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Impact of maternal serum uric acid on perinatal outcome in women with hypertensive disorders of pregnancy: A prospective study

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ABSTRACT

Introduction: Worldwide hypertensive disorder of pregnancy is major cause of maternal and perinatal morbidity, mortality. *Aim:* To study impact of maternal serum uric acid on perinatal outcome in women with hypertensive disorder of pregnancy. *Methodology:* Present study was conducted in Obstetrics and Gynecology Department of rural tertiary care centre of Northern India over seven months (October 2016–May 2017). Total 110 pregnant women > -34 weeks with hypertensive disorder of pregnancy were divided into three groups; Gestational hypertension (n = 35), Pre-eclampsia (n = 49), Eclampsia (n = 26). Maternal serum uric acid and its co-relation with perinatal outcome were assessed in each group. *Results:* Of total 111 babies delivered to women with hypertensive disorder of pregnancy, 52 (46.85%) were preterm and 59 (53.15%) term. Of these; 43 (38.74%) were born healthy (APGAR > 7), 31 (27.93%) suffered minimal respiratory distress, 14 (12.61%) severe birth asphyxia and required ventilator support, of which two died, 19 (17.12%) babies died in utero and 4 (3.60%) were still births. Mean neonatal birth weight in all three groups was 2.956 ± 0.273 kg, 2.475 ± 0.324 kg and 2.177 ± 0.282 kg respectively. Mean serum uric acid in gestational hypertension women with healthy foetuses was 5.16 ± 1.74 mg/dl and with distressed foetuses was 6.52 ± 2.31 mg/dl, in pre-eclampsia it was 5.3 ± 1.44 mg/dl and 7.29 ± 2.63 mg/dl and in eclamptic women 5.7 ± 0 mg/dl and 8.83 ± 2.96 mg/dl respectively. *Conclusion:* Adverse perinatal outcome was maximum in eclampsia group, followed by pre-eclampsia and lastly in gestational hypertension. Hence, higher maternal serum uric acid was associated with poor perinatal outcome ($p < .05$).

1. Introduction

Worldwide around 287,000 women die annually during pregnancy and childbirth and India accounts for approximately 19% (56,000) of these total deaths [1]. Hypertensive disorders of pregnancy (HDP) and their associated complications account for maximum burden of maternal morbidity and mortality followed by obstetric haemorrhage, pre-existing medical diseases, infections and abortions all over the world [2,3]. HDP affects approximately 2–10% of all pregnancies [4], with 10% occurring during first pregnancy and 20–25% in women with past history of chronic hypertension [5] and contributes significantly to maternal and perinatal morbidity and mortality [6–11]. Annually HDP is responsible for 40,000 maternal deaths worldwide [12]. In developing countries the scenario is far worse with HDP affecting 7–10% of all pregnancies, second to anaemia [13] and is responsible for one quarter of all admissions in antenatal wards [14].

According to the National High Blood Pressure Education Program (NHBPEP) working group; spectrum of HDP mainly consist of Gestational hypertension (GH), preeclampsia (PE), and eclampsia [15]. Pre-eclampsia and eclampsia are considered as “diseases of theories” with unknown aetiology with multisystem involvement [16]. Endothelial cell dysfunction appears to be the key feature in its pathophysiology [17]. According to recent figures the estimated global incidence of pre-eclampsia is 3–10% [18–20] with about 6% incidence rate in primigravida women [21]. The incidence in developing countries ranges between 4 and 18% with an increasing trend [6,22,23].

The major reasons for such a high maternal and foetal morbidity and mortality associated with HDP are unavailability of tests that can identify pregnant women at risk of developing HDP precisely [24]. One such test that can be used as a biomarker for severity of disease as well adverse maternal and perinatal outcome is serum uric acid levels. This association was first reported in 1917 by Slemons et al. [25]. Since then, uric acid levels were considered for monitoring of maternal and foetal outcomes in pregnant women with HDP. There are several

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reasons for elevated serum uric acid levels such as decreased urinary clearance due to fall in glomerular filtration rate and increased re-absorption rate [26]. Furthermore the elevated serum uric acid levels not only reveal severity of HDP but it also contributes in its pathology [27] and has significant effects on maternal and perinatal outcomes [28–30].

Hence, the present study was conducted with the aim of having information about the effects of elevated maternal serum uric acid levels on overall perinatal outcome.

2. Material and methods

2.1. Study design

Prospective comparative study.

2.2. Study population

The present study was conducted in the Obstetrics and Gynaecology department of a rural tertiary care centre of Northern India from October 2016 to May 2017 on all pregnant women with period of gestation > -34 weeks admitted with features of Hypertensive Disorders of pregnancy as study subjects.

2.3. Study duration

Seven months (October 2016–May 2017).

2.4. Exclusion criteria

All pregnant women with period of gestation < 34 completed weeks or history of pre-existing medical disorders such as Type II diabetes mellitus, chronic hypertension, renal disease, liver disease, cardiovascular, thyroid or any other endocrinological disorders were excluded from the study.

2.5. Definitions

Hypertension during pregnancy: It is defined as diastolic blood pressure of 90 mmHg or greater on two occasions more than 4 h apart or a single diastolic blood pressure above 110 mmHg [31].

Severe hypertension in pregnancy: It is defined as systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg, or both [32].

Gestational hypertension: It is defined as new onset hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or both) presenting at or after 20 weeks gestation without proteinuria or other features of preeclampsia [33,34].

Preeclampsia: It is defined as systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or both with proteinuria and, potentially, other end-organ dysfunction [33].

Severe preeclampsia: It includes presence of any one of the following: severe hypertension (systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg, or both), epigastric pain, cerebral/visual disturbances, decreased urine output, pulmonary oedema, thrombocytopenia, deranged liver functions, or intrauterine growth restriction [35].

Eclampsia: It is defined as new onset grand-mal seizures in women with features of preeclampsia [31,33].

2.6. Data collection

The present prospective comparative study was conducted in the department of Obstetrics and Gynaecology of a rural tertiary care centre of Northern India over a period of seven months from October 2016 to May 2017 after Institutional Ethical Clearance and informed written consent from the participants. Every effort was made not to disclose the identity of any of the participants. All pregnant women with gestational age 34 weeks or more admitted with the features of HDP in the department of obstetrics were enrolled in the study. After admission a detailed medical and family history of all the cases was taken to ensure that they fulfil the inclusion criteria for the study. Also a thorough physical examination of every case was done and recorded. The blood pressure of all cases at the time of admission and after two hours of rest was carefully recorded according to the Society of Obstetricians and Gynaecologists of Canada clinical practice Guidelines [33], with the woman in sitting position with her arm at the level of heart using an appropriately sized cuff (i.e., length 1.5 times the circumference of the arm). Korotkoff phase V sound was used to measure diastolic blood pressure. Also if blood pressure was consistently higher in one arm, the arm with the higher values was used for all blood pressure measurements. At the same time, under all aseptic precautions 5 ml of venous blood sample was drawn from the patient's ante-cubital vein with the patient in supine position, prior to commencement of any treatment, into properly labelled tubes for measurement of serum uric acid levels by enzymatic colour test using Uricase and Peroxidase enzymes. The normal values used for reference in third trimester ranges between 3.1 and 6.3 mg/dl [36]. For urinary protein analysis, 10 ml mid stream urine was collected. Urine protein was measured by dipstick and graded as Trace to 4+ (Trace, 0.1 g/L; 1+, 0.3 g/L; 2+, 1 g/L; 3+, 3.0 g/L; 4+, 10 g/L). Guidelines of the National Clinical Chemistry Laboratory Standards were followed for collection, handling, and transportation of samples to the laboratory [37,38].

Finally on the basis of presence or absence of urinary protein and features of convulsion; the study population was divided into 3 groups; Group I included antenatal women with Gestational hypertension, Group II; women with preeclampsia and Group III; antenatal women with features of eclampsia. All the participants were age matched and the cases were followed until delivery for final maternal and foetal outcomes, which were recorded.

2.7. Statistical analysis

The data was analysed using SPSS-20 version and the final results were compiled thereafter. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Quantitative variables were compared using unpaired *t*-test/Mann-Whitney Test and qualitative variables were correlated using Chi-Square test/Fisher's exact test. P value of < .05 was considered statistically significant.

3. Results

Of total 110 women; 35 (31.81%) suffered from Gestational hypertension with a mean age of 26.51 ± 3.82 years, 49 (44.54%) had Pre-eclampsia with mean age at presentation 27.14 ± 3.64 years and remaining 26 (23.63%) had eclampsia with mean age 24.73 ± 4.01 years. (Table1). Of total 111 babies (including one twin gestation) delivered to all women with hypertensive disorders of pregnancy, 52 (46.85%) [13 (25%) in gestational hypertension group; 23 (44.23%) in pre-eclampsia group and 16 (30.77%) in eclampsia group] were born prematurely and the remaining 59 (53.15%) [23 (38.98%) in gestational hypertension group; 26 (44.07%) in pre-eclampsia group and 10 (16.95%) in eclampsia group] were born at term.

Of 36 babies in gestational hypertension group 8 (22.2%) were delivered by lower segment caesarean section (LSCS), including one twin gestation (7 term and 1 preterm) and 28 (77.78%) by vaginal delivery (16 term and 12 preterm), in preeclampsia group of 49 babies; 15 (30.61%) were delivered by LSCS (9 term and 6 preterm), 32 (65.31%) by vaginal delivery (17 term and 15 preterm) and 2 (4.1%) by vaginal birth after caesarean section, in eclampsia group of 26 babies, 12 (46.15%) were delivered by LSCS (5 term and 7 preterm), 13 (50%)