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Original article

Fetal Outcome of Pre-eclamptic Mothers with Hyperuricemia

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ABSTRACT

Pre-eclampsia (PE) is considered as a major cause of maternal and fetal morbidity and mortality. When a pre-eclamptic woman develops associated hyperuricemia then fetal outcome may become worse. To observe the fetal outcome of hyperuricemic pre-eclamptic pregnancy in relation to normo-uricemic pre-eclamptic pregnancy in a hospital based comparative and cross-sectional study 62 pre-eclamptic patients were selected purposively. PE was diagnosed by hypertension and proteinuria. PE patients were divided into two groups by there serum uric acid level - Hyperuricemic & Normo-uricemic. Then fetal outcome markers (Stillbirth and low birth weight fetus) of the study groups were observed. In this study significant increased number of low birth weight fetuses was observed in babies born to hyperuricemic pre-eclamptic mothers in comparison with babies born to normo-uricemic pre-eclamptic mothers. According to the observation the estimation of serum uric acid may be considered in management of pre-eclamptic mothers, especially in lowering the rate of poor fetal outcome.

Key Words: Pre-eclampsia (PE), Hyperuricemic, Normo-uricemic, Fetal outcome, Stillbirth, Low birth weight (LBW) fetus.

Introduction

Pre-eclampsia is one of the major causes of maternal and fetal morbidity and mortality world-wide[1,2,3]. Overall perinatal mortality in PE is around 35 per thousand of total births but may reach 160 per thousand in severe diseases. 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 labour, accidental haemorrhage etc.) and remote (residual hypertension and recurrent PE)[6] complications. Fetal outcome of PE may be normal or abnormal. In complicated PE the abnormal outcomes are low birth weight (LBW) fetuses, birth asphyxia, perinatal death i.e. stillbirth and death of fetus within a week after birth etc. Among them stillbirth and LBWs are the immediate fetal outcome[7].

Uric Acid is the end product of purine metabolism. Which is filtered through glomeruli and most is reabsorbed from the proximal tubular lumen[8]. Hyperuricemia most commonly is defined by serum or plasma uric acid concentrations greater than 7.0 mg/dl in men or greater than 6.0 mg/dl in women[9]. Uric acid is a low molecular weight substance that passes 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 a low nephron number. It was showed that mothers at risk for having LBW babies were frequently pre-eclamptic, which was associated with elevated uric acid level[10].

An association of uric acid with PE has been known since long. Several studies have correlated the rise in uric acid with the severity of the PE. Although hyperuricemia does co-relate with maternal morbidity, there is an even stronger association of increased uric acid with the risk for small or LBW infants and with overall fetal mortality[11,12,13]. Association of raised uric acid in PE and its effect on pregnancy may provide alternative approach to decrease maternal and fetal mortality and morbidity by an attempt to reduce serum uric acid level in PE. The study was designed to observe the fetal outcome of hyperuricemic pre-eclamptic pregnancy in relation

to normo-uricemic pre-eclamptic pregnancy.

Subjects and methods

This comparative cross-sectional study was conducted at Sylhet MAG Osmani Medical College (SOMCH) during the period of July'07 to June'08. Admitted 32-40 weeks pregnant pre-eclamptic patients from Gynecology and obstetrics ward of SOMCH were taken as study subjects. A total 62 patients were selected for the study. Subjects were divided into two groups: Group-I included 25 pre-eclamptic mothers with hyperuricemia and Group-II 32 pre-eclamptic mothers having normal serum uric acid level. 5 subjects were excluded due to hyperglycemia during observation.

PE was diagnosed by hypertension and proteinuria. The fetal outcome markers (Stillbirth and LBW) of the study groups were observed.

Result was expressed as mean ± SD. Analysis of the collected data was done by SPSS software program, using unpaired 't' test, Chi square ('x^2') test. A level of P <0.05 was accepted as statistically significant.

Results

The mean age of group-I and group-II (years) were 24.9 ± 4.44 and 26.59 ± 4.72 and the mean gestational age (years) of group-I and group-II were 37.43 ± 2.52 and 38.69 ± 1.33 respectively. No significant difference of maternal age between the study groups was observed but there was a significant difference of gestational age ($p < 0.05$) between the study groups seen (Table-1). In group-I, the mean of systolic blood pressure (mmHg) was 156.30 ± 18.60 and diastolic blood pressure was 102.61 ± 12.42. In group-II, the mean of systolic blood pressure was 151.72 ± 12.09 and diastolic blood pressure was 98.59 ± 7.54. No statistically significant difference ($p > 0.05$) of both systolic and diastolic blood pressure was found between the study groups (Table-1).

Table-1: Age, gestational age and blood pressure status of the study groups.

Parameters	Group-I (Mean ± SD)	Group-II (Mean ± SD)	p
Age	24.9 ± 4.44	26.59 ± 4.72	> 0.05
Gestational age	37.43 ± 2.52	38.69 ± 1.33	< 0.05
Systolic blood pressure (mmHg)	156.30 ± 18.60	151.72 ± 12.09	> 0.05
Diastolic blood pressure (mmHg)	102.61 ± 12.42	98.59 ± 7.54	> 0,05

Means compared using Student's unpaired 't' test.

Mean serum uric acid concentration in group-I was 7.09 ± 1.09 mg/dl and in group-II, it was 4.62 ± 0.76 mg/dl. There was significant difference of serum uric acid levels ($p < 0.001$) between study groups (Table-2).

Table-2: Uric acid status of the subjects.

Groups	Number of population (n)	Serum uric acid level (mg/dl) (Mean ± SD)	p
Group-I	25	7.09 ± 1.09	<0.001*
Group-II	32	4.62 ± 0.76	

Means compared using Student's unpaired 't' test.

In group-I, normal birth weight (NBW) fetuses were 5 (20%) and low birth weight (LBW) fetuses were 18 (72%) and in group-II NBW fetuses were 29 (90.62%) and LBW fetuses were 3 (9.38%). There was significant difference of fetal birth weight status ($p < 0.001$) between the study groups (Table-3).

Table-3: Fetal outcome of the study groups.

Fetal outcome	Group-I (n = 25)	Group-II (n = 32)	p
Stillbirth	2 (08%)	0 (00%)	
Low birth weight (gms)	18 (72%)	03 (9.38%)	< 0.001
Normal birth weight (gms)	5 (20%)	29 (90.62%)	

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

In group-I live birth was 23 (92%) and stillbirth was 2 (8%) and in group-II live birth was 32 (100%) and stillbirth was 0%.

Discussion

Pregnancy brings about certain physiological changes in renal function and metabolic processes of the mother. The changes are often exaggerated in PE and eclampsia. Raised uric acid in pre-eclamptic mothers affects fetal growth, which in turn gives rise to poor fetal outcome.

Two events, hyperuricemia and impaired fetal well being or fetal outcome may be a completely separate expression of pre-eclampsia. Although LBW fetuses are frequently seen, stillbirth is also very common in fetal outcomes. It is not fully clear that why fetal outcome is poor in pre-eclamptic mother. In this situation it is important to evaluate biochemical changes of pre-eclamptic mothers during pregnancy, which may predict probable fetal outcome. Among the various biochemical parameters fetal outcome of pregnant woman with raised blood uric acid is implicative[11,13]. The precise mechanism which leads to accumulation of uric acid in the blood of pre-eclamptic mothers is still uncertain but its adverse effects on fetal outcome are now well known[12,14,15,16].

The relationship of high blood uric acid in pre-eclamptic women with poor fetal outcome (LBW fetus and stillbirth) was observed in this study. In hyperuricemic subjects serum uric acid concentration was 7.09 ± 1.09 mg/dl and in normo-uricemic group it was 4.62 ± 0.76 mg/dl. Significant differences of the uric acid levels between the two groups were observed. In hyperuricemic group among 25 fetuses NBW fetuses were 5 (20%) and LBW fetuses were 18 (72%). In normo-uricemic group among 32 subjects NBW fetuses were 29 (90.62%) and LBW fetuses were 3 (9.38%). Significant difference of fetal birth weight status between the study groups was

observed. In the study it was also observed that LBW fetal outcome was 72% in hyperuricemic subjects whereas in normo-uricemic subjects it was 9.38%, which is very negligible in contrast to hyperuricemic group. D'Anna et al. 2000[16] and Feig et al. 2004[17] performed same type of study. They got significant relationship between hyperuricemia and LBW fetus. Redman et al. 1976[14] and Chesley, 1985[18] also saw a similar linear trend in patients of PE with hyperuricemia. This trend of increased uric acid with poor fetal outcome indicates that probably increased uric acid causes growth retardation, that the consequence is reflected as LBW. In this view it may be assumed that, for poor fetal outcome in PE, the main culprit may be hyperuricemic status associated with PE, in other words in PE, the incidence of poor fetal outcome increased as uric acid increases.

Among the 32 normo-uricemic subjects no incidence of stillbirth was observed but in hyperuricemic subjects it was 2 in 25 subjects. Although it is not significant but due to small sample size the probability of stillbirth in hyperuricemic PE cannot be neglected.

Conclusion

Hyperuricemia associated with PE is an important risk factor for poor fetal outcome. Significant increased number of LBW fetuses was observed in babies born to hyperuricemic pre-eclamptic mothers in comparison with babies born to normo-uricemic pre eclamptic mothers. There was 2 incidence of stillbirth in hyperuricemic pre-eclamptic mothers, which was not negligible.

It is assumed from the study that in PE, the incidence of poor fetal outcome increases as uric acid increases. So, serum uric acid estimation can play a good diagnostic measure in recognizing the severity of the disorders and also to take prior decision to make the delivery safe and hazardless both for mother and the fetus. Estimation of serum uric acid may be also considered in management of pre-eclamptic mothers, especially in lowering the rate of poor fetal outcome.

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