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Fetal Outcome of Preeclamptic Mother with Hyperuricemia

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ABSTRACT:

Introduction: Hypertension is a universal problem, and it complicates at least 10% of all pregnancies. Preeclampsia is defined as the triad of hypertension, proteinuria and edema occurring after 20 weeks gestation in previously normotensive women. Pre-eclampsia is one of the leading causes of maternal and fetal morbidity and mortality worldwide. And hyperuricemia is a common finding in preeclamptic pregnancies with adverse fetal outcomes.

Aims and Objectives: This study aimed to determine serum Uric acid levels in preeclamptic women and to compare them with normal pregnant women in the third trimester of pregnancy. Serum Uric acid levels were also correlated with fetal outcome.

Material and Methods: Subjects were divided into two groups: Group-I included 100 preeclamptic women with hyperuricemia and Group-II 100 healthy normouricemic, age-matched pregnant women. Serum uric acid was estimated by the Uricase method in ERBA CHEM-5.

Results: Serum Uric acid levels were significantly higher in the case of group I than the control group II (7.45±1.04 mg/dl vs. 4.64±1.02mg/dl); It has also been observed that there was a significant increase in the number of low-birth-weight babies born to hyperuricemic preeclamptic women in comparison to babies born to normouricemic pregnant women (2.4±0.2 Kg vs. 3.2±0.3 Kg).

Conclusion: Hyperuricemia identifies higher-risk women and may act as a useful marker to manage preeclamptic women to reduce the rate of poor fetal outcome.

Keywords: Hyperuricemia, Preeclampsia, Serum Uric Acid

INTRODUCTION

The anatomical, physiological and biochemical adaptations that take place in women during the short span of human pregnancy are profound [1]**.** Pregnancy is a normal physiological phenomenon with many biochemical changes ranging from alterations in electrolyte concentrations to more complex changes in cortisol and Calcium metabolism. Pregnancy is associated with normal physiological changes that assist in nurturing and survival of the fetus. Biochemical parameters reflect these adaptive changes and are distinct from the non-pregnant state. Preeclampsia is an idiopathic multisystem disorder specific to human pregnancy. Hypertension is a universal problem, and it complicates at least 10% of all pregnancies [2]. Preeclampsia is defined as the triad of hypertension, proteinuria and edema occurring after

20 weeks gestation in previously normotensive women [3]. It is a transient but potentially dangerous complication of pregnancy. Preeclampsia is still one of the leading causes of maternal and fetal morbidity and mortality [4]. The pathophysiological mechanism is characterized by a failure of the trophoblastic invasion of the spiral arteries; leading to maladaptation of maternal spiral arterioles, which may be associated with increased vascular resistance of the uterine artery and a decreased perfusion of the placenta [5]. Hyperuricemia is one of the earliest and most consistent observations noted in preeclamptic pregnancies. Increased Uric acid often precedes clinical manifestations of the disease, including reduced glomerular filtration rate [6]. Hyperuricemia is believed to result from the decreased renal excretion that occurs as a consequence of preeclampsia; also increased production may be secondary to tissue ischemia and oxidative stress. Soluble Uric acid impairs nitric oxide generation in endothelial cells. Hyperuricemia induces endothelial dysfunction and may induce hypertension and vascular diseases [5&7]. In pregnancy, Uric acid concentrations initially fall 25-35% due to the effects of oestrogen, expanded blood volume and increased glomerular filtration rate [8]. However, concentrations slowly rise to those observed in non-pregnant women by term gestation (4-6 mg/dL) [9]. Since the late 1800s, numerous reports have demonstrated a relationship between Uric acid concentrations and severity of disease [6&10]. Recently studies examined the relationship of high Uric acid elevations in pregnant hypertensive women to the endpoints of preterm birth (largely indicated preterm birth for the management of Preeclampsia) and growth restriction [6]. The increased frequency of preterm birth and growth restriction was present in hypertensive women with elevated concentration of Uric acid even in the absence of proteinuria.

AIMS AND OBJECTIVES:

Nowadays biochemical approach is implicated to prevent complications in pregnancy and to improve the fetal outcome. The aim of this study was:

• To measure serum Uric acid levels in preeclamptic women and to compare it with normal pregnant women in the third trimester of pregnancy.

• To correlate maternal serum Uric acid levels (of Normal as well as of Preeclamptics) with fetal outcome.

MATERIALS AND METHODS:

The present study was conducted in the Departments of Biochemistry and Obstetrics & Gynaecology, Sri Aurobindo Medical College & P.G. Institute, Indore. An institutional ethical committee has approved this research work. Subjects were divided into two groups: Group-I included 100 preeclamptic women with hyperuricemia and Group-II 100 healthy normouricemic, age-matched pregnant women. The two groups did not differ in respect to age and socioeconomic strata.

- *Inclusion criteria:*
    - Mild preeclamptic women with gestational age more than 28 weeks of pregnancy who had Proteinuria +1 or +2 detected by Dip-stick Urine Analysis method with Base-line Blood pressure more than or equal to 140/90 mm of Hg and may or may not had pitting Edema over feet.
    - Asymptomatic pregnant women with gestational age more than 28 weeks of pregnancy with Blood pressure less than 130/80 mm Hg & no traces of Protein in urine.
- *Exclusion criteria:*
    - Women with a history of Preeclampsia/Eclampsia, Diabetes mellitus, Chronic Hypertension, Renal diseases and any other Chronic illness.
    - Women with a history of multiple pregnancies, under-treatment of Anti-epileptic Drugs and family history of Diabetes mellitus or Hypertension.
    - Blood pressure was measured in a semi-recumbent position. Proteinuria was measured by testing urine sample by the Dip-stick method.
    - After taking written consent from the subjects, venous blood will be collected in Vacutainer, allowed to clot and then immediately sent to the biochemistry lab. Where the samples will be centrifuged at 4000rpm× for 10 minutes, then serum will be separated and analysed for the tests.

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- The test performed in our department:
- Serum uric acid was estimated by the Uricase method in ERBA CHEM-5 (Enzymatic Kit method).
- All subjects were followed till 48 hours after delivery and various parameters for fetal outcomes were noted. Fetal birth weight, Apgar score at 1 min and 5min and other neonatal complications were noted.

RESULTS:

We have collected data into two groups: Group-I included 100 preeclamptic women with hyperuricemia and Group-II 100 healthy normouricemic, pregnant women.

- *Blood pressure:*

The systolic blood pressure and diastolic blood pressure was measured using a sphygmomanometer in the women left arm.

The Mean systolic blood pressure and diastolic blood pressure for Preeclamptic women were 148.32±5.06 mmHg and 94.9±6.00 mmHg respectively. For the Control group, Systolic BP was 110±6.5 mm Hg and Diastolic BP was 75.1±2.05 mm Hg as presented in table 1 & the Bar chart (FIGURE 1).

- *The Gestational age:*

The Gestational age of Preeclamptics and Control groups is taken at the time of delivery. The Mean Gestational age (in weeks) for Preeclamptic women was 36.24 ±2.58 and for the Control group were 38.30 ±1.97 as presented in Table 2 & the Bar chart (FIGURE 2).

- *Serum Uric Acid:*

The Mean Serum Uric acid level in Preeclamptic cases was 7.45±0.4mg/dL and in the Control group, it was 4.6±1.02mg/dL. Table 3 & the Bar chart (FIGURE 3) shows that there was an extremely statistically significant increase in the Mean Uric acid levels in Preeclamptic cases when compared to the normal healthy pregnant women taken as Controls (p-value<0.0001).

- *Birth Weight*

The Mean birth weight of newborn in Preeclamptic cases was 2.4±0.2Kg and in the Control group, it was 3.2±0.3Kg. Table 4 & the Bar chart (FIGURE 4) shows that there was an extremely statistically significant decrease in the Mean birth weight of newborn in Preeclamptic cases when compared to the normal healthy pregnant women taken as Controls (p-value<0.0001).

Data in all the concerning tables are shown as Mean±SD; p-value was determined with student's t-test.

TABLES:

Table 1: Mean and Standard deviation of Blood pressure in Preeclamptics and Control groups

Group	Mean Systolic blood pressure (mm Hg) with SD	Mean Diastolic blood pressure (mm Hg) with SD
Preeclamptics	148.32±**5.06**	94.9±**6.00**
Control	110±**6.5**	75.1±**2.05**
p-value	<0.0001	<0.0001

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Table 2: Mean and Standard deviation of Gestational age in Preeclamptics and Control groups

Group	Gestational age (weeks)	p-value	Inference
Preeclamptics	**36.24 ±2.58**	<0.0001	Difference is statistically significant
Control	**38.30 ±1.97**	<0.0001	Difference is statistically significant

Table 3: Showing Mean±SD and the significant difference in the Mean Serum Uric acid levels (mg/dL) between the Preeclamptic and Control groups

Group	Serum Uric-acid (mg/dL) Mean±SD	p-value	Inference
Preeclamptics	7.45±0.4	<0.0001	Difference is extremely statistically significant
Control	4.6±1.02		

Table 4: Mean and Standard deviation of Birth weight and Apgar score of newborns in Preeclamptics and Control groups

Group	Birth weight of new born (Kg)	Apgar score		p-value	Inference
		1 min	5 min		
Preeclamptics	2.4±0.2	8.16±1.84	9.22±0.88	<0.0001	Difference is extremely statistically significant
Control	3.2±0.3	8.89 ±1.11	9.57 ±0.43		

Table 5: Comparative Study of Serum Uric acid In Different Research Papers

AUTHOR (YEAR)	PREECLAMPTIC WOMEN (mg/dL)	NORMAL PREGNANT WOMEN (CONTROL) (mg/dL)
Chanvitya P[12] (2008)	7.01±1.93	5.33±1.23
Alavi A[13] (2012)	5.32±1.41	4.55 ±1.14
Sendhav S[14] (2013)	7.25 ± 1.08	5.03±0.73
Present study (2013)	7.45± 0.40	4.60± 1.02
Khalil SSH (2018)	7.39±0.94	3.14±0.28
Zulfu AA(2018)	7.35	4.47

Data in all the above concerning tables are shown as Mean±SD; p-value was determined with student's t-test.

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FIGURES/GRAPHS:

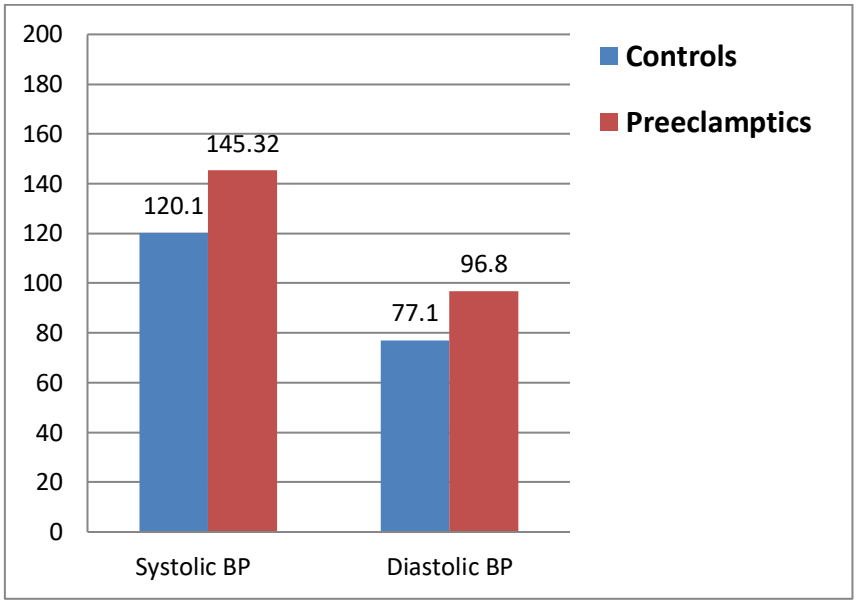

Figure 1: Comparison of Blood pressure in Preeclamptics and Control groups

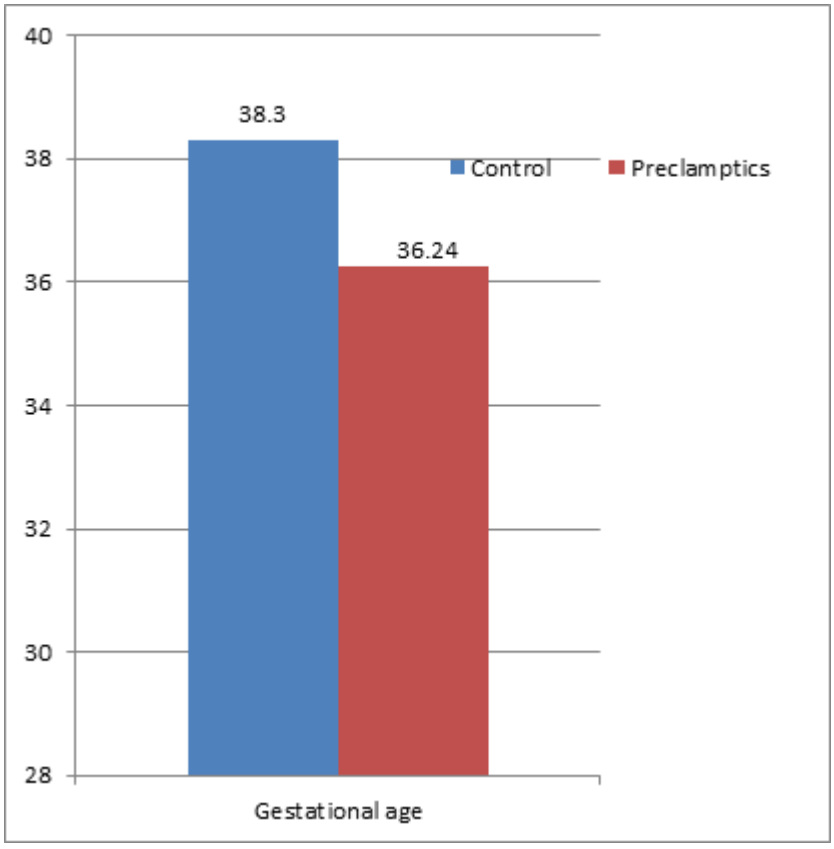

Figure 2: Comparison of Gestational age between Preeclamptics and Control groups

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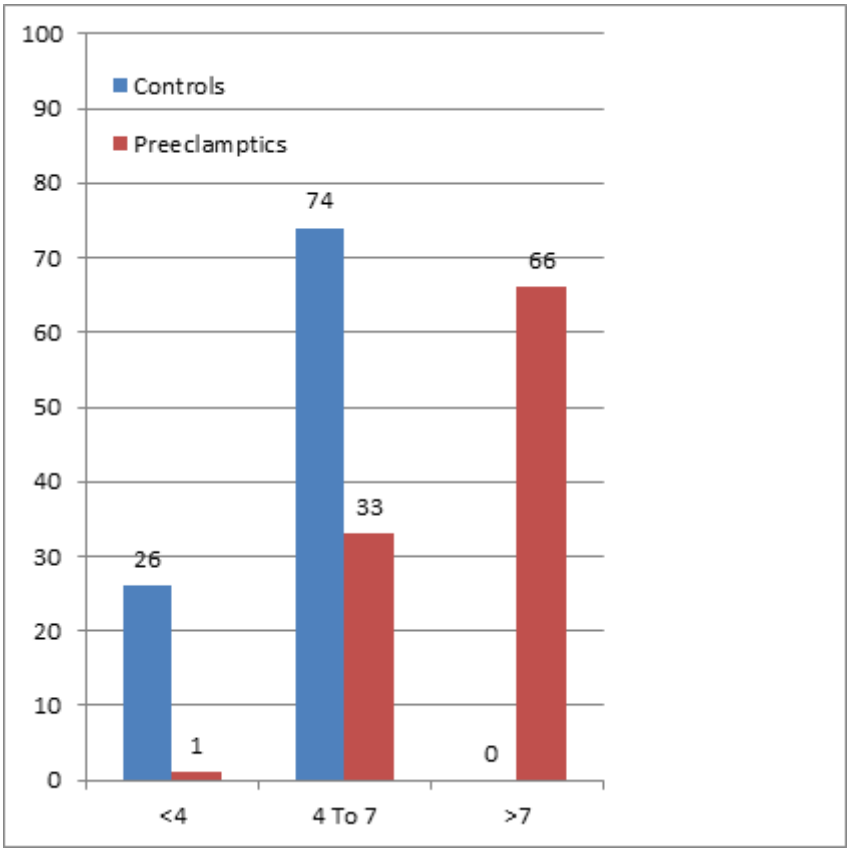

Figure 3: Comparison of Serum Uric acid levels (mg/dL) in the Preeclamptic and Control groups

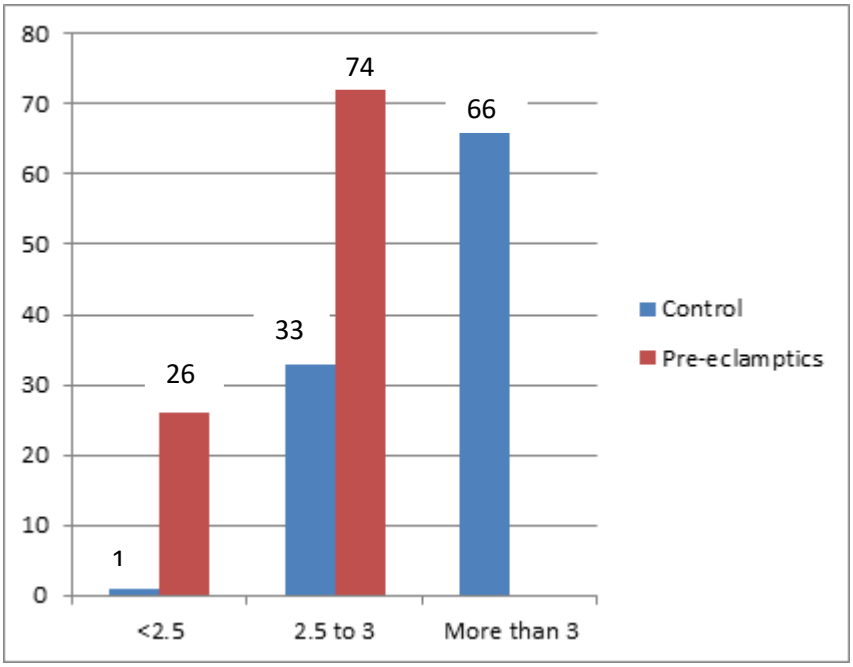

Figure 4: Comparison of Birth weight of new born between Preeclamptics and Control groups

DISCUSSION:

Hypovolemia, an early change in Preeclampsia, increases Uric acid reabsorption which could increase Serum Uric acid concentrations. However, increased Uric acid precedes the reduction in plasma volume [11].

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Increased Uric acid production from maternal, fetal or placental tissues through heightened tissues breakdown (i.e. increased substrate availability) and/or increased XO activity could also explain the increased concentration.

Uric acid is capable of damaging adult vasculature and could have similar effects in the placentae of preeclamptic women.

A similar vasoconstrictive effect of uric acid in the placentae of women with preeclampsia would compromise placental perfusion and could inhibit fetal growth.

Uric acid could contribute to being failed placental bed vascular remodelling by impeding trophoblast invasion with resultant reduced placental perfusion, setting the stage for ischemia-reperfusion injury to the placenta and oxidative stress.

In the present study, we found that the birth weight of a newborn in the hyperuricemic group was 2.4±0.2 (Kg) and in the normouricemic group was 3.2±0.3.

D'Anna et al [15] **(**2000) and Feig et al [16] (2004) performed the same type of study. They got a significant relationship between hyperuricemia and LBW fetus. Redman et al [17] (1976) and Chesley [18] (1985) also saw a similar linear trend in patients of PE with hyperuricemia. Wu Y et al [19] showed the association of higher serum uric acid level with the development of adverse infant conditions. Livingstone et al [20] conducted a study which concluded that serum uric acid is clinically useful in predicting adverse perinatal outcome. This trend of increased uric acid with poor fetal outcome indicates that probably increased uric acid causes intrauterine growth retardation. Serum uric acid estimation can play a vital role to diagnose preeclamptic women to make the delivery safe and improve fetal outcome.

Thus hyperuricemia identifies higher-risk women and it is a useful biomarker to manage preeclamptic women. Thereby we can reduce fetal morbidity and mortality.

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