

ASSOCIATION OF SERUM URIC ACID AND SERUM LIPID PROFILE IN PRE- ECLAMPSIA- A HOSPITAL BASED CASE-CONTROL STUDY

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ARTICLE INFO

Received : 15 October, 2019

Accepted : 24 December, 2019

Published : 31 December, 2019

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ORA 141

DOI: <http://dx.doi.org/10.3126/bjhs.v4i3.27032>

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Citation

Rizal S, Joshi BR, Dhakal A, Sagtani RA. Association Of Serum Uric Acid And Serum Lipid Profile In Pre- Eclampsia- A Hospital Based Case-control Study. BJHS 2019;4 (3)10: 831-834.

ABSTRACT

Introduction

Pre-eclampsia, one of the most common medical complication in pregnancy results in considerable maternal and fetal morbidity and mortality. Endothelial dysfunction is a central feature of pre-eclampsia. Elevated serum uric acid level may serve as a marker for early diagnosis of the disease as well as a surrogate for clinical severity of the condition. High serum values of triglycerides, total cholesterol, low-density lipoprotein and low levels of high density lipoprotein are all significantly related to risk of developing preeclampsia.

Objective

To find out the association between serum uric acid level and lipid profile in pre-eclamptic women and compare it with the normal pregnant women.

Methodology

A case control study was conducted among 180 pregnant women (90 cases of pre-eclamptic women and 90 cases of age matched normal pregnant women) between 21-35 years who were admitted in the Gynaecology and Obstetrics ward of Nobel Medical College and Teaching Hospital, Biratnagar.

Blood pressure was measured. Serum from all the patients were analyzed for the following biochemical parameters: serum uric acid, triglyceride, total cholesterol, low density lipoprotein cholesterol (LDL-C) and high density lipoprotein cholesterol (HDL-C). The data were collected and entered in MS-Excel and analyzed using Statistical Package for Social Sciences (SPSS) ver. 16 software.

Result

Mean serum uric acid of pre-eclamptic women was higher than those of normal pregnant women which was found to be statistically significant with p value <0.001. Among the lipid parameters, serum triglyceride and total cholesterol was significantly higher in pre-eclamptic women whereas high density lipoprotein was significantly lower in pre-eclamptic. Also there was a positive co-relation between triglyceride and blood pressure and a negative co-relation between HDL-C in preeclamptic women.

Conclusion

Development of simple and inexpensive methods to predict and prevent pre-eclampsia in early stage is very important. Thus, our study concludes the utility of measurement of serum uric acid and lipid profile for screening patients at risk of developing pre-eclampsia.

KEYWORDS

Blood pressure, HDL-C, pre- eclampsia, triglyceride, uric acid



INTRODUCTION

Gestational hypertension is defined as a systolic blood pressure (SBP) of at least 140 mm Hg and/or a diastolic blood pressure (DBP) of at least 90 mm Hg on at least two occasions at least 6 hours apart after 20th week of gestation in women known to be normotensive before pregnancy and before 20th week of gestation.¹ Pre-eclampsia is primarily defined as gestational hypertension with proteinuria which is 300 mg or more in 24-hour. If 24-hour urine collection is not available, then proteinuria is defined as a concentration of at least 30 mg/dL in at least two random urine samples collected at least 6 hours apart.² Preeclampsia is one of the most common complication during pregnancy affecting 2-8% of all the pregnancies resulting in considerable maternal and fetal morbidity and mortality.^{3,4} It is believed to be due to suboptimal uteroplacental perfusion associated with maternal inflammatory response and maternal vascular endothelial dysfunction.⁴

Elevated serum uric acid is one of the most consistent and earliest detectable parameter of pre-eclampsia. It is found that the elevation in uric acid levels precedes the onset of hypertension and proteinuria which are considered as the clinical manifestation for diagnosis of pre-eclampsia.⁵ It is further hypothesized that an elevated concentration of uric acid in pre-eclamptic women is not simply a marker of disease severity but rather contributes directly to the pathogenesis of the disorder.⁶ Decreased renal clearance owing to decreased glomerular filtration rate, increased renal reabsorption and decreased tubular secretion, increased tissue break down and increased activity of the enzyme xanthine oxidase/dehydrogenase are the possible causes for elevated serum levels of uric acid in women with preeclampsia.^{7,8}

Maternal endothelial dysfunction is the classic hallmark of pre-eclampsia. The accumulation of markers of endothelial dysfunction in the endothelial cells is the result of increased level of circulating lipids.⁹ In normal pregnancy, there is maternal hyperlipidemia owing to fetal growth and development. High levels of atherogenic lipids i.e high total cholesterol (TC), triglyceride (TG) and low density lipoprotein cholesterol (LDL-C) and low levels of high density lipoprotein cholesterol (HDL-C) are all contributing factors for endothelial damage through oxidative stress mechanism in the arterial wall leading to pathophysiology of pre-eclampsia.¹⁰ Thus, lipid level assessment in early pregnancy may be a tool to detect women at risk of pre-eclampsia.

Thus, our study aims to assess serum uric acid level in pre-eclamptic women and compare it with normal pregnant women and evaluate the diagnostic utility of serum uric acid in pre-eclampsia. Our study also aims to compare the changes in lipid parameters in pre-eclamptic women and normal pregnant women.

METHODOLOGY

A case control study was conducted among 180 pregnant women (90 cases of pre-eclamptic women and 90 cases of

normal pregnant women) who were admitted in the Gynaecology and Obstetrics ward of Nobel Medical College and Teaching Hospital, Biratnagar. The study was conducted from 1st June, 2018 to 31st May, 2019. Ethical approval was taken from the Institutional Review Committee of Nobel Medical College. Informed consent was taken from each patient before data collection.

Diagnosed cases of pre-eclampsia (cases) and age matched normal pregnant women in the age group between 21-35 years were included in our study. Preeclampsia was diagnosed based on the "ACOG Task Force on Hypertension in Pregnancy 2013" as follows: Women known to be normotensive who developed a systolic BP \geq 140mm Hg or diastolic BP \geq 90mm Hg on two occasions at least 4 hours apart after the 20th week of gestation and proteinuria \geq 300mg/24 h urine collection or a protein/creatinine ratio \geq 0.3.¹¹ Women with previous history of hypertension or hypertension before 20th week of gestation were excluded from the study. Also women with history of Diabetes Mellitus, Renal Disease and other diseases known to alter the blood pressure were also excluded from the study.

Blood pressure was measured by sphygmomanometer cuff on both hands in sitting position and mean was taken and recorded.

Blood samples from all the patients were collected from ante-cubital vein after overnight fast. Blood was allowed to clot and serum was separated. Serum from all the patients were analyzed for the following biochemical parameters: serum uric acid, triglyceride, total cholesterol, LDL-C and HDL-C.

The data were collected and entered in MS-Excel and analyzed using Statistical Package for Social Sciences (SPSS) ver. 16 software. All the biochemical parameters were expressed as mean \pm standard deviation for each group. Biochemical parameters were compared using Student's unpaired t test. P < 0.05 was considered statistically significant.

RESULT

Table 1: Comparison of age, SBP, DBP and uric acid among cases and control. (n = 180)

Parameter	Normal Pregnant Women (Control) (Mean \pm SD)	Pre-eclamptic women (Cases) (Mean \pm SD)	Mean diff.	95% CI of mean diff.		P value
				Lower	Upper	
Age (in years)	27.19 \pm 3.88	27.53 \pm 5.23	-0.344	-1.70	1.01	0.617
SBP (mm/Hg)	106.93 \pm 9.87	151.13 \pm 9.28	-44.20	-47.02	-41.38	<0.001*
DBP (mm/Hg)	69.09 \pm 6.77	101.96 \pm 7.43	-32.86	-34.95	-30.77	<0.001*
Serum Uric Acid (mg/dl)	3.59 \pm 0.84	5.510 \pm 0.74	-1.91	-2.147	-1.67	<0.001*

*statistically significant.

In this study, the mean age of pregnant women of both the groups was around 27 years and thus, did not show statistical difference. In case of both systolic and diastolic blood pressure, the mean pressure was significantly higher among the pre-eclamptic women with mean difference of 44.2 mmHg and 32.8 mm Hg respectively. Similarly, the mean serum uric acid of pre-eclamptic women was higher



than the normal pregnant women which was found to be statistically significant with p value <0.001. Thus, high blood pressure and higher levels of serum uric acid is associated with pregnant women with pre eclampsia. (Table 1)

Table 2: Comparison of parameters of lipid profile among cases and control. (n = 180)

Parameter	Normal Pregnant Women (Control) (Mean ± SD)	Pre- eclamptic women (Cases) (Mean ± SD)	Mean Diff.	95% CI of mean diff.		P value
				Lower	Upper	
TG(mg/dl)	172.06 ± 39.29	210.46 ± 45.41	- 38.39	-50.88	-25.90	<0.001*
TC(mg/dl)	179.99 ± 32.16	277.97 ± 47.42	- 97.98	-109.90	-86.06	<0.001*
LDL-C (mg/dl)	111.02 ± 17.97	111.48 ± 19.12	- 0.46	- 5.92	4.99	0.867
HDL-C (mg/dl)	50.51 ± 4.02	44.47 ± 7.92	6.03	4.18	7.88	<0.001*

*statistically significant.

Table 2 shows that mean triglycerides and total cholesterol are significantly higher among the pre-eclamptic women with mean difference of 38.39 mg/dl and 97.98 mg/dl respectively. On the other hand, there is no significant difference in LDL cholesterol between both the groups. In case of HDL cholesterol, the mean levels are significantly higher among the normal pregnant women group with p value <0.001. Thus, higher serum triglycerides, high total cholesterol and low HDL levels are associated with pregnant women with pre eclampsia.

Table 3: Correlation of TG and HDL with SBP among women with pre - eclampsia. (n = 90)

Correlation of SBP with	Correlation coefficient (R)	P value
TG	+0.517	<0.001*
HDL	-0.391	<0.001*

*statistically significant.

The results showed that serum triglycerides was positively correlated with SBP i.e. the women with higher SBP had higher TG level. On the other hand, HDL was negatively correlated with SBP i.e. women with higher SBP had lower levels of HDL. Both these correlations were statistically significant with p value <0.001. (Table 3)

Table 4: Correlation of TG and HDL with DBP among women with pre - eclampsia. (n = 90)

Correlation of DBP with	Correlation coefficient (R)	P value
TG	+ 0.473	<0.001*
HDL	- 0.387	<0.001*

*statistically significant.

Similar to SBP, the results showed that serum triglycerides were positively correlated with DBP i.e. the women with higher DBP had higher TG level and lower HDL levels. Also, these correlations were statistically significant with p value <0.001. (Table 3)

DISCUSSION

Pre-eclampsia accounts for 10-15% of all the maternal deaths occurring worldwide. The most common reason for such high maternal and fetal morbidity and mortality is the unavailability of precise and specific test that can identify pregnant women at risk of developing pre-eclampsia.¹²

Thus, we attempted to find the association of serum uric acid along with serum lipid levels to diagnose pre-eclampsia.

In our study, the mean age group for pre-eclamptic women was 27.53 ± 5.23 years and those for control was 27.19 ± 3.88, which did not show any statistical significance.

The systolic and diastolic blood pressure was 151.13 ± 9.28 mm Hg and 101.96 ± 7.43 mm Hg respectively in the pre-eclamptic women (cases) whereas it was 106.93 ± 9.87 mm Hg and 69.01 ± 6.77 mm Hg respectively for normal pregnant women (control). The difference of blood pressure between the cases and control was statistically significant with p value <0.00. Our finding was consistent with the studies done by Asgharnia et.al¹³ and Bishoni et.al.⁸

Serum uric acid level was significantly higher in pre-eclamptic women (mean ± SD = 5.51 ± 0.74 mg/dl) in comparison to normal pregnant women (mean ± SD = 3.59 ± 0.84 mg/dl) (p<0.001). Our finding was consistent with the studies done by Sultana et.al,¹⁴ Asgharnia M et.al¹³ and Bishoni et.al.⁸ Elevated serum uric acid and its association with severity of pre-eclampsia has been reported since late 1800s.¹⁵ Studies suggests that hyperuricemia was present in 16% of women with gestational hypertension without proteinuria whereas it is present in 75% of women diagnosed with pre-eclampsia.⁶ Decreased renal clearance and increased renal reabsorption owing to decreased glomerular filtration rate,¹⁶ along with placental hypoxia and placental cell destruction, both being the source of purine for production of uric acid by xanthine oxidase.⁸ explains the presence of hyperuricemia in preeclampsia. Studies has shown that uric acid increases the blood pressure by increasing salt sensitivity and vascular smooth muscle proliferation.¹⁷ In initial phases of normal pregnancy, uric acid level decreases owing to uricosuric action of estrogen, expanded blood volume and increased GFR.⁶ Studies has shown that there is no significant difference in serum uric acid levels between gestational hypertension and normal pregnancy, suggesting increased uric acid to be a predictor of pre-eclampsia.^{18,19}

Among the lipid parameters, serum TG and serum TC was higher in pre- eclamptic women compared to normal pregnant women and the difference was statistically significant with p<0.001. Also serum HDL- C was significantly (p<0.001) lower in the pre-eclamptic women when compared to normal pregnant women whereas serum LDL-C did not show any statistical difference. This was consistent with many studies done in different part of the world.^{20,21} Alteration in lipid parameters are expected in normal pregnancy also but results from many meta-analysis suggest that women with pre-eclampsia experience greater changes in lipid metabolism than normotensive women.²² An abnormal lipid profile has a direct effect on vascular endothelial dysfunction as seen in pre-eclampsia.⁸ High levels of TG in pre-eclampsia is primarily due to hypoestrogenemia which leads to decreased expression of VLDL/apoE receptors resulting in reduced transport of VLDL to fetal compartment and so there is maternal hypertriglyceridemia owing to increased biosynthesis of endogenous TG, which is carried by VLDL.^{8,23} Among the lipid parameters, serum TG showed a positive correlation with both the systolic and diastolic blood pressure



which was statistically significant with $p < 0.001$. This was consistent with the studies done by A Siddiqui²⁴ and Ghaffar et.al.²⁵ indicating the implication of raised serum triglyceride levels in the pathogenesis of pre-eclampsia. Also serum HDL showed a negative correlation with both systolic and diastolic blood pressure and was statistically significant with $p < 0.001$. This finding was also consistent with the findings of the study done by A Siddiqui²⁴ and Ghaffar et.al.²⁵ Dyslipidemia mediated activation of endothelial cells leads to production of endothelia disturbing factors like lipid peroxides which are responsible for the pathologic changes in PIH.³ Thus, results of our study add to the existing evidence to support pathophysiological role of both dyslipidemia and hyperuricemia in the clinical manifestations of preeclampsia.

CONCLUSION

Serum uric acid levels are raised in pregnancies complicated by pre-eclampsia which may serve as a marker for early diagnosis. Maternal lipid levels are also altered in pre-eclampsia and showed a significant relation with the blood pressure. Thus, measurement of serum uric acid levels and lipid profile, which are simple, inexpensive and readily

available test can be evaluated to add to the diagnosis of pre-eclampsia and define the severity of pre-eclampsia.

LIMITATION OF THE STUDY

We just evaluated uric acid and lipid profile in pre-eclamptic women, but we could have attempted to evaluate many other biochemical parameters to show its association with pre-eclampsia.

ACKNOWLEDGEMENTS

We would like to express our sincere thanks to the Department of Obstetrics and Gynecology for their help in recruiting patients for data collection. This study would have never been possible without the co-operation of each of the patients. My sincere thanks to Dr. Shanti Subedi for guiding me in data collection.

CONFLICT OF INTEREST

None

FINANCIAL DISCLOSURE

None

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