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EFFECT OF HYPERURICEMIA ON PRE-ECLAMPTIC, ECLAMPTIC PATENTS AND THEIR FETAL OUTCOME

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ABSTRACT

Background: Pre-eclampsia and eclampsia are global problem. They are considered as a major cause of maternal and fetal morbidity and mortality. Hyperuicemia complicates pre-eclamptic and eclamptic patients as well as their fetal outcome. **Aim:** To evaluate the serun uric level of both pre-eclamptic and eclamptic patients, and to correlate the serum uric level to the outcome of pregnancy. **Material and Methods:** It was a comparative horizontal cross-sectional study of pre-eclamptic and eclamptic patients attending State Specialst Hospital, Maiduguri, Nigeria. **Results:** Serum uric acid concentrations were significantly higher in both pre-eclamptic and eclamptic subjects (436 + 36 µmol/L and 527 + 80 µmol/L respectively) ($P < 0.05$) as compared with the age-matched control group (245 + 67 µmol/L). The mean birth weight of infants of eclamptic patients was significantly lower (2.48 + 0.33kg) ($P < 0.05$) as compared to normal birth weight (>2.80 kg). **Conclusion:** These results suggest that maternal hyperuricemia is a strong predictor of maternal disease in pre-eclampsia and eclampsia with increased perinatal morbidity and mortality.

KEYWODS: Pre-eclampsia, eclampsia, pregnancy, serum uric morbidity, birthweght, hyperuricemia, mortality, Northeastern Nigeria.

INTRODUCTION

Pre-eclampsia is one of the major causes of maternal and fetal morbidity worldwide.[1,2,3] Overall perinatal motality in PE is around 35 per thousand of total births but may reach 160 per thousand in severe disease. Mortality is increased two fold if the fetus is small for gestational age.[4] PE complicates between 5% to 8% of pregnancies in United States and 3% to 14% of pregnancies worldwide.[5] The complications of PE may be considered as immediate (eclampsia, preterm labor, accidental hemorrhage etc).

Eclampsia is depined as seizure activity or coma unrelated to other cerebral condition in an obstetrical patient with pre-eclampsia.[7] Pre-eclampsia and eclampsia have been associated with increased serum uric acid concentration, decreased glomerular fillration rate, and marked proteinuria.[8] The incidence of eclampsia varies from one part of the world to another. The incidence has been decreasing and its outcome improving in the developed countries, where there is excellent antenatal care and special management protocols have been employed. For instance, the incidence in the UK is quoted as approximately 1 in 2000 pregnancies while that of a referral institution in Nigeria is 11.8 per 1000 deleveries.[9] Eclampsia accounts for approximately 50,000 maternal deaths world wide annually.[10]

The hyperuricemia of pregnancy-induced hypertention is partly due to the failure of tubular secretion but placental ischemia may contribute to the elevation of uric acid in PET (pre-eclamptic toxemia) secondary to ischemia.[8] Therefore, pre-eclamptic hyperuricemia is probably caused by a combination of increased production, intrarenal (peritubular) vasoconstriction and hypovolemia.[8] Hyperuricemia which is an increase in uric acid level in blood, a persistent increase of 60 µmol/L or more over a patient's established non gravid value should be considered significant.[11] Uric acid is a low Molecular weight substance that pass freely into fetal circulation where it has the potential for inhibiting glomerular endothelial cell proliferation. A rise in uric acid in the third trimester would preferentially affect nephron development since kidney development occurs late in pregnancy. The child would then be born with low nephron number. It was shown that mothers at risk for having LBW (low birth weight) babies were frequenthy pre-ealanptic/eclamptic, which was associated with elevated uric acid.[12]

An assiciation of uric acid with pre-eclampsia and eclampsia has been known since long. several studies have correlatd the rise in serum uric acid with the severity of pre-eclansia and eclampsia. hperunicemia was reported by many authors to co-relate with maternal morbidity and mortality. There is an even stronger association of increased serum uric acid with the risk for small or LBW infants and with overall fetal mortality.[13,14,15,16] Association of raised uric acid in pre-eclampsia and eclampsia and its effect an pregnancy would provide atternative approach to reduce maternal and fetal morbidity and mortality by an attempt to decrease serum acid levels in pre-eclampsia/eclampsia patients, and to correlate the serum uric acid to the outcome of pregnancy.

MATERIAL AND METHODS

The setting was the Obstetrics and Gynecology ward of State Specialist Hospital Maiduguri, North-Eastern Nigeria. Maiduguri, the state capital of Borno State is the largest of the six states in the North-Eastern zone of Nigeria. It lies on latitude 11^0 North and longitude 13^0 East. Borno State shares borders with Republic of Niger to the north, chad to the north-east and Cameroon to the East. The estimated population of Borno State in 2006 is 4,098,391.

The study is a comprative horizontal study of eclamptic and pre-eclamptic patients attending State Specialist Hospital, Maiduguri, Nigeria. Forty (40) consecutive eclamptic patients and twenty (20) pre-eclamptic patients were recruited for the study, while the control group was forty (40) apparently healthy age-matched pregnant women attending antenatal clinic within the period of the study. Five milliliters (5MIS) of blood was collected by vein puncture using a five 5ml syringe and needle under septic techniques using 75% methylated spirit. The blood was then transferred into a new 10ml specimen vial and allowed to clot at room temperature, it was then centrifuged of 4000 rpm for 5 minutes and the serum harvested using Pasteur's pipette into a serum container for uric acid estimation. The sample was then refrigerated at-30^0 until analysis. Serum uric acid was measured by enzymatic (uricase) method using semichemistry autoanalyzer.

Result was expressed as mean + SD. Analysis of the collected data was done by SPSS software version 13.0, using unpaired 't' test. A level of $P < 0.05$ was accepted as statistically signficant.

RESULTS

The mean and standard deviations for serum uric acid concentration of values obtained from the various groups are presented. Statistical analysis was by student t-test, and the level of significance was (at $P < 0.05$) as shown in table 1 The mean serum uric acid concentration in control group was 245 + 67 µmol/L, in pre-eclampsia was 436 + 36 µmol/L, and in eclampsia was 527 + µmol/L. There was a statistically significant increase in serum uric acid levels in pre-eclampsia 436 + 36 µmol/L as compared with control subjects 245 + 67 µmol/L ($P < 0.05$). The mean serum uric acid levels of eclamptic subjects were significantly higher 527 + 80 µmol/L than those of their control subjects 245 + 80 µmol/L ($P < 0.05$).

Table 1: Showed the Mean serum uric acid concentrations of study groups

Uric Acid Values (Mean + SD) in				
Parameters	**Per-eclampsia (n=20)**	**Eclampsia (n=40)**	**Control (n=40)**	**P-value**
Serum Uric Acid (µmol/L)	436 + 36	527 + 80	245 + 67	< 0.05

The mean age of preeclamptic, eclamptic patients and control group were 25.6 + 8.3, 36.1 + 6.2 and 24.2 + 7.3 respectively. No significant difference of maternal age between The study groups was observed ($P < 0.05$) The systolic blood pressure of pre-eclamptic, eclamptic and control group were 151.72 + 12.1mmHg, 156.2 + 18.3 mmHg, and 118.7 + 14.4 mmHg, respectively. Similarly, the diastolic blood pressure of pre-eclamptic, eclamptic and normal pregnant women (control group) were 98.6 + 7.2 mmHg, 102.5 + 12.1 mmHg, and 79.2 + 8.1 mmHg, respectively. There was significant difference in both systolic and diastolic blood pressures of case subjects and control subjects ($P < 0.05$).

Table 2: Showed age, systolic and diastolic blood pressure.

Parameters	**Per-eclampsia (Mean + SD)**	**Eclampsia (Mean + SD)**	**Control**	**P-value**
Age (yrs)	25.6 + 8.3	36.1 + 6.2	24.2 + 6.2	P > 0.05
Systolic blood pressure (mmHg)	151.7 + 12.1	156.2 + 18.3	118 + 14.4	P < 0.05
Diastolic blood pressure(mmHg)	98.6 + 7.2	102.5 + 12.1	79.2 + 8.1	P < 0.05

In Pre-eclampsia, normal birth weight (NBW) Fetuses were 14 (70%) and low birth weight fetuses, were 5.5 (27.7%); in eclampsia, NBW were 30 (75%) and LBW fetuses were 8(20%), and the NBW and LBW of control group were 38(95%) and 1.8 (4.5%) respectively. There was significant difference of fetal birth weight status ($P < 0.05$) among the study groups.

Table 3: Showed fetal outcome of the study groups.

Fetal Outcome	Pre-eclampsia (n=20)	Eclampsia (n=40)	Control (n=40)	P-value
Stillbirth	0.5 (2.5%)	2 (5%)	0.2 (0.5%)	
Low birth weight (kg)	5.5 (27.7%)	8 (20%)	1.8 (45%)	< 0.05
Normal birth weight (kg)	14 (70%)	30 (75%)	38 (95%)	

Numeric and percent value of different types of fetal outcome. X^2 test was done and $P<0.05$ was taken as the level of significant.

DISCUSSION

Significant hyperuricemia was found in pre-eclampsia and eclampsia 436 + 36 µmol/L and 527 + 80 µmol/L repectively ($P < 0.05$).

Hyperuricemia has been demonstrated in both pre-eclamptic and eclamptic subjects and has been associated with decrease in glomerular fillration rate; increased production, intrarenal (peritubular) vasoconstriction and hypovolemia due to increased tubular reabsorption of urate.[8,17]

The hyperuricemia in the eclamptic subjects was significantly higher (at $P < 0.05$) when compared with the age-matched normal pregnant women. Changes in serum uric acid concentration and its renal handling occur in pre-eclampsia/eclampsia. A large literature attests to observations that serum urate levels rise and its renal clearance decreases in this disease.(18) The hyperuricemia observed in this study among pre-eclamptic and eclamptic subjects confirms previous reports of Mustaphi et al,[19] Lam et al,[20] on the status of serum uric acid in pre-eclamptic and eclamptic women.

Maternal urate levels have also been correlated with fetal outcome.[18] Since some authors consider an increasing serum uric acid levels or a decrease in its clearance (particularly if the ratio C_{urate}/C_{inulin} decreae below 0.07) as virtually pathognomonic of pre-eclampsia, a discussion of other physiologic or pathophysiologic influences on urate excretion is warranted.[18]

An increased serum uric acid levels found in this study is a clinical feature of pre-eclampsia/eclampsia, higher levels correlate with signifcant maternal and fetal morbidity and Mortality This Finding corresponds with the work of Lam et al.[20]

Perinatal mortality was markedly increased when maternal serum urate concentrations were raised, generally in association with severe pre-eclampsia and eclampsia of early onset These findings suggest that in term of fetal health, changes in renal handling of urate may be a more inportant feature of pre-eclampsia. This corroborates the work of Radmen et al[16] and Mustaphietal.[19] who reported that hyperuricemia more than 5.5mg% is associated with increased perinatal morbidity and mortality.

Moreover, mean gestational age at delivery was 39 + 2 weeks for patients with uric acid levels of < 430 µmol/L with a mean fetal birth of 2.8kg and 15% babies being small for gestational age. Wherease with serum uric acid of 743 µmol/L mean gestational age at delivery became 35 + 2 week with a mean birth of 2.68kg and 25% babies were small for gestational age. These findings are similar to those reported for pakistan's women.[20] This raised level of serum uric acid was a better indicate than blood pressure as an index of fetal prognosis. contrary to other studies that stated that maternal serum uric acid levels are not good prognostic indicators for of the severity of the maternal or fetal complication.[22]

Hussain et al[23] reported that there were significant increased number of low birth weight fetuses in babies born to hyperuricemic pre-eclamptic/eclamptic mothers in comparison with babies born to normouricemic mothers, Other authors also saw similar linear trend in patient of pre-eclampsia with hyperuricemia[16,20,21] this trend of increased uric acid with poor fetal outcome indicates that probably raised uric acid causes growth retardation, reduced placental function that the consequence is reflected as LBW.[23,24,25,26]

CONCLUSION

In conclusion the result of this study shows that there is significant increae in serum uric acid concentration in both pre-eclamptic and eclamptic patients as compared with the age-matched normal pregnant women (control). Maternal hyperuricemia is a strong indicator of maternal disease progression in pre-eclampsia/eclampsia with increased perinatal morbidity and mortality. An elevated levels of serum uric acid is not simply a marker of disease severity but rather contributes directly to the pathogenesis of the disorders.

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