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Association of Serum Uric Acid Level and Perinatal Outcome in Pregnancy Induced Hypertension

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Abstract

Introduction: Preeclampsia is a multisystem disorder that associated with significant maternal and neonatal morbidity and mortality. Hyperuricemia has been linked with preeclampsia hemce having a predictive role in perinatal outcome.

Objectives: Objective was intended to study uric acid as an important biomarker in early identification and measurement of severity of preeclampsia and prediction of maternal and perinatal complication.

Material and Methods: A prospective observational antenatal control study was done at GMCH Udaipur, Rajasthan from January 2018 to July 2018. Total no. of 191 patients with PIH were included in our study. Maternal outcome noted in the terms of the mode of delivery, maternal complications and maternal end result. Fetal outcome assessed by perinatal morbidity and mortality, need for admission in NICU and neonatal end result. Patients were divided into two groups according to the level of uric acid. Patients with uric acid <5.0 mg/dl and >5.0 mg/dl.

Results: Out of 191 patients, 39 (20.52%) patients with mild preeclampsia, 24 (12.56%) with moderate preeclampsia and 6 (3.14%) with severe preeclampsia while 3 (1.57%) patients had eclampsia. All the patients with Severe pre eclampsia and eclampsia and majority of moderate preeclampsia had uric acid >5 mg/dl (p value <001). In which higher level of mean of uric acid level in severe preeclampsia (8.67 ± 2.32) and eclampsia (10.37 ± 4.85) have been noted in our study. Majority of maternal as well as fetal complicatios have been noticed in patients with uric acid levels >5 mg/dl. Majority of low birth weight and NICU admissions were also seen in uric acid levels >5 mg/dl.

Conclusion: The presence of hyperuricemia, especially >5 mg/dl levels identifies PIH patients at increased risk of maternal and fetal complications. By serum uric acid laboratory test, the severity of the disease can be predicted with more accuracy timely intervention gives us better perinatal outcome.

Keywords: Pregnancy; Preeclampsia; Uric acid; Pregnancy complications.

Introduction

Preeclampsia is defined as a multisystem disorder occurring in pregnancy and puerperium characterized by development of hypertension of 140/90 mm hg and after 20 weeks of pregnancy in previously normotensive patients [1]. It complicates 10–17% of pregnancies and responsible for 14% of maternal deaths [2].

Uric acid is the final product of purine metabolism oxidation and then finally excreted in urine. Uric acid is a marker of oxidative stress, injury and renal dysfunction and therefore might be helpful in the prediction of complication of preeclampsia [3].

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Raised serum uric acid is associated with on almost doubled risk of severe complications, such as eclampsia, HELLP syndrome, APH and perinatal deaths [4].

Hyperuricemia from decreased renal excretion, as a consequence of preeclampsia or production secondary to tissue ischemia and oxidative stress has been cited as better predictor of fetal outcome than blood pressure [5]. It may identify women at risk of adverse maternal and particularly fetal outcome [6].

There is a positive correlation between the raised serum uric acid levels and adverse fetal outcomes like IUGR, Prematurity, Low birth weight, neaonatal death, Intrauterine death. After knowing the effect of uric acid on severity of preeclampsia and maternal and neonatal complications can help early diagnosis, control and treatment. Results can be used for clinical decision making and prevent from maternal and neonatal complications [7]

Objectives

Objective was intended to study uric acid as an important biomarker in early identification and measurement of severity of preeclampsia and prediction of maternal and perinatal complication. Because laboratory investigation of serum uric acid is simple, cheap and can be easily performed in any laboratory.

Material and Methods

A prospective observational antenatal control study was done at GMCH Udaipur, Rajasthan from January 2018 to July 2018. The study was approved by institutional ethical committee. All PIH patients were taken for uric acid measurement. Total no. of 191 patients were included in our study. Hypertensive pregnant females were grouped as per the criteria described according to the American College of Obstetricians and Gynecologists.

- Mild to Moderate PET.
- Severe PET.
- Eclampsia.

Maternal outcome noted in the terms of the mode of delivery, maternal complications and maternal end result. Fetal outcome assessed by perinatal morbidity and mortality, need for admission in NICU and neonatal end result.

A proforma with detailed history and all relevant investigations prepared of all admitted PIH patients. Informed consent taken from all included patients.

Determination of uric acid was carried out by quantitative estimation on colorimetric methods (by enzymatic uricase method). The colour intensity formed is directly propotional to uric acid concentration and determined by measuring its absorbance. Reagent/Materials used in uric acid testing is COBAS integra 400 plus Uric acid : cassette UA2.

Patients were divided into two groups according to the level of uric acid. Patients with uric acid <5.0 mg/dl and >5.0 mg/dl.

Results

A total number of 191 patients were examined, out of which 119 (62.31%) patients being with gestational hypertension, 39 (20.52%) patients with mild preeclampsia, 24 (12.56%) with moderate preeclampsia and 6 (3.14%) with severe preeclampsia while 3 (1.57%) patients had eclampsia. All the patients with Severe pre eclampsia and eclampsia and majority of moderate preeclampsia had uric acid >5 mg/dl (p value <001) which has been explained in Table 1.

Table 1: Uric acid and PIH

Category	URIC ACID		Total	Chi square value	p- value
	≤ 5 mg/dl	> 5 mg/dl			
Gestational Hypertension	88 (85.44%)	31 (35.23%)	119 (62.31%)	54.731	<0.001
Mild Pre Eclampsia	12 (11.65%)	27 (30.68%)	39 (20.52%)		
Moderate Pre Eclampsia	3 (2.91%)	21 (23.86%)	24 (12.56%)		
Severe Pre Eclampsia	0	6 (6.82%)	6 (3.14%)		
Eclampsia	0	3 (3.41%)	3 (1.57%)		
Total	103 (100%) (53.93%)	88 (100%) (46.05%)	191 (100%) (100%)		

The mean uric acid levels of all hypertensive patients is described in Table 2, which shows higher level of mean of uric acid level in severe preeclampsia (8.67 ± 2.32) and eclampsia (10.37 ± 4.85) (Table 2).

Majority of maternal complications observed in patients with uric acid levels >5 mg/dl (p value 0.002) shown in Table 3.

Majority of fetal complicatios have been noticed in patients with uric acid levels >5 mg/dl. Majority of babies with low birth weight (27.90%) were of patients with > 5 mg/dl uric acid levels. Fetal complications are shown in Table 4.

Low apgar score at the end of 1 min of time period were also associated more with uric acid levels >5 mg/dl (p value 0.003) shown in Table 5.

Table 2: PIH and Mean Uric acid

Category	URIC ACID						T test	p- value
	N	≤ 5 mg/dl Mean ± SD	N	> 5 mg/dl Mean ± SD	N	Total Mean ± SD		
Gestational Hypertension	88	3.84 ± 0.72	31	6.31 ± 1.13	119	4.47 ± 1.38	14.01	<0.001
Mild Pre Eclampsia	12	4.39 ± 0.68	27	6.81 ± 1.02	39	6.07 ± 1.46	7.48	<0.001
Moderate Pre Eclampsia	3	3.83 ± 0.70	21	6.82 ± 1.16	24	6.45 ± 1.49	4.30	<0.001
Severe Pre Eclampsia	0	-	6	8.67 ± 2.32	6	8.67 ± 2.32		
Eclampsia	0	-	3	10.37 ± 4.85	3	10.37 ± 4.85		
Anova		3.14		8.24		30.44		
P Value		0.048		<0.001		<0.001		

Table 3: Maternal Complications

Category	URIC ACID		Total N = 191	p- Value
	≤ 5 mg/dl N = 103	> 5 mg/dl N = 88		
Polyhydroaminios	1	0	1	
Placenta previa	1	1	2	
Antepartum Haemmorage	2	1	3	
Oligo	31	25	56	
PPROM	2	2	4	
Chronic hypertension	6	5	11	
DM 2	1	0	1	0.002
GDM	10	12	22	
Maternal intrapartum cardiomyopathy	0	1	1	
Maternal hypertensive cardiomyopathy	0	1	1	
Hypertensive cardiac failure	0	1	1	
HELLP	0	1	1	
Acute renal failure	0	1	1	

Table 4: Fetal outcomes

Category	URIC ACID		Total N = 215	p- Value
	≤ 5 mg/dl N = 114	> 5 mg/dl N = 101		
Fetal anomaly	1	0	1	
Low birth	30	60	90	
Very low birth weight	16	41	57	
IUGR	11	27	38	
Neonatal death	2	18	20	
Prematurity	17	38	55	0.0024
Neonatal complication	11	33	44	
NICU admission	24	44	68	
Neonatal sepsis	0	1	1	
Fetal distress	3	1	4	
Asphyxia	0	1	1	
Congenital anomaly	1	0	1	
IUD	1	5	6	

Table 5: Relationship with APGAR

APGAR score	URIC ACID		Total	Chi square value	p- value
	≤ 5 mg/dl	> 5 mg/dl			
0–3	2 (1.75%)	9 (8.91%)	11 (5.12%)	11.882	0.003
4–7	4 (3.51%)	12 (11.88%)	16 (7.44%)		
8–10	108 (94.74%)	80 (79.21%)	188 (87.44%)		
Total	114 (100%)	101 (100%)	215 (100%)		

Discussion

Gestational Hypertension, Preeclampsia and eclampsia are all various types of PIH. A rising serum uric acid level has been recognized as an early feature of preeclampsia and its measurement increases the accuracy of the diagnosis and also helps in differentiation from other essential or chronic forms of preexisting hypertension complicating the pregnancy [8].

In our study, the uric acid levels were significantly high in patients with Severe preeclampsia and eclampsia than Geststional hypertension and mild preeclampsia. Result shows mean uric acid levels in patients with gestational hypertension were 4.47 ± 1.38 mg/dl, whereas in patients with severe preeclampsia and eclampsia were 8.67 ± 2.32 mg/dl and 10.37 ± 4.85 mg/dl. which shows significant rise in uric acid with increased severity. According to Mustaphi et al. mean serum uric acid in mild PIH patients were 5.42 ± 0.55 mg/dl and in severe PIH were 6.65 ± 0.60 which was significantly higher than normal women [9]. Williams *et al.* and Lim *et al.* study shows the mean uric acid levels in women with preeclampsia were 6.2 ± 1.4 mg/dl which was significantly higher than controls in his study which is comparable to our study [10]. Elevation of serum uric acid levels tends to increase severity of the PIH and appears to correlate with the severity of glomerular involvement. In our study serum uric acid levels were significantly higher in patients with severe pre eclampsia and eclampsia compared to Gestational hypertensive patients.Kamath *et al.* [11]. Nischinta *et al.* [12] and Sirajwala *et al.* [13] have Made similar observations. It likely occurs due to diminished glomerular filtration, increased tubular reabsorbtion and decreased secretions from tubules, though increased placental urate production, compensatory to increased oxidative stress has also been taken into consideration [14].

Maternal complications were also noted to be higher in hypertensive pregnant women especially in serum uric acid levels >5 mg/dl as compared to uric acid levels <5 mg/dl (Table 3) Complications like Oligo, Hypertensive cardiomyopathy, Hypertensive cardiac failure, HELLP, Acure renal failure were seen in patients with uric acid levels >5 mg/dl. Similar findings have also been noted by Nischinta *et al.* [12] and Pereira *et al.* [15]. In our study Abruptio placenta and APH were seen in patients with uric acid levels <5 mg/dl which is not related to other studies. During healthy early pregnancies the serum uric acids are low (<3 mg/dl) due to effects of oestrogen and increased renal blood, but the levels in women who are on the verge of developing preeclampsia are relatively high even during their 1st trimester and continue to rise with increasing complications of reduced placental perfusion, platelet consumption etc. The uric acid levels usually comes down rapidly by sixth day of delivery [16].

Hyperuricemia in the PIH patients is also associated with various foetal complications. In our study out of 215 babies, 90 babies (41.86%) were low birth weight babies, out of which 60 babies were of the patients with uric acid levels >5mg/dl. 57 babies (26.51%) were very low birth weight babies (<2.0 Kg weight) out of which 41 babies were of the patients with uric acid levels >5 mg/dl. Other complications like prematurity (25.58%) and IUGR (17.67%) have also been noted in our study, out of which majority of babies were of patients with uric acid levels >5 mg/dl. There has been 20 (9.30%) neonatal deaths observed in our study out of which 18 (8.37%) deaths were of patients with uric acid levels >5 mg/dl. Simillar findings have been observed for low birth weight in Pereira *et al.* [15] and Kamath *et al.* [11] and Alam *et al.* [17]. There was also an association of serum uric acid levels with low APGAR scores. Total 27 (12.55%) babies were having APGAR score <7. Out of them 20 (9.30%) babies were of patients with uric acid levels >5 mg/dl. There are also chances of more NICU admissions with hyperuricemia which has been observed in our study. Out of 68 (31.62%) NICU admissions 44 (20.46%) admissions were of patients with uric acid levels >5 mg/dl. Simillar studies of Low APGAR scores and NICU admissions were observed in Alam *et al.* [17] and Patel *et al.* [18] showing clear association of hyperuricemia with adverse foetal outcome.

The value of serum uric acid in hypertensive pregnancy is greatest in between 24 to 32 weeks of

gestation. The low serum uric levels indicates good prognosis of fetus. Rising or high values at this time indicate high risk cases which are better managed and treated in hospital. Early bed rest, monitoring of fetal well being inutero and anticipation of maternal problems related topreeclampsia then ensure the best chances for bringing the pregnancy to stage where planned delivery prevents serious maternal complications and gives the best possible chance of fetal survival [18].

Conclusion

Our study shows that the measurement of serum uric acid level is of great diagnostic as well as prognostic value mainly for fetal outcome. The presence of hyperuricemia, especially >5 mg/dl levels identifies PIH patients at increased risk of maternal and fetal complications and timely intervention can reduce the adverse events. By serum uric acid laboratory test, the severity of the disease can be predicted with more accuracy regarding fetal and maternal outcome and timely intervention gives us better perinatal outcome.

Further studies are required to compare uric acid in PIH and non PIH patients. Post partum uric acid measurement was not included in our study due to poor follow up visits.

It is a cheap, highly accessible, easily available and a non invasive method, deserves to be considered as a routine diagnostic and prognostic tool in risk identification and management of PIH.

Ethical approval: Ref: GU/HREC/EC/2017/1520.

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