

Uric Acid Levels in Pregnancy Induced Hypertension (PIH) in Relation to Maternal and Perinatal Outcomes

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Abstract

Background: Preeclampsia is one of the common conditions of unknown etiology which increases the risk of maternal and perinatal morbidity and mortality. According to some studies, serum uric acid lacks sensitivity and specificity as a diagnostic tool whereas another group of the researchers indicated uricemia as a predictor of preeclampsia in pregnant ladies.

Objective: The present study was designed to assess whether serum uric acid can be used as a biochemical indicator or not, in pregnancy induced hypertensive (PIH) patients.

Study period & Method: Total number of 98 PIH patients admitted in GMERS Medical College, Dharpur, from Dec 2013 to Feb 2015 were included in this study and 60 normal healthy pregnant ladies served as control. Serum uric acid levels were estimated using modified Trinder's test.

Results: Out of the 98 cases mild preeclampsia was 60(61.2±%), severe Preeclampsia 24 (24.5%) and eclampsia 14(14.3%). Serum Uric acid levels significantly increased with the severity of PIH, normal pregnant women (4.58±0.37), mild preeclampsia (5.32±0.40), severe preeclampsia (6.29±0.57) and eclampsia (7.88±1.26). Out of these women with uric acid levels more than 5.5mg/dl was seen in 28(46.6%) mild preeclampsia, 19(79.2%) severe preeclampsia and 12 (85.7%) eclampsia. Maternal mortality was observed in 05(5.1%)PIH cases and out this 04(80) had uric acid level > 5.5mg/dl. Perinatal mortality was observed in 25 (25.1%) cases, out of these 19(76%) were stillbirths and 06(24%) were neonatal deaths. Out of the 25 perinatal deaths 18(72%) had uric acid level >5.5mg/dl.

Conclusion: Serum uric acid level could be used as a biochemical indicator of preeclampsia/eclampsia and its complications.

Key words: Preeclampsia, Uric acid, Mortality

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Introduction

Hypertensive disorders are amongst the most common medical disorders during pregnancy and considered to be a major cause of maternal and perinatal morbidity and mortality.⁽¹⁾ In developing countries they rank second only to anaemia with approximately 7-10% of all pregnancies complicated by some form of hypertensive disorder and lead to various maternal and fetal complications.⁽²⁾ In India incidence of preeclampsia as recorded from hospital statistics vary widely from 5-15%.⁽³⁾ Pre-eclampsia and eclampsia is still regarded as "a disease of theories" and its etiology is still obscured. The central feature in the pathophysiology of pre-eclampsia appears to be endothelial cell dysfunction.⁽⁴⁾

Preeclampsia is associated with uricemia.⁽⁵⁾ Nevertheless; some studies reported no significant difference in serum uric acid level between normal and preeclamptic women.⁽⁶⁾ Furthermore, one study also

reported serum uric acid lack sensitivity and specificity as a diagnostic tool,⁽⁷⁾ Whereas most of the researchers indicated uricemia as a predictor of preeclampsia.⁽⁸⁾ This study was conducted to confirm that maternal serum uric acid level during pregnancy can be used as a biomarker for preclampsia/eclampsia and that it corresponds to its severity. So we wanted to revisit uric acid as a useful biomarker, which is extremely cheap & widely available, as studies with new biomarkers have shown variable and inconsistent result.⁽⁹⁾

Materials and Methods

Study Population: This study was conducted from Dec 2013 to Feb 2015 and all the patients admitted in the Obstetrics and Gynecology department, at the GMERS medical college, Dharpur, Patan were examined.

Exclusion Criteria: Patients with history of hyperuricemia, preexisting diabetes, hypertension, renal disease, cardiovascular illness, and symptomatic infectious diseases were excluded.

Sample size and Sampling: All pregnant women admitted during the study period were examined. Blood pressure was measured by mercury sphygmomanometer in reclining position in right brachial artery. Three readings were taken at 10 minutes interval. Out of the total 752 women admitted during this period, 98 women having average systolic blood pressure \geq 140 mm Hg and/or diastolic blood pressure \geq 90 mm Hg

were included in the present study and 60 normotensive pregnant women were also recruited in this study. All were singleton pregnancy and were comparable with the study group in age, parity, period of gestation.

Definitions⁽¹⁰⁾: Pre-eclampsia is hypertension presenting after 20 weeks with significant proteinuria. Severe pre-eclampsia is pre-eclampsia with severe hypertension and/or with symptoms, and/or biochemical and/or haematological impairment. Eclampsia is a convulsive condition associated with pre-eclampsia.

Data collection: After enrolment participants were grouped into mild preeclampsia, severe preeclampsia and eclampsia. Informed consent was taken from all the participants. The history of all participants was taken. Blood samples of participants were taken from right or left cubital vein, were collected in plain tubes and serum levels of uric acid was measured by modified Trinder's test [11] using a semi autoanalyzer. Participants were observed throughout the pregnancy for maternal and perinatal outcomes.

Statistical Analysis: The data were validated and analysed with the help of free statistical software. We used unpaired t test for comparing the mean uric acid level with the maternal and perinatal outcomes. p value < 0.05 was considered statistically significant

Results and Discussion

Comparison of Normal and different PIH cases with serum uric acid:

Table 1: *P<0.05 statistically significant

	Number	Serum uric acid
Control group	60	4.58±0.37
Mild PIH	60 (61.2%)	5.32 ±0.40*
Severe Preclampsia	24 (24.5%)	6.29 ±0.57*
Eclampsia	14 (14.3%)	7.88 ±1.26*

Comparison of PIH cases with serum uric acid:

Table 2: number and percentage

PIH	Uric acid >5.5mg/dl	Uric acid <5.5mg/dl
Mild PIH (60)	28(46.6%)	32(53.4%)
Severe Preclampsia(24)	19(79.2%)	05(20.8%)
Eclampsia (14)	12(85.7%)	02(14.3%)

Comparison of Maternal Outcome and serum uric acid levels

Table 3: number and percentage

Complications	Uric acid >5.5mg/dl	Uric acid <5.5mg/dl
Eclampsia (14)	12(85.7%)	02(14.2%)
Abruptio placenta (07)	05(71.5%)	02(28.5%)
Post partumhemorrhage (PPH)(05)	04(80%)	01(20%)
HELLP (05)	03(60%)	02(40%)
ARF (02)	01(50%)	01(50%)
Maternal mortality (05)	04(80%)	01(20%)

Comparison of Perinatal Outcome and serum uric acid levels

Table 4: number and percentage

Complications	Uric acid >5.5mg/dl	Uric acid <5.5mg/dl
Preterm delivery(40)	32(80%)	08(20%)
Birthweight		
<2.5Kg (70)	55(78.5%)	15(21.5%)
>2.5Kg (28)	10(35.7%)	18(64.3%)
Perinatal mortality(25)	18(72%)	07(28%)

A total of 752 women were admitted for deliveries during the study period. Out of these 98 women were diagnosed as having pregnancy induced hypertension (PIH). So the overall incidence of PIH was 13.0%. Out of the 98 cases mild preeclampsia was 60(61.2%), severe preeclampsia 24(24.5%) and eclampsia 14(14.3%). (Table 1) Maternal mortality occurred in 05(5.1%) cases with PIH. While perinatal mortality occurred in 25(25.1%) women with PIH. Out of these 25, 19 (76%) were stillbirths and 06(24%) were neonatal deaths. Maximum cases were 71(72.4%) unbooked, 69(70.4%) had not taken antenatal care (ANC), age group 20-25yrs age52(53.0%), primigravidas 51(52.0%), preterm deliveries 40(40.8), 65(66.3%) belonged to Low socioeconomic (LSE) status and 78(79.5%) from rural areas. Maternal complications was seen in 33 (33.6%) cases. Most common complication was 14(14.2%) eclampsia, followed by abruptio placenta, post-partum hemorrhage, HELLP and acute renal failure(ARF). (Table 3) Serum Uric acid levels significantly increased with the severity of PIH, normal pregnant women (4.58±0.37), mild preeclampsia (5.32±0.40), severe preeclampsia (6.29±0.57) and eclampsia (7.88±1.26) (P<0.0001) (Table 1).

Uric acid is a terminal metabolite of the degradation of nucleotides. It is influenced by diet (i.e. high protein and fructose), alcohol consumption, increased cell turnover, enzymatic defects in purine metabolism or altered kidney function.⁽¹²⁾ In pregnancy uric acid concentrations initially fall 25-35% due to the effects of estrogen, expanded blood volume and increased glomerular filtration fate.⁽¹³⁾ However, concentrations slowly rise to those observed in non-pregnant women by term gestation (4-6mg/dl).⁽¹⁴⁾

However in preeclampsia uricemia occurs, it most likely results from reduced uric acid clearance from diminished glomerular filtration, increased tubular reabsorption and decreased secretion.⁽¹⁵⁾ It was once thought to result solely from reduced renal clearance but increase in uric acid levels are now also thought to be due to increased uric acid produced and caused by trophoblast breakdown, cytokine release and ischemia.⁽¹⁶⁾

Uric acid clearance is a key feature of preeclampsia. The serum level of uric acid rises as preeclampsia progresses; a level >5.5 mg/dl is a strong indicator of the disease and a level >7.8 mg/dL is associated with significant maternal morbidity.⁽¹⁷⁾ These observations were more or less similar in our study. Uric acid levels >5.5 mg/dl was observed in 28(46.6%) cases of mild preeclampsia, 19(79.2%) severe preeclampsia and 12(85.7%) cases of eclamptic women.(Table 2).

Maternal mortality was observed in 5 cases and out of these 4(80%) had uric acid levels more than 5.5 mg/dl. All the patients who had abruptio 5(71.5%) PIH women had serum uric acid more than 5.5mg/dl. Uric acid levels more than 5.5mg/dl was also observed in cases with maternal complications like 4(80%) PPH, 3(60%) HELLP, and 1(50%) ARF. (Table 3). Increasing blood levels of uric acid is a valuable marker as it helps to differentiate PIH from all other causes of hypertension complicating pregnancy where decrease in uric acid clearance does not occur. Therefore, an increased level of Uric Acid reflects the disease severity in PIH and fetal outcome.⁽¹⁸⁾

In PIH women with serum uric level >5.5mg/dl, 72.0% had perinatal deaths. All the mothers who delivered babies with birth weight less than 2.5kg 55(78.5%) and with preterm deliveries 32(80%) showed uric acid levels more than 5.5 mg/dl. (Table 4).

Authors have reported serum uric acid to be a sensitive index of severity of preeclampsia,⁽¹⁹⁾ others have even reported that its elevation will simply confirm the diagnosis.⁽¹⁷⁾ It was noted that in an established preeclampsia case, the diagnosis is usually clinically evident, its measurement is of greater value where the diagnosis is in doubt.⁽²⁰⁾ Low uric acid values indicate a good prognosis for the fetus. Rising or high values at this time indicate high-risk cases which are better managed and treated in hospital.⁽²⁰⁾ Studies have shown decreasing uric acid levels with allopurinol improved endothelial dependant vasodilation in diabetic and congestive heart failure patients. So by reducing uric acid level it might be a potential therapeutic method for preeclamptic women also.^(21,22)

Conclusion

Results of the present study indicated strong association of elevated serum uric acid level with preeclampsia/eclampsia, which could be used as a

biochemical indicator of maternal and fetal complications.

References

1. Shah M R. Hypertensive disorders in pregnancy. 1st edn published by Jaypee. 2007:1-10.
2. Barrilleaux PS, Martin JN; Hypertensive therapy during pregnancy. ClinObstet Gynecol., 2002;45(1):22-34.
3. Dutta DC; Hypertensive disorders in pregnancy. In Text book of Obstetrics including perinatology and contraception. 6th edition, Calcutta: New central book agency, 2004:221-242.
4. Cotter AM, Molloy AM, Scott JM, Daly SF. Elevated plasmahomocysteine in early pregnancy: a risk factor for the development of severe preeclampsia. American Journal of Obstetrics and Gynaecology.2001;185(4):781-85.
5. Wu Y, Xiong X, Fraser WD, Luo ZC. Association of uric acid with progression to preeclampsia and development of adverse conditions in gestational hypertensive pregnancies. Amer J Hypertens2012;25:711-17.
6. Punthumapol C, Kittichotpanich B. Serum calcium, magnesium and uric acid in preeclampsia and normal pregnancy. J Med Assoc Thai 2008; 91:968-73.4
7. Lim KH, Friedman SA, Ecker JL, Kao L, Kilpatrick SJ. The clinical utility of serum uric acid measurements in hypertensive diseases of pregnancy. Am J ObstetGynecol1998;178:1067-71.
8. Kang DH, Finch J, Nakagawa T, Karumanchi SA, Kanellis J, Granger J, Johnson RJ. Uric acid, endothelial dysfunction and pre-eclampsia: searching for a pathogenetic link. J Hypertens2004;22:229-35.
9. Kleinrouweler CE, Wiegerinck MM, Ris-Stalpers C, et al. Accuracy of circulating placental growth factor, vascular endothelial growth factor, soluble fms-like tyrosine kinase 1 and soluble endoglin in the prediction of pre-eclampsia: a systematic review and meta-analysis. BJOG.2012;119(7):778-787.
10. NICE clinical guideline 107. Hypertension in pregnancy: The management of hypertensive disorders during pregnancy [Internet] [Issued: August 2010; last modified: January 2011; Cited 2014 January 16]. Available from: www.nice.org.uk/nicemedia/live/13098/50418/50418.pdf.
11. Bauer, P.J. Anal Biochem.1981;110(1):61-72.
12. Johsao RJ, Kang DH, Feig D, Kivlighn S, Kanellis J, Watanabe S, Tuttle KR. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension 2003;41:1183-90.
13. Carter J, Child A. Serum uric acid levels in normal pregnancy. Aust N Z J Obstet Gynaecol 1989;29:313-4.
14. Powers RW, Bodnar LM, Ness RB, Cooper KM, Gallaher MJ, Frank MP, Daftary AR, Roberts JM. Uric acid concentration in early pregnancy among preeclampsia women with gestational hyperuricemia at delivery. Am J Obstet Gynecol. 2006;194:160.
15. Lindheimer MD, Conrad K, Karumanchi SA: Renal physiology and disease in pregnancy. In Alpern RJ, Hebert SC, editors. Seldin and Giebisch's the kidney: physiology and pathophysiology (4th ed.). New York: Elsevier 2008a: 2339.
16. Martin AC, Brown MA. Could uric acid have a pathogenic role in pre-eclampsia? Nat Rev Nephrol 2010;6:744-8.
17. Mustaphi R, Gopalan, S, Dhaliwal, L and Sarkar AK. Hyperuricemia and PIH- reappraisal. Indian J Med Sci 1996;Vol.50(3):68-71.

18. Laxmi Narayana s, M Dsulemanand B Vodelu. Study of serum uric acid levels in Pregnancy induced hypertension Int J Pharm Bio Sci 2014 Oct; 5(4): (B) 97 – 103.
19. Pramanik T, 1 Khatiwada B 2, Pradhan P. Serum uric acid level in normal pregnant and preeclamptic ladies: a comparative study .Nepal Med Coll J 2014;16(1):30-32.
20. Patel T, Dudhat A. Relationship of Serum Uric Acid Level to Maternal and Perinatal Outcome in Patients with Hypertensive Disorders of Pregnancy. Gujarat Medical Journal -2014 Vol. 69 No. 2:45-47.
21. Butler R, Morris AD, Belch JJ, Hill A, Struthers AD. Allopurinol normalizes endothelial dysfunction in type 2 diabetics with mild hypertension. Hypertension. 2000;35:746-51
22. Farquharson CA, Butler R, Hill A, Belch JJ, Struthers AD. Allopurinol improves endothelial dysfunction in chronic heart failure. Circulation. 2002;106:221-6.