (50%) between 5.1-8.0 mg/dl of uric acid (Table 3).

Table 1: Age distribution of patients in both groups

Age (years)	Group A		Group B	
	No.	%	No.	%
18-26	20	40.0	13	26.0
27-35	30	60.0	37	74
Mean±SD	27.32±4.04		29.24±4.15	

In group A, 35 (70%) patients were hyperuricemic and 17 (34%) patients were in group-B. In group-A, 15 (30%) patients

were non-hyperuricemic while in group -B, 33 (66%) patients were non hyperuricemic. Most of the patients in both groups 52 (52%) were hyperuricemic. There were odd cases 2.3, odd control 0.51 and Odd's ratio was 4.5 (Table 4).

Table 2: Distribution of gestational age of patients in both groups

Gestational age	Group A		Group B	
	No.	%	No.	%
27-33	23	46.0	1	2.0
34-40	27	54.0	49	98.0
Mean±SD	33.0±2.60		38.02±1.33	

Table 3: Frequency of uric acid of patients in both groups

Uric acid	Group A		Group B	
	No.	%	No.	%
2.8-5.0	15	30.0	20	40.0
5.1-8.0	31	62.0	19	38.0
8.1-11	4	8.0	11	22.0
Mean±SD	1.78±0.58		1.82±0.77	

Table 4: Frequency of hyperuricemia of patients in both groups

Variable	Group A		Group B	
	No.	%	No.	%
Hyperuricemia	35	70.0	17	34.0
Non-hyperuricemia	15	30.0	33	66.0

Odd Cases 2.3
 Odd Controls 0.51
 Odd's Ratio 4.5

DISCUSSION

A study carried out by Mohieldein et al¹⁰ mean age of study participants was 27.4±6.1 years. Another study reported by Malas et al¹¹ the mean age was 23.40±5.10 years in study group. In present work, mean age of both study groups was 28 years which is comparable with other national and international studies.

In study done by Baulon et al¹², gestational age of study population at the time of delivery was 39.30±1.55 weeks. Result of study presented by Powers et al¹³ the gestational age was 39.4 weeks in study group. Different studies reported, regular checkups are recommended for prevention and timely diagnosis of eclampsia.^{13,14} The present study shows 46%patients of 27-33 weeks of gestational age was present in group A and 12% patient had group B. Twenty-seven (54%) patients from group A had 34-40 weeks of gestational age and 44 (88%) of females from group B had preeclampsia at term which is comparable with other studies.^{13,14}

Study reported by Laughon et al¹⁵ the high level of uric acid cause insulin resistance in mid gestation and insulin resistance without hyperuricemia cause low birth weight infant. In comparison of the present study the mean uric acid was almost similar in both groups. Values of serum uric acid in the current study were also similar with other findings. In group A, majority of women with hyperuricemia were present in contrast to group B which is comparable with the other studies.^{14,15}

In study reported by Lind et al¹⁶ uric acid is synthesized by purine metabolism with the help of enzyme, xanthine oxidase. During pregnancies, uric acid level gets elevated throughout the pregnancy. This high serum uric acid level might be due to altered renal functioning. This might also indicate the underlying renal disease in some females.¹⁷⁻¹⁹ These alterations cause escalation in uric acid level especially in the third trimester of pregnancy, also cause glomerular filtration changes. Though, these alterations not only changes glomerular filtration rate but also cause changes in the secretion of xanthine oxidase.

The women with preeclampsia and high uric acid escalate the chances of preterm and SGA infants.²⁰ Moreover, it is

noteworthy to state that the women with gestational hypertension and high uric acid concentration have same pregnancy outcome just like women with pre-eclampsia.

CONCLUSION

Several mechanisms cause higher uric acid level in pregnant females mainly changes in renal functioning. There are 70% women who had hyperuricemia and pre-eclampsia deliver pre term and 34% women who had hyperuricemia and pre-eclampsia deliver at term. Serum uric acid concentration significantly raised in pregnant females throughout the pregnancy and it escalates the chances of pre-term delivery.

REFERENCES

- Koopmans CM, Pampus MG, Green Home. Accuracy of serum uric acid as a predictive test for maternal complications in preeclampsia. *Eur Obstet Gynecol* 2009;146:8-14.
- Shennan A. Dewhurst textbook of obstetrics & gynaecology 7th ed. London: Keith Edmonds 2007;227.
- Channel P, Brown M, Simpson JM, Devoe G. Proteinuria in preeclampsia how much matters? *Because J Obstet Gynecol* 2005;112:280-5.
- Roberts D, Bonded LM, Lain KY. Poor pregnancy outcome increased uric acid. *Hypertension* 2005;67:759-1.
- Barclay L. Uric acid levels may help to identify preterm delivery in women with gestational hypertension. *Hypertension* 2005;51:538-9.
- Fakhri M, Shirvani MA, Tahmtan RM. Comparative study of serum uric acid levels in pre-eclamptic and normal pregnant women and it's related out comes. *J Mazandaran Uni* 2005;15:47.
- Marian C, Limacher MD. Uric acid adds to clinical risk assessment in preeclampsia. *J Watch Women Health* 2006;5:307.
- Roberts JM, Bonded LM, Lain KY. Uric acid as important as proteinuria identifying fetal risk in women with gestational hypertension. *J Am Heart Assoc* 2005.
- Bainbridge SA, Roberts JM. Uric acid as pathogenic factor in preeclampsia. *Placenta* 2008;29:67-72.
- Mohieldein AH, Dokem AA, Osman YHM, Hamza MA, Idris HMA. Serum calcium level as a marker of pregnancy induced hypertension. *Sudan JMS* 2007;2:245-48.
- Malas NO, Zaid M, Shurideh ZM. Does serum calcium in preeclampsia and normal pregnancy differ? *Saudi Med J* 2001;22:868-71.
- Baulon E, Fraser WD, Piedboeuf B, Buekens P, Xiong X. Pregnancy induced hypertension and infant growth at 28 and 42 days postpartum. *Bio Med Center* 2005;5:5-10.
- Prowers RW, Bodnar LM, Ness RB, Cooper KM, Gallagher MJ, Frank MP et al. Uric acid concentration in early pregnancy among preeclampsia women with gestational hyperuricemia at delivery. *Am J Obstet Gynaecol* 2006;194:160-8.
- Brown CM, Garovic VD. Drug treatment of hypertension in pregnancy. *Drugs* 2014;74(3): 283-96.
- Laughon SK, Catov J, Roberts JM. Uric acid concentrations are associated with insulin resistance and birth weight in normotensive pregnant women. *Am J Obstet Gynecol* 2009; 201:582;1-6.
- Lind T, Godfery KA, Otun How, Philips PR. Changes in serum uric acid concentrations during normal pregnancy. *British J Obstet Gynaecol* 1994;91:128-32.
- Chappell LC, Seed PT, Briley A, Kelly FJ, Hunt BJ, Charnock-Jones DS, et al. A longitudinal study of biochemical variables in women at risk of pre-eclampsia. *Am J Obstet Gynecol* 2002; 187:127-36.
- Guberby P, Tasta O, Swiader A, Pont F, Bujold E, Parant O, et al. Role of oxidative stress in the dysfunction of the placental endothelial nitric oxide synthase in preeclampsia. *Biology* 2021; 40: 101861.
- Hooijschuur MCE, Ghossein-Doha C, Kroon AA, De Leeuw PW, Zandbergen AAM, Van Kuijk SMJ, et al. Metabolic syndrome and pre-eclampsia. *Ultrasound ObstetGynaecol* 2019; 54(1): 64-71.
- Koopmans CM, van Pampus MG, Groen H, Aarnoudse JG, van den Berg PP, Mol BWJ. Accuracy of serum uric acid as a predictive test for maternal complications in pre-eclampsia: bivariate meta-analysis and decision analysis. *Eur J Obstet Gynecol Reprod Biol* 2009; 146(1): 8-14.