

Fetal Outcome in Pre-Eclamptic Women with High Serum Uric Acid Level

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Abstract

Background:

Pre-eclampsia is a major cause of morbidity and mortality for the woman and her child.

Objective:

To determine the fetal outcome in pre-eclamptic women with high uric acid

MATERIAL AND METHODS:

SETTING:

This descriptive case series study was carried out in the department of obstetrics and gynaecology wards of Liaquat University Hospital Hyderabad for six months from 1st March 2013 to 30 August 2013.

RESULTS:

This study was carried out on 130 preeclamptic women. In the present study 73 (56.0%) mothers had normal serum uric acid levels and 57 (44.0%) mothers had higher serum uric acid. There was significant difference of serum uric acid levels ($p < 0.0001$) between study groups. Among 57 patients who had hyperuricaemia, 54 (95.0%) babies had IUGR. Among 73 patients who had no hyperuricaemia, **Intrauterine growth restriction** was present in 46 (63.0%) babies. This difference was statistically significant (P-Value 0.02). Among 57 patients who had hyperuricaemia, 45 (78.94%) had alive babies, 1 (1.75%) had stillbirth and 11 (19.29%) had **Intrauterine death**. Among 73 patients who had no hyperuricaemia, 57 (78.0%) had alive babies, 2 (2.73%) patient had stillbirth and 14 (19.17%) had **Intrauterine death**. This difference was not statistically significant; $p = 0.89$.

CONCLUSION

High uric acid associated with PE is an important risk factor for poor fetal outcome.

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

INTRODUCTION

Pre-eclampsia is a syndrome that is defined usually as the onset of hypertension and proteinuria after 20 weeks of gestation in previously normotensive, nonproteinuric pregnant women.¹ It occurs in about 5-10% of all pregnancies and results in substantial maternal and neonatal morbidity and mortality.² A worldwide incidence of pre-eclampsia has been estimated 8,37,000 per year in developing countries. In Colombia 42% of

maternal death occurs.³ runs in families. Aprimigravida is 8 times more likely to develop pre-eclampsia if her sister had the condition and 4 times more likely if her mother was affected. It complicates 3% of women during first pregnancy. Multigravidas who had severe pre-eclampsia have 5-10% risk of recurrence and 15-20% risk of pre-eclampsia over all.⁴ Hyperuricemia is one of the characteristic findings in pre-eclampsia. In clinical practice, uric acid determination is considered to be a part of the work upon women with pre-eclampsia to monitor disease severity and aid in the management of the disease. Reduced uric acid clearance secondary to reduce glomerular filtration rate, increased absorption and decrease secretion may be the reason for elevated serum uric acid level in women with pre-eclampsia.⁵ Uric acid is used as a sensitive indicator of the severity of pre-eclampsia.

A study shows that preterm, IUD, IUGR, still birth, are 5.3 times higher in the hyperuricemic group as compared to low serum uric acid level.⁸ Studies shows that pre-eclampsia is responsible for 10-15% of maternal death.⁷ Adverse perinatal outcomes occurred in 45% of births in pre-eclamptic hyperuricemic patients.⁸

Hypertension in pregnancy is a significant management problem if associated with proteinuria, a multisystemic disease occurs as pre-eclampsia.⁹ Pre-eclampsia is a major cause of maternal morbidity and mortality world wide and causing 15% of all direct maternal death.¹⁰ Measurement of 24 hour urine protein is one of the most important test ordered in the investigation of renal disease. The collection of urine for 24 hours is boring, and errors may take place during the process. For this reason, the protein/creatinine ratio (P/C) in spot urine was developed as a diagnostic alternative.^{11,12} Spot urine is collected during the second urination of the morning, and the first 20-25ml are discarded After this, without disrupting urination, the middle urine is collected in the receptacle, and the last portion is also discarded.¹³ The potential error in determining proteins in a spot urine sample as a result of daily variation does not exceed the error in collecting a 24 hour urine sample.¹⁴ The wide spread use of 24 hours urine protein excretion measurement forced the researchers to find a simpler and quicker method to get the result. One of the simpler methods is use of spot single voided urine protein/creatinine ratio as an alternative to 24 hours urine collection. A number of papers are published on this subject in the western world but the data is relatively lacking in Pakistani population.^{15,18} In Pakistan maternal mortality due to pre-eclampsia and eclampsia is about 11.7%. It effects 2 to 8% of all pregnancies.¹⁸ and it is defined as blood pressure of 140/90 or higher after 20 week of gestation and urine albumin of more than +1 by dipstick test or chronic hypertension with new onset urine protein of more than +1 or greater by dipstick test.¹⁹

Objective of this study was to determine the fetal outcome in pre-eclamptic women with high uric acid

MATERIAL AND METHODS

Setting:

The study was carried out in the department of obstetrics and gynaecology of Liaquat University Hospital Hyderabad.

Duration of the study:

Six months from March 2013 to August 2013.

Study design:

Descriptive, case series.

Inclusion criteria:

Those pregnant women **with systolic blood pressure from 130 to 200 mmHg** and protein urea > 1 on drip stick or >300 mg/l in 24 hour urinary specimen with gestational age 32 weeks or more and serum uric acid level >6 mg/dl were included in this study.

Exclusion criteria:

Those pregnant women with glucose intolerance, renal disease, multiple pregnancy, congenitally abdominal fetus and use of drugs affecting uric acid levels were the excluded from the study.

DATA COLLECTION PROCEDURE:

130 pre-eclamptic women with serum uric acid level 6 mg/dl collected from all units of obstetrics and gynaecology, Liaquat University Hospital Hyderabad were included in this study based on inclusion criteria. Patients were carefully evaluated by detailed history, clinical examination pulse, BP, edema and obstetrical examination and investigation, serum uric were noted on a structured proforma birth, intrauterine growth restriction, apgar score and intrauterine death. These data were collected and entered into proforma. Women who fulfill the inclusion criteria and willing and admitted in obstetrics/Gynae wards were registered and included in study.

STATISTICAL ANALYSIS:

The data were entered and analyzed is statistical program SPSS version 16 Qualitative data (frequency and percentage) such as booking status. Parity, fetal outcome, hypertension, age (In groups) and mode of delivery were presented as n(%). Numerical parameters like gestational age, apgar score <7 and serum uric acid and levels were expressed as Mean \pm Standard Deviation. **Student t-test was applied to calculated p value.** Stratification was done with regard to serum uric acid level, maternal age, gestational age and parity to see the effect of these variables on outcome.

RESULTS

This study was conducted in the department of obstetrics and Gynaecology, Liaquat University Hospital (Tertiary care hospital) to determine the fetal outcome in pre-eclamptic women with high uric acid level in the department of Obstetrics and Gynaecology LUH Hyderabad and Jamshoro.

In this study out of 130 women, most of women i.e. 63(48.460%) were between 31 to 40 years of age, 26(20%) women were between 41 to 50 years of age, while 41(31.5%) women were below <30 years of age.

Women mean gestational age \pm SD was 34.0 ± 2.88 weeks, ranged from 32 to 42 weeks. Most of women i.e. 114(87.6%) had Gestational age from 34 to 40 weeks, 12(9.2%) women had the gestational age 40-42 weeks and only 4(3.2%) women had gestational age >40 weeks. Mean systolic blood pressure \pm SD was 160.23 ± 8.23 , ranged from 130

to 200 mmHg. Mean diastolic blood pressure + SD was 101.17 ± 7.762 , ranged from 130 to 200 mmHg.

Distribution of mean serum uric acid for pre-eclamptic mothers was $5.58 \pm \text{SD}$. In the present study 73(56.0%) mothers had normal serum uric acid levels (Non-hyperuricaemic) and 57 (44.0%) mothers had higher serum uric acid (Hyperuricemic). Mean serum uric acid concentration in hyperuricemic mothers (elevated) was 7.45 ± 0.89 mg/dl and in non-hyperuricemic mothers, it was 4.11 ± 1.0 mg/dl. There was significant difference of serum uric acid levels (<0.0001) between study groups.

Among 57 patients who had hyperuricaemia, 54(95.0%) babies had IUGR. Among 73 patients who had no hyperuricaemia, IUGR was present in 46(63.0%) babies. This difference was statistically significant (P-Value 0.02).

Among 57 patients who had hyperuricaemia, 45(78.94%) babies were admitted to NICU. Among 73 patients who had no hyperuricaemia 26(36%) babies were admitted to NICU. This difference was statistically significant (p value 0.01).

The mean birth weight of babies of hyperuricemic mothers was 7.35 ± 1.42 kg as opposed to non-hyperuricemic mothers in whom the mean birth weight of babies was 8.52 ± 0.55 kg; this difference was statistically significant, $p=0.03$.

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 7.45 ± 0.89 mg/dl and in normo-uricemic group it was 4.11 ± 1.0 mg/dl. Significant differences of the uric acid levels between the two groups were observed. In hyperuricemic group NBW fetuses were 10(17%) and LBW fetuses were 40 (70.1%). In normo-uricemic group, NBW fetuses were 58 (79.45%) and LBW fetuses were 7 (9.58%). Significant differences of fetal birth weight status between the study groups was observed. In the study it was also observed that LBW fetal outcome was 70.1% in hyperuricemic subjects whereas in normo-uricemic subjects it was 9.58%, which is very negligible in contrast to hyperuricemic group. There was significant difference of stillbirth ($p<0.05$) between hyperuricemic and normo-uricemic groups.

TABLE NO.2

**AGE DISTRIBUTION OF THE WOMEN (IN GROUPS)
(n= 130)**

Age groups	Number	Percentage
<30 years	41	31.5%
31-40 years	63	48.46%
>40 years	26	20.00%

TABLE NO.3
BOOKING STATUS OF THE WOMEN
(n=130)

Status	Number	Percentage
Booked	80	61.53%
Un-booked	50	38.46%

TABLE NO.4
PERIOD OF GESTATION OF THE WOMEN
(n=130)

Mean	34.0
Median	34
Mode	33
Standard Deviation	2.68
Range	32 to 42 weeks
Minimum	32
Maximum	42

TABLE NO.5
AGE DISTRIBUTION OF THE WOMEN (IN GROUPS)
(n=130)

Gestational Age in weeks	Number	Percentage
34-37	114	87.6%
37-40	12	9.2%
40-42	04	3.2%

TABLE NO.6
SYSTOLIC BLOOD PRESSURE
(n=130)

Mean	160.23
Median	150.0
Mode	150.0
Standard Deviation	8.23
Range	130 to 200
Minimum	130
Maximum	200

TABLE NO.7

**DIASTOLIC BLOOD PRESSURE
(n=130)**

Mean	101.17
Median	100.0
Mode	100.0
Standard Deviation	6.76
Range	90 to 120
Minimum	90
Maximum	120

TABLE NO.8

**DISTRIBUTION OF SERUM URIC ACID
(n=130)**

Mean	5.58
Median	5.65
Mode	4.90
Standard Deviation	1.93
Range	2.50-2.10
Minimum	2.50
Maximum	2.10

TABLE NO.9

**DISTRIBUTION OF SERUM URIC ACID LEVELS
(n=130)**

Serum uric acid level (mg/dl)	Mean \pm SD (Range)	Number	Percentage
Normal	4.11 \pm 1.0 (2.50-5.90)	73	56.0%
	7.45 \pm 0.89 (6.25-9.10)	57	44.0%

P value = <0.0001 (highly significant) calculated by student "t" test

TABLE NO.10
FETAL OUTCOME AMONG HYPERURICAEMIC VERSUS NON-HYPERURICAEMIC GROUPS

Fetal outcome	Hyperuricaemic group N=57	Non-Hyperuricaemic group n=73	P Value
IUGR	54 (95.0%)	46 (63.0%)	0.02
Intrauterine death	11 (19.29%)	14 (19.17%)	0.89
Still birth	02 (3.50%)	01 (1.3%)	0.01
Admission to NICU	40 (70.1%)	26 36%)	0.03
Birth Weight	1.52±1.42	2.15±0.43	<0.001*
Apgar Score	7.35±1.42	8.52±0.55	<0.001*
Low birth weight	40(70.1%)	07 (9.58%)	<0.001*
Normal birth weight	10(17.5%)	58 (79.45%)	<0.001*

*P value= <0.0001 (highly significant) calculated by student "t" test

DISCUSSION

Hypertensive disorders during pregnancy increase maternal and infant risks. The greatest impact is associated with the pregnancy specific syndrome, preeclampsia.²⁰ Preeclampsia conventionally diagnosed by the gestational onset of hypertension and proteinuria increases perinatal mortality 5-fold and kills 50,000 women yearly worldwide.²¹ Its management in the form of delivery to halt the progression of the pathophysiology, is responsible for 15% of preterm births in developed countries.²²

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. 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.

Among the various biochemical parameters fetal outcome of pregnant woman with raised blood uric acid is implicative.^{23,24}

Although low birth weight can be influenced by genetic factor, nutrition status, environmental effects. The relationship of high blood uric acid in pre-eclamptic women was also associated with low birth weight and still birth. In hyperuricemic subjects serum uric acid concentration was 7.45 ± 0.89 mg/dl and in normo-uricemic group it was 4.11 ± 1.0 mg/dl. Significant differences of the uric acid levels between the two groups were observed. In hyperuricemic group NBW fetuses were 10(17%) and LBW fetuses were 40(79.45%). In normo-uricemic group, NBW fetuses were 58 (79.45%) and LBW fetuses were 7 (9.58%). 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 70.1% in hyperuricemic subjects whereas in normo-uricemic subjects it was 9.58%,

which is very negligible in contrast to hyperuricemic group. D'Anna et al, 2000²⁵ and Feig et al. 2004²⁶ performed same type of study. They got significant relationship between hyperuricemia and LBW fetus. Redman et al. 1976¹⁴ and Chesley, 1985²⁷ 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 consequences 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

The average birth weight of patient with pre-eclampsia is 2.6 Kg in my study. In normotensive patient the average weight is 3 Kg. In August P. Helseth et al. Study the average weight for pre-eclampsia is 2.4 Kg and in normotensive is 3.0 Kg which is nearer to this study. This parameter supports this study.²⁸

CONCLUSION

High uric acid associated with PE is an important risk factor for poor fetal outcome. 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.

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