

Association of hyperuricemia and dyslipidemia in primigravida with preeclampsia during third trimester of gestation at tertiary care hospital

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ABSTRACT

Introduction: It is still difficult to identify women who are more likely to develop preeclampsia, even after decades of research into the condition. Determining whether women are "at-risk" is a crucial goal because a marker that identified high-risk women would enable greater surveillance in secondary care, recruiting for studies of possible therapeutic drugs, accurate diagnosis, and prompt action when issues arise. Predicting preeclampsia in women with underlying medical disorders would also be beneficial for tailored therapy.

Objective: To determine the association of hyperuricemia and dyslipidemia with pre-eclampsia in primigravida.

Materials & Methods: A descriptive cross-sectional study was conducted in Chemical Pathology section, Sheikh Zayed Hospital, Rahim Yar Khan, from June 15, 2023, to December 16, 2023, on primigravida aged 18-35 years in their third trimester attending OPD and Indoor Gynecology Department of the hospital. Patients with already known diabetes, gestational diabetes mellitus, chronic hypertension, HBV, HIV, chronic obstructive pulmonary disease (COPD), using aspirin, corticosteroids, and antihypertensive medication were excluded. Lipid profile and uric acid were estimated in preeclampsia and normal pregnancy and results compared between the groups. SPSS 23 was used for data analysis and $p \leq 0.05$ was taken as statistically significant.

Results: Mean serum cholesterol in study subjects with preeclampsia was 260.97 ± 36.74 mg/dl, mean serum triglyceride was 248.88 ± 34.55 mg/dl, mean serum HDL-c was 37.57 ± 5.17 mg/dl, and mean LDL-c was 160.06 ± 27.85 mg/dl. The difference of mean serum cholesterol, triglyceride, HDL-c, LDL-c was found statistically significant with p value < 0.05 . Mean serum uric acid level was found higher in preeclampsia as compared to normal pregnancy with statistically significant difference ($p = 0.0001$).

Conclusion: Hyperuricemia and dyslipidemia were found as significant biochemical abnormalities in females with preeclampsia when compared to normal pregnancy.

Keywords: Pregnancy; Primigravidity; Preeclampsia; Lipidemia; Hyperlipidemia; Dyslipidemia; Uric Acid; Hyperuricemia; Inflammation.

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INTRODUCTION

Pre-eclampsia (PE) is a condition that affects about 3% of pregnancies globally. Symptoms usually appear in the late second or third trimester, usually after 32 weeks of gestation. With time, the definition of PE has evolved. Having a systolic pressure ≥ 140 mm Hg, diastolic blood pressure of 90 mm Hg or more on two separate occasions at least 4 hours apart was deemed as a hypertensive condition of pregnancy.^{1,2} Early diagnosis of this issue is necessary to avoid future difficulties for the mother and the fetus. Given that levels of renin, aldosterone, and angiotensin II are lower in afflicted pregnancies than in normal pregnancies, it appears that the hypertension associated with preeclampsia is not mediated by the renin-angiotensin-aldosterone system (RAAS).³

Elevated uric acid in preeclampsia may be caused by a number of causes, including accelerated tissue breakdown, altered renal function, increased enzymatic activity such as xanthine oxidase or dehydrogenase and acidosis. Preeclampsia is thought to be the result of a cascade involving aberrant maternal inflammatory response, endothelial cell activation or damage, along with a dysregulated hemodynamic milieu and dysregulated immunity.⁴

Dyslipidemia in the early stages of pregnancy is linked to a higher risk of PE. Lipid parameters such as phospholipid, triglycerides, low-density lipoprotein (LDL-C), high-density lipoprotein (HDL-C), and total cholesterol (TC) all gradually rise during a normal pregnancy. This increase begins in the 12th week of gestation and continues through the second and third trimesters. The need of fetal growth and physiological changes is met by this increase in lipids. The two main alterations in lipid metabolism during pregnancy are the buildup of maternal fat depots and hyperlipidemia.^{5,6}

The mother is in anabolic condition during the first trimester of pregnancy, and the lipid provides energy to both the developing fetus and the mother in the third trimester. Numerous data suggest that lipid profile abnormalities may be linked to an increased risk of pre-eclampsia.

Pre-eclamptic women had higher levels of Triglyceride, LDL-c, total cholesterol (TC), and very low-density lipoprotein (VLDL) lipid profiles than women with normal pregnancies; however, pre-eclamptic women have reduced levels of high-density lipoprotein (HDL).^{7,8}

The present study was conducted to determine the association of uric acid and dyslipidemia with preeclampsia in primigravida during third trimester. Early detection of dyslipidemia could be helpful in identifying and preventing the possible development of complication resulting in pre-eclampsia and its related morbidity.

MATERIALS & METHODS

A descriptive cross-sectional study was conducted in the Chemical Pathology section of the Pathology department at Sheikh Zayed Hospital, Rahim Yar Khan for a period of six months, from June 15, 2023, to December 16, 2023. Data were collected using consecutive sampling technique after receiving ethical approval from the institutional review board. Included subjects were primigravida women in their third trimester, aged 18–35 years who were attending the OPD and the indoor gynecology department of Sheikh Zayed Hospital, Rahim Yar Khan. Individuals who had a history of diabetes, gestational diabetes mellitus, chronic hypertension, HIV, HBV, chronic obstructive pulmonary disease (COPD), as well as women who were currently on antihypertensive drugs, corticosteroids, or aspirin were excluded.

Informed consent was taken from patients or their attendants. Data were collected from OPD and Inpatients of gynaecology department of Sheikh Zayed Hospital, Rahim Yar Khan. Blood specimens for lipid profile (cholesterol, triglycerides, LDL-C, HDL-C) and uric acid were collected in gel tubes. Lipid profile and uric acid were analyzed on fully automated chemistry

analyzer Atellica CH-930. Results were recorded on pre-designed Performa.

Data were collected on pre-designed Performa and was entered and analysed using SPSS23. Qualitative variables were presented in terms of frequency and percentages (pre-eclamptic and non-preeclamptic pregnant women). Mean and SD were calculated for quantitative variables (Age, Serum cholesterol, Serum triglycerides, Serum LDL-C, Serum HDL-C and Serum uric acid). Post-stratification Independent Sample T-test was applied. A $p \leq 0.05$ was considered as significant.

RESULTS

Of the total 90 pregnant females, 45(50%) were having preeclampsia while 45(50%) were having normal pregnancy. The distribution of mean lipid profile in study subjects with respect to presence and absence of preeclampsia is shown in Table 1. Mean total serum Cholesterol (mg/dl) in preeclampsia was 260.97 ± 36.74 while in non-preeclampsia was 229.48 ± 14.06 with statistically significant difference between two groups ($p=0.0001$). Mean serum triglyceride level (mg/dl) in preeclampsia was 248.88 ± 34.55 while in non-preeclampsia was 202.46 ± 18.94 ; the difference of mean triglyceride level was statistically significant between two groups ($p=0.0001$). Mean LDL-c level (mg/dl) in preeclampsia was 160.06 ± 27.85 while in non-preeclampsia it was 141.15 ± 18.81 with statistically significant difference between the groups ($p=0.0003$). Mean HDL-c (mg/dl) in preeclampsia was 37.57 ± 5.17 while in non-preeclampsia was 42.15 ± 6.67 with statistically significant difference between two groups ($p=0.0005$). Mean serum uric acid level (mg/dl) in preeclampsia was 8.01 ± 0.97 while in normal pregnant females was 4.84 ± 1.53 with statistically significant difference between two groups ($p=0.0001$).

Table 1: Distribution of lipid profile and serum uric acid level with respect to Preeclampsia and Normal Pregnancy (n=90).

Lipid Profile (mg/dL)	Pregnancy Groups (n=45 each)		p value
	Preeclampsia	Normal Pregnancy	
Total Cholesterol	Preeclampsia	260.97 ± 36.74	0.0001
	Normal Pregnancy	229.48 ± 14.06	
Triglyceride	Preeclampsia	248.88 ± 34.55	0.0001
	Normal Pregnancy	202.46 ± 18.94	
LDL-c	Preeclampsia	160.06 ± 27.85	0.0003
	Normal Pregnancy	141.15 ± 18.81	
HDL-c	Preeclampsia	37.57 ± 5.17	0.0005
	Normal Pregnancy	42.15 ± 6.67	
Serum uric acid	Preeclampsia	8.01 ± 0.97	0.0001
	Normal Pregnancy	4.84 ± 1.53	

The distribution of mean lipid profile in preeclampsia and non-preeclampsia with respect to age subgroups is shown in Table 2. Mean total cholesterol (mg/dl) in age subgroup 18-26 years in preeclampsia was 256.55 ± 31.70 while in non-preeclampsia was 227.34 ± 13.10 with statistically significant difference between the groups ($p=0.0001$). In age subgroup 27-35 years preeclampsia, mean Cholesterol (mg/dl) was 278.66 ± 48.38 while in non-preeclampsia was 241.14 ± 12.26 with no statistically significant difference between subgroups ($p=0.0667$). Mean serum triglyceride level (mg/dl) in age

subgroup with respect to presence and absence of preeclampsia was found statistically significant ($p=0.0001$). Mean serum LDL-c level in age subgroup 18-26 years with respect to presence and absence of preeclampsia was found statistically significant with ($p=0.0003$) while no significant difference of mean serum LDL-c level was found in age subgroup 27-35 years with respect to presence and absence of preeclampsia with ($p=0.1883$). Mean serum HDL-c level in age subgroups with respect to presence and absence of preeclampsia was found statistically significant ($p=0.0166$ and $p=0.0029$ respectively).

Table 2: Distribution of Lipid profile (Total Cholesterol, Triglyceride, LDL-c and HDL-c) and mean serum uric acid level in Preeclampsia and Normal Pregnancy with respect to age groups (n=90).

Lipid Profile (mg/dL)	Age Subgroups (Years)	Preeclampsia	Normal Pregnancy	p value
Total Cholesterol	18 - 26	256.55 ± 31.70	227.34 ± 13.10	0.0001
	27 - 35	278.66 ± 48.38	241.14 ± 12.26	0.0667
Triglyceride	18 - 26	243.80 ± 35.25	201.73 ± 19.75	0.0001
	27 - 35	269.22 ± 21.98	206.42 ± 10.96	0.0001
LDL-c	18 - 26	159.94 ± 29.72	138.00 ± 18.20	0.0003
	27 - 35	160.55 ± 16.06	151.00 ± 9.70	0.1883
HDL-c	18 - 26	38.72 ± 4.67	42.15 ± 7.05	0.0166
	27 - 35	33.00 ± 4.52	40.42 ± 3.45	0.0029
Serum Uric acid	18 - 26	07.99 ± 1.00	04.97 ± 1.49	0.0001
	27 - 35	08.12 ± 0.76	04.17 ± 1.44	0.0001

DISCUSSION

In the present study, association of dyslipidemia and uric acid has been evaluated in primigravida with respect to presence and absence of preeclampsia. Mean serum cholesterol level (mg/dl), mean serum triglyceride level (mg/dl), mean serum LDL-c and mean HDL-c level showed statistically significant difference with respect to presence and absence of preeclampsia with p value <0.05 (Table 1). The association has been investigated between dyslipidemia and preeclampsia with respect to age showed that the difference of mean level of serum cholesterol was found statistically significant with P value <0.05 in subgroup 18-26 years while non-significant in subgroup 27-35 years with p value >0.05 as shown in Table 2. On the basis of our study, the mean serum triglyceride level with respect to age subgroups was found statistically significant in subgroup 18-26 years with p value <0.05 while non-significant in subgroup 27-35 years with p value >0.05 as shown in Table 2. Mean serum LDL-c level in age subgroup 18-26years with respect to presence and absence of preeclampsia was found statistically significant with p value 0.0003 while no significant difference of mean serum LDL-c level was found in age subgroup 27-35years with respect to presence and absence of preeclampsia with p value 0.1883 (Table 2). Mean serum HDL-c level in age subgroups with respect to presence and absence of preeclampsia was found statistically significant with p values 0.0166 and 0.0029 respectively (Table 2).

Increased maternal triglyceride levels have been linked to pre-existing hyperlipidemia and are thought to have a role in the pathophysiology of preeclampsia.⁹ These results are in line with those of our investigation, which suggests that there is a substantial difference in blood triglyceride levels between preeclampsia and a normal pregnancy. Additionally, a recent study revealed a significant association between preeclampsia and high maternal serum lipid levels.¹⁰ Furthermore, compared to normal pregnant women, preeclamptic women had low levels of high-density lipoprotein (HDL) (P=0.0005). On the other hand, elevated TG and decreased HDL have led to the development of cardiovascular complications in pregnancy. Conversely, in preeclamptic women, insulin resistance may result in a decrease in HDL. Nonetheless, the current study's findings of higher LDL and lower HDL in preeclamptic women may be regarded as a risk factor for the development of atherosclerosis.¹¹

The underlying dysregulation that causes preeclampsia has been linked to a number of atherogenic risk factors, including decreased HDL-C (high-density lipoprotein cholesterol) and raised LDL-C and blood triglycerides.¹²⁻¹⁶ The findings of our study are suggestive of dyslipidemia with high serum cholesterol, high triglyceride, high LDL-c and low HDL-c with statistically significant difference between preeclampsia and normal pregnancy.

Owing to the pathophysiologic similarities between adult cardiovascular disease and preeclampsia, there is growing interest in assessing the use of lipid-modifying medications for the prevention and treatment of preeclampsia. Residual confounding factors, such as those resulting from medical comorbidities, have hampered previous observational investigations of lipids and preeclampsia risk.¹⁷⁻¹⁹ A review by Wojcik-Baszko D et al²⁰ demonstrates the potential role of lipid imbalance in the pathophysiology of preeclampsia. A recent lipidomics study has been examined to identify lipid parameters present in the blood, umbilical cord arteries and placenta of preeclamptic women. Hypertension with proteinuria or hypertension and end-organ failure with or without proteinuria appear in the second part of pregnancy as a new sign of preeclampsia, a multisystem, progressive disease. Presently one of the top three causes of maternal morbidity and death, the disorder affects about 4.6 percent of pregnancies globally. Therefore, it is imperative to develop broadly applicable, cost-effective diagnostic techniques that would allow for the early detection of high-risk women and facilitate close observation, focused preventive intervention, and treatment. The ultimate long-term goal is to avoid maternal deaths from preeclampsia earlier.²⁰

Mejia et al²¹ conducted a meta-analysis and demonstrated the role of hyperuricemia as a risk for developing preeclampsia. In order to rule out reverse causality, a meta-analysis and systematic review of cohort studies evaluating uric acid less than 20 weeks of gestation were also carried out. Pre-eclampsia was positively correlated with high uric acid levels in a linear fashion. By increasing uric acid levels, the odds ratio (adjusted) in pre-eclampsia was 1.21 (95% Confidence interval 1.11–1.33). There were no discernible variations in the strength of the correlation between early and late pre-eclampsia. Studies conducted in pregnant females with preeclampsia at or before 20 weeks of

gestation showed odds ratio of uric acid in pre-eclampsia as 1.46 (95% confidence interval 1.22-1.75. Levels of maternal uric acid are linked to a higher risk of preeclampsia.²¹

A study conducted by Hosier H et al²² found that raised HDL-c is associated with reduced risk of preeclampsia, findings consistent with our study. Dyslipidemia is considered as a component along the pathway of developing preeclampsia.^{23,24} A study conducted by Melekoglu et al²⁵ demonstrated that pregnant women with preeclampsia had high serum total cholesterol and high triglyceride level with low HDL-c level. These findings are consistent with our study findings, however some other studies showed conflicting results.²⁶ Corominas A et al²⁷ discussed in their study that uric acid level increased significantly after twenty weeks of gestation in females who develop preeclampsia before 34 weeks of gestation. A review study conducted by Pecoraro et al,²⁸ found no strong evidence of measuring serum uric acid level to predict maternal as well as fetal adverse outcome.

CONCLUSION

A state of hyperuricemia and dyslipidemia exists in females with pre-eclampsia when compared to normal pregnancies. Early detection of these biochemical abnormalities may identify and prevent the possible development of pre-eclampsia and its related morbidity.

LIMITATIONS

Our study had certain limitations. It was a single centered study. Results were not compared with non-pregnant females.

RECOMMENDATIONS

Samples should be taken serially at regular intervals in third trimester and further research is warranted to compare the results of lipid profile and mean serum uric acid level in non-pregnant females in the same age group to evaluate the effect of pregnancy in causing these derangements such as dyslipidemia and hyperuricemia.

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