Raised Uric Acid Level and Fetal Outcome in Hypertensive Disorders of Pregnancy

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Aims: This study was done to find the relation of raised uric acid with fetal outcome in hypertensive disorders of pregnancy and to compare the fetal outcome with normal and raised uric acid level .

Methods: This was a hospital based cross-sectional prospective comparative study done in Paropakar maternity and Women's hospital conducted over three month period.

Results: During the study period, a total of 126 cases of hypertensive disorders of pregnancy were identified among 3819 obstetric cases. The incidence of hypertensive disorders of pregnancy in this study was 3.3%. Fifty seven of them were found to have serum uric acid level <5.5 mg% (Group A), 43 of them were found to have serum uric acid level ≥5.5mg% (Group B). In those developing hyperuricemia 54.81% had mild hypertension, 40.91% had severe hypertension. Adverse perinatal outcome with serum uric acid level ≥5.5mg/dl had stillbirth in 7%, had low birth weight in 27.9%, 11.6 % were admitted in special care baby unit and 18.6 % had apgar <7 at five minute.

Conclusions: Perinatal morbidity and mortality was increased in women with raised uric acid level except admission to special baby care unit Hypertensive disorders of pregnancy are associated with high maternal and perinatal morbidity and mortality.

Keywords: fetal outcome, hypertensive disorder of pregnancy, uric acid.

INTRODUCTION

Hypertensive disorders are the most common medical complications of pregnancy, affecting between 7 -15% of all pregnancies.[1] Hypertensive disorders of pregnancy results in 12% of maternal deaths globally and 10% associated with eclampsia.[2]. The major risks to the fetus result from decreased placental perfusion leading to decreased supply of oxygen and nutrients necessary for fetal growth and well being.

In 1917 Slemons and Bogert first observed an association between serum uric acid concentration and presence of preeclampsia and Redman was first to note that high serum uric acid level was associated with increased perinatal mortality rate.[3,4]

Hyperuricemia is one of the characteristic findings in pre-eclampsia. Uric acid determination is considered to be a part of the workup in women with pre-eclampsia to monitor disease severity and aid management of these women. It is also considered a good predictor of low birth weight and fetal outcome. In this study an attempt was made to see the relationship of serum uric acid level and perinatal outcome .

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METHODS

This was a hospital based cross sectional prospective comparative study done in Maternity Hospital, Thapathali, Kathmandu. This is the largest maternity hospital in Nepal where about 18660 deliveries take place in a year. The study was conducted over three month period.

All the cases admitted in the hospital with diagnosis of hypertensive disorders of pregnancy after 28 weeks of gestation with singletons pregnancy were enrolled .The criteria were adopted from National high blood pressure education program (NHBPEP).

All primi and multigravid patient with blood pressure ≥140/90 mmHg after 28 weeks of pregnancy were enrolled whereas women with a blood pressure ≥140/90 mmHg at or before 20 weeks of gestation, with past history of renal disease, previous hypertension or on anti hypertensive drugs, hypertension in multiple gestation, intrauterine fetal death, ultrasonograph showings abnormal fetuses were excluded from the

study.

Permission from hospital was taken before the study begans. General and systemic examination of a women was carried out thoroughly and findings, time, place was recorded . Diagnosed cases of hypertensive disorder of pregnancy were noted and their blood pressure was rechecked after 4-6 hours, if the diastolic blood pressure ≥90 mmHg then they were enrolled for study. If DBP ≥110mmHg then after single reading they were also enrolled for study and were classified as severe hypertension. Blood pressure was measured by sphygmomanometer cuff on the both arms in sitting position. Koratokoff 5(K5) was used for diastolic blood pressure.

A delivered case with diagnosis of hypertensive disorder in pregnancy was taken in the study with attention given to fetal outcome. All women who developed hypertension during intrapartum and postpartum period (within 24hours of delivery) was also enrolled as study case if the criteria were met.

Urine for protein was tested by sulphosalicylic acid method 12 hourly apart and proteinuria was considered significant if it is 1+ in two or more occasion. If proteinuria, urine routine examination was done to exclude urinary tract infection. Serum uric acid level was done by pap colorimetric enzymatic method. The cases were divided into 2 groups according to serum uric acid level. Those with serum uric acid <5.5mg % were grouped as Group A and those with serum uric acid ≥5.5mg% as Group B. Serum uric acid was repeated once a week till delivery and initial value was taken. The cases with interval between delivery and uric acid investigation >24 hours were excluded from data analysis. The subjects and their babies were followed till discharge and any adverse events of baby during delivery or hospital stay was noted.

Special attention was given to still birth, low birth weight(<2.5 kg), low apgar (<7 at one minute and 5 minute), special care baby unit admission. Babies that were admitted in special baby care unit because the mothers were admitted in maternal intensive care unit for severe preeclampsia, eclampsia, and HELLP syndrome were not taken as special care baby unit admission.

The data was entered in SPSS program. The rate and proportion was calculated .These findings were presented in figures and comparison was done by chi-square test and Z test for proportion. The resultant p- value was considered significant if $p<0.05$.

RESULTS

During the study period, 126 cases of hypertensive disorders of pregnancy were identified from among 3819 obstetric cases. Out of these 126 cases, 100 cases that fulfilled the criteria were entered into the study. The incidence of hypertensive disorders of pregnancy in this study was 3.3%.

Serum uric acid level < 5.5 mg% (Group A) were found in 57 cases, 43 were found to have serum uric acid level ≥ 5.5mg% (Group B). Overall 40.96% patient with mild hypertension and 52.9% patient with severe hypertension developed hyperuricemia.

Adverse perinatal outcome was seen with the stillbirth rate of 1.8% versus 7%, low birth weight rate of 21% versus 27.9%, Low apgar score rate of 8.8% versus 18.6% in women with serum uric acid level <5.5mg% compared to ≥ 5.5mg%.But admission to special baby care unit was 15.8% versus 11.6% with serum uric acid level <5.5mg% compared to ≥ 5.5mg% respectively. The findings were statistically not significant. Perinatal morbidity and mortality was increased in women with increased uric acid level except admission to special care baby unit.

Table1. Distribution of adverse perinatal outcome in relation to Serum uric acid level.

Characteristics	Group A SUA <5.5mg/dl (n=57)	Group B SUA ≥5.5mg/dl (n=43)	Total	P value
Stillbirth	1 (1.8%)	3 (7%)	4	0.18
LBW	12 (21%)	12 (27.9%)	24	0.42
SCBU admission	9 (15.8%)	5 (11.6%)	14	0.55
Low Apgar	5 (8.8%)	8 (18.6%)	13	0.14
NND	0	0	0	

Table 2. Birth weight in relation to serum uric acid level.

Birth weight in kg	Group A (SUA <5.5mg/dl)	Group B (SUA ≥5.5mg/dl)	Total	P value
<2.5	12 (21%)	12 (27.9%)	24	0.52
2.5-3.0	23 (40.3%)	20 (46.5%)	43	
3.1-3.5	16 (28%)	9 (20.9%)	25	
>3.5	6 (10.5%)	2 (4.65%)	8	
Total	57	43	100	

LBW was 21% in group A and 27.9% in group B. Normal birth weight (2.5 -3.0) kg was more common with serum uric acid level ≥5.5mg% (46.5% versus 40.3%).

DISCUSSION

Various studies had shown the increased incidence of preterm birth, intrauterine growth restriction, low birth weight, still birth in hypertensive disorder of pregnancy. Association between serum uric acid level and fetal outcome has also been demonstrated by many studies.

The incidence of hyperuricemia in this study was 43% of hypertensive pregnancy which is lower than the studies done in United States 58% , UK and Argentina 23.5% and 26.5%.[5,6,7]

Redman CW in their study done in 332 pregnant women with hypertension reported excellent fetal prognosis with severe maternal hypertension without hyperuricemia. Conversely when maternal hypertension was mild and hyperuricemia was severe, prognosis for fetus was poor.[8] In a study done in United states of America by Shah DM , Reed G found that when serum uric acid ≥ 6 mg/dl patient had a relative risk of 4.2 for adverse perinatal outcome (95 % CI ,2.0-8.9 ; p <0.0001) which suggest the elevated serum uric acid may be clinically useful predictor of perinatal mortality, more importantly of perinatal morbidity.[9] There was 1.8% still birth with serum uric acid level <5.5mg% and 7% with serum uric acid level ≥5.5mg% but was not statistically significant probably due to the small sample size. There was no early neonatal death in this study group.

Different studies have found that hyperuricemia is related with preterm birth and low birth weight .In this study 21 % with serum uric acid <5.5 mg/dl and 27.9 % with serum uric acid ≥ 5.5 mg/dl had low birth weight which was also not significant statistically and this finding is lower than the study done in Chandigarh who showed 69% low birth weight in patients with hyperuricemia but the study done in Argentina reported 10 % low birth weight with serum uric acid <5.5 mg /dl and 20 % with serum uric acid ≥ 5.5 mg/dl which is lower than this study.[10,7]

In this study two intrauterine growth restriction were identified. Both were at 36 weeks with severe pre eclampsia, both had cesaerean section ,one weighed 1600gm with serum uric acid 6.8gm% and another weighed 1800gm with serum uric acid 5.5mg%. This finding was probably because most of them were identified to be hypertensive only during admission as only admitted cases with hypertensive disorder of pregnancy were included in the study as the study period was short and has not followed those patients who developed hypertension after 28 weeks of gestation till delivery. A comparative study done in Spain showed that intrauterine growth restriction was present in 44.5 % of cases with serum uric acid >6 mg% and 27.5% in cases with serum uric acid <6 mg% group which is not comparable as the intrauterine growth restriction of only 4.7 % with serum uric acid ≥5.5 mg% was found in this study group.[11]

In this study special care baby unit admission was 15.8 % in group A and 11.6 % with group B which is lower than the study done in Spain which showed 25.2% of babies with maternal serum uric acid <6mg% were admitted to special care baby unit in comparison to 36.7% in uric acid >6mg% that was also not significant statistically.[11]

This study showed perinatal mortality rate with group A was 17.5/1000 live birth and with group B was 69.76/1000. The perinatal mortality rate in this study was lower than the study done in Chandigarh , India who have found the perinatal mortality rate (PNMR) 200/1000 with serum uric acid ≥5.5mg% which

reflects the perinatal outcome with this serum uric acid level whereas Varma TR found Perinatal mortality rate (PNMR) 100/1000 in serum uric acid >330mmol/L (5.5 mg %) with pre existing hypertension and the perinatal mortality rate 101.7/1000 in preeclampsia with serum uric acid >330mmol/L (>5.5mg %) whereas perinatal mortality rate was 7.1/1000 in pre eclampsia patient with normal uric acid ($p < 0.01$) [6]

Range of birth weight (2.5– 3.0) kg in this study population was 40.3 % with group A and 46.5% with group B. Low birth weight was 21% in group A and 27.9 % with group B in this study which is not statistically significant. In a study of 576 cases which was done in Islamabad, patients with serum uric acid level of ≤ 6.4mg/dl had a mean fetal birth weight of 3125 grams and with serum uric acid of ≥6.4 mg/dl had a mean birth weight of 2774 grams.[12]

CONCLUSIONS

Perinatal morbidity and mortality was increased in women with raised uric acid level except admission to special baby care unit though the adverse perinatal outcome was not statistically significant probably due to small sample size. Further study is needed with large population to predict its relation for perinatal outcome.

DISCLOSURE

The authors report no conflicts of interest in this work.

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REFERENCES

1. Arias F, Daftary S, Bhide A. Practical guide to high risk pregnancy and delivery:a South Asian perspective. 3rd ed. 2011.
2. Sibai BM. Chronic hypertension during pregnancy. Sci J Gynaecol and obstet. Philadelphia JB Lippincott: 1989: 1-8.
3. Cunningham FG, Gant NF, Levono JK, Haut CJ, Wenstrom DK. Hypertensive disorders in pregnancy. Williams Obstetrics. 21st ed. McGraw – Hills, 2001;pp.761-808.
4. Redman CWG, Williams GF, Jonesa DD. Plasma urate and serum deoxycytidylate deaminase measurements for early diagnosis of pre eclampsia. Br J Obstet Gynecol. 1977;84: 904.
5. Lim K H. The clinical utility of serum uric acid measurements in hypertensive disease of pregnancy. Am J Obstet Gynecol. 1998;178(5):1067-71.
6. Varma TR. Serum uric acid level as an index of fetal prognosis in pregnancies complicated by pre-existing hypertension and pre eclampsia of pregnancy. Int J Gynaecol and Obstet. 1982;20(5):401-8.
7. Voto LS, Darbon Grosso HA, Illia R, Margulies M. Uric acid levels: a useful index of the severity of pre eclampsia and perinatal prognosis. J Perinatal Med. 1988;16(2):123-6.
8. Redman CW, Beilin LJ, Bonnar J, Wilkinson RH. Plasma urate measurements in predicting fetal death in hypertensive pregnancy. Lancet. 1976;1(7974):1370-3.
9. Shah DM, Reed G. parameters associated with adverse perinatal outcome in hypertensive pregnancies. J Human Hypertension. 1996;10(8):511-5.
10. Mustaphi R, Gopalan S, Dhaliwal L, Sarkar AK. Hyperuricemia and perinatal outcome in pregnancy induced hypertension. J Ind Med Assoc. 1994;92(10):331-2.
11. Acien P, Lioret M, Lioret G. Perinatal morbidity and mortality in pregnancy of hypertensive disorder: Prognostic value of the clinical and laboratory findings. Int J Gynaecol and Obstet. 1990; 32(3):229-35.
12. Saeed GA, Hamid R, Khattak NB. Serum Uric Acid level as a marker for predicting progression of gestational hypertension to pre-eclampsia and fetal morbidity. Pak Armed Forces Med J. 2003; 53(2):136-41.