Assessment of Lipoprotein (a) and Lipid Profile Pattern in patients of Pre-Eclampsia

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Abstract

Introduction: Preeclampsia is a hypertensive disorder of pregnancy characterized by endothelial dysfunction. The present study was planned to assess and compare the levels of serum Lipoprotein (a) and lipid profile in preeclampsia and normal pregnant women and to determine the association of Lp (a) with severity of the disease.

Materials and Method: The study comprised of 60 preeclamptic women and 30 normal pregnant women in third trimester of pregnancy. The serum levels of lipoprotein (a) [Lp (a)], triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and very low density lipoprotein (VLDL) were determined.

Results: A significant alteration in Lp (a) and lipid profile parameters was observed in preeclamptic patients. Serum Lp (a), TG and VLDL were significantly increased while HDL was significantly decreased in preeclamptic group compared to normal pregnant women. Positive correlation was found between serum Lp (a) and blood pressure in preeclampsia patients.

Conclusion: The present study demonstrates a dyslipidemic profile in preeclamptic patients. These findings are significant in understanding the pathologic processes of preeclampsia and may help in developing strategies for prevention and early diagnosis of the disorder.

Keywords: Pre-eclampsia, Dyslipidemia, Lipid profile, Lipoprotein (a)

Introduction

Preeclampsia is a hypertensive disorder of pregnancy. Its incidence is about 7-10% of all the pregnancies.[1] It is a progressive, multisystem disorder associated with hypertension (Systolic /diastolic blood pressure ≥ 140/90 mmHg), proteinuria ≥ 300mg /24 hour or 1+ dipstick response induced by pregnancy after 20th week. Without intervention, pre-eclampsia progresses to eclampsia which is characterized by malignant hypertension and epileptiform convulsions requiring termination of pregnancy.[2] Pre-eclampsia and eclampsia are associated with various fetal complications like intrauterine growth retardation, death and prematurity with attendant complications where as mother is at risk of renal failure, pulmonary edema, stroke and death.[3]

The mediator of this disorder of preeclampsia is the abnormal placental products that reach the maternal circulation and trigger endothelial dysfunction. This evokes various cardiovascular complications like vasospasm, increased endothelial permeability and activation of thrombogenic mechanisms. These features contribute to the early events of atherosclerosis. There are various predisposing factors for preeclampsia such as chronic hypertension, diabetes or obesity which contributes to the intense vascular reactivity seen in these patients.[4]

Women with preeclampsia have shown peculiar vascular lesions at the placental implantation site which simulate to those found in patients of atherosclerosis. These lesions are characterized by formation of fibrofatty plaque surrounded by foam cells.[4] These microscopic lesions mimic to those found in atherosclerosis in general population.

Although much research has taken place into mechanism of pre-eclampsia, its exact pathogenesis still remains a mystery. There is no single biomarker that can be used for early prediction of this disorder, delaying the implication of preventive and therapeutic strategies before irreparable damage occurs.[3]

Abnormalities in lipoprotein pattern are considered as one of the predisposing factor for Pre-eclampsia.[3] Hypertension and proteinuria in Pre-eclampsia is mainly attributed to the disturbed lipoprotein metabolism. In view of the above findings it is postulated that alteration of lipid metabolism may play a key role in the development of symptoms of Pre-eclampsia.[3] Lipoprotein (a) [Lp (a)] is a heterogeneous macromolecule that consists of a glycoprotein apolipoprotein (a) molecule, bound by a sulfhydryl link to the apolipoprotein B-100 moiety of low density lipoprotein (LDL) particle.[5] The structure of lipoprotein (a) is similar to plasminogen and tissue plasminogen activator. It competes with plasminogen for its binding site, leading to reduced fibrinolysis and thereby thrombogenesis. Concentration of Lp (a) is increased in pre-eclampsia and correlates with severity of disease. Its levels may reflect the underlying pathogenic process and contribute to the adverse pregnancy outcome.[6]

In preeclampsia, characteristic pathological lesions seen in the placenta are villus necrosis, fibrin deposits and acute atherosis.[7] Acute atherosis of placenta has been compared to the vascular lesion of atherosclerosis. Atheroma have been observed in uterine spiral arteries in normal pregnancies as well as in preeclamptic pregnancies, although in preeclampsia it is much more common and widespread, especially in the decidual segments.[8] Various epidemiologic studies have identified increased Lp (a) as a risk factor for coronary thrombosis, atherosclerosis and cerebrovascular diseases. The similar pathological lesions found in preeclampsia and atherosclerosis suggests that a common pathway is operative in pathogenesis of these disorders.[7]

In this background of increased Lp (a) being a potential risk factor for atherosclerotic cardio-vascular diseases, the significance of elevated Lp (a) in the preeclampsia needs to be evaluated.[6]

Aims and Objectives
1. We designed the present study to compare the alteration in lipid profile [Total Cholesterol (TC), Triglycerides (TG), High Density Lipoprotein (HDL) Cholesterol, Low Density Lipoprotein (LDL) Cholesterol and Very Low Density Lipoprotein (VLDL) Cholesterol] and Lp (a) among preeclamptic women and normal pregnant women.
2. Secondary objective of the study was to find out the correlation between serum Lipoprotein (a) and Systolic / Diastolic blood pressure.

Materials and Method
In the present Cross Sectional Study, which was conducted in Government Medical College and Hospital Aurangabad, Maharashtra, 60 pregnant women were selected as cases after confirmed diagnosis of preeclampsia and 30 normal healthy pregnant women as controls. The institutional ethical committee for clinical research approved the study protocol. Written Informed consent was taken from the study participants.

Preeclampsia was diagnosed according to the criteria proposed by American College of Obstetrics & Gynecologist,[6] i.e. systolic blood pressure ≥ 140 mmHg or a rise of 30 mmHg and diastolic blood pressure ≥ 90 mmHg or a rise of 15 mmHg (manifested on two occasion 6 hrs apart) & proteinuria ≥ 300 mg in 24 hour urine samples (manifested on two occasion 6 hrs apart). The cases and controls were matched for

maternal age, gestational age and body mass index (BMI). Preeclampsia is of two degree:[9] Mild - diastolic BP < 110 mmHg and Severe - diastolic BP > 110 mmHg.
We divided the subjects into following 3 groups:
Group I: 30 Normal pregnant women (controls)
Group II: 30 pregnant women with mild pre-eclampsia (cases)
Group III: 30 pregnant women with severe pre-eclampsia (cases)

Cases included were from age group 20-30 years, primigravida with gestational age 24 weeks to term. While women with pre-existing hypertension, cardiovascular disease, renal diseases, diabetes mellitus, thyroid disorders, obesity, smoking or drug addiction were excluded from the study. Fasting blood samples were collected from all participants and analyzed for triglycerides, total cholesterol, LDL, HDL and VLDL. Levels of Lp (a) were determined by immunoturbidometric assay method.[6] Urine samples were collected and urinary protein that is proteinuria is detected by dipstick method.

Statistical Analysis: The results were analyzed by Graphpad prism software, version 5. The data were expressed as mean ± standard deviation (SD). Differences in demographic characteristics and biochemical parameters were statistically analyzed using one way ANOVA test. Pearson's correlation was used to study the correlation among the parameters (r value). P value < 0.05 was considered statistically significant.

Results
A description of the demographic characteristics of the study and the control groups is shown in Table 1. The systolic and diastolic blood pressure were significantly increased (P < 0.05) in cases as compared to normal controls.

Patients of preeclampsia had significantly increased levels of Lp(a), triglycerides and VLDL when compared with controls. HDL level was significantly decreased in cases than controls. (P < 0.05) (Table 2)

We also found a significant positive correlation between serum lipoprotein (a) and blood pressure. (Table 3)

We analyzed urine samples of the patients for proteinuria by the dipstick method. Mild preeclampsia patients showed 1+ or 2+ dipstick responses while severe preeclampsia patients showed 3+ or 4+ dipstick responses.

Table 1: Comparison of Demographic Characteristics in Studied Groups: (One Way ANOVA Test)

Sr. No.	Clinical parameters	Normal Pregnancy	Mild Pre-eclampsia	Severe Pre-eclampsia	'P' value
1.	Age (years)	24.80 ± 4.7	24.80 ± 3.9	25.0 ± 4.5	> 0.05
2.	BMI (Kg/m^2)	25.75 ± 2.48	26.76 ± 3.31	24.61 ± 3.03	> 0.05
3.	Systolic BP (mmHg)	117.13 ± 8.66	152.62 ± 7.48	176.39 ± 10.63	< 0.05*
4.	Diastolic BP (mmHg)	78.8 ± 6.29	98.1 ± 4.51	118.53 ± 6.52	< 0.05*

Table 2: Comparison of Biochemical Parameters in Studied Groups: (One Way ANOVA Test)

Sr. No.	Biochemical parameters	Normal Pregnancy	Mild Pre-eclampsia	Severe Pre-eclampsia	'P' value
1.	Lp (a) (mg %)	21.40 ± 5.89	42.58 ± 6.27	68.87 ± 5.74	< 0.001*
2.	TG (mg %)	126.30 ± 16.2	192.0 ± 25.01	250.0 ± 21.8	< 0.001*
3.	VLDL (mg %)	28.13 ± 8.42	42.15 ± 12.60	57.8 ± 11.20	< 0.001*
4.	TC (mg %)	174.30 ± 20.20	172.0 ± 17.40	180 ± 13.53	> 0.4
5.	HDL (mg %)	51.4 ± 9.7	40.2 ± 5.82	30.3 ± 3.24	< 0.05*
6.	LDL (mg %)	123.2 ± 16.4	133.8 ± 13.3	127.8 ± 16.9	> 0.1

Table 3: Correlation between Lp (a) and Systolic / Diastolic blood pressure: (Pearson's Correlation)

Group	Biochemical Parameters		'P' value
		Systolic BP	Diastolic BP	
Normal Pregnancy	Lp (a)	0.22	0.18	-
Mild Pre-eclampsia	Lp (a)	0.46	0.52	< 0.01*
Severe Pre-eclampsia	Lp (a)	0.57	0.63	< 0.01*

Discussion

Preeclampsia is one of the leading causes of maternal and fetal morbidity and mortality. Classically, the condition presents with new-onset hypertension and proteinuria after 20 weeks of gestation. In developing countries where access to healthcare is limited, it is responsible for about 60,000 maternal deaths worldwide per year.[4] Endothelial dysfunction has been reported as an important biologic feature in women with preeclampsia.[1]

The preeclamptic patients in our study showed dyslipidemia, characterized by high levels of TG and VLDL and decreased HDL. In preeclampsia, there is increase in hepatic lipase and decrease in lipoprotein lipase activities, resulting in increased serum TG and VLDL levels.[2] High triglyceride levels increase the risk of placental vascular disorders, which trigger endothelial dysfunction, atherosclerosis and thrombosis. The development of atherosclerosis in the placental spiral arteries of preeclamptic women indicates that dyslipidemia is involved in this disorder. This also indicates that a common pathophysiological mechanism is operative between the endothelial lesions of preeclampsia and atherosclerosis.[4]

Preeclampsia affects the function of various organs involved in lipoprotein metabolism. Development of vascular endothelial lesions found in the placenta of preeclampsia and lesions of atherosclerotic plaque share a common pathophysiological pathway in which lipoproteins sequestered from plasma play an important role. Besides dyslipidemia, Lp (a) is the proposed cytotoxic factor that damages endothelial cells.[6] Lp (a) is an acute phase reactant and it is elevated in response to widespread inflammatory endothelial cell damage seen in preeclampsia. Lp (a) is also involved in the transport of cholesterol for deposition at the site of endothelial dysfunction.[10] Lp (a) traverses the vascular endothelium, interacts with extracellular matrix proteins like glycosaminoglycans, proteoglycans and gets incorporated into the intima of the arteries. This incites an inflammatory response with foam cell formation. Lp (a) binds to tissue plasminogen activator and fibrinogen, inhibits fibrinolysis and promotes thrombosis. Pregnancy is a state of hypercoagulability and impaired fibrinolysis. These changes are aggravated in preeclampsia. The presence of fibrin deposits in preeclampsia suggests that intravascular coagulation plays an important role in the etiopathogenesis of this pregnancy specific disorder.[6]

We found a strong positive correlation between serum lipoprotein (a) and systolic and diastolic blood pressure in this study. This suggests that serum Lp (a) may be involved in the pathogenesis of preeclampsia. So, increased serum Lp (a) is linked with the severity of the disease.[11] Findings in our study suggest that estimation of Lp (a) in preeclampsia along with other lipoproteins helps in the better understanding of pathophysiology of this disorder.[6] Studies conducted by Vibha C et al,[6] Saila Parvin et al,[11] B Demiret et al[15] showed increased serum Lp (a) in preeclamptic women as found in our study. The Dyslipidemia documented in our study is also reported by many researchers worldwide.[2,3,13,14] They suggested that lipid profile assessment between 24 to 32 weeks of gestation can be used for the early prediction of preeclampsia.[12]

To reduce the healthcare burden associated with preeclampsia and to implement preventive measures, early disease diagnosis is very important. Dyslipidemia and raised blood pressure before conception are the predisposing factors for this disorder. Such women should be motivated for regular health check-up by their obstetrician.[12] Better understanding of abnormal lipoprotein pattern in preeclampsia and its association with endothelial dysfunction is crucial from a public health perspective.[4]

From results of our study, we can hypothesize that preeclamptic lesions may predispose these women to adverse cardiovascular complications later on in their

life. Elevated levels of serum Lp (a) has atherogenic potential and may result in adverse cardiovascular outcome. Further studies are needed to establish its usefulness in assessing future cardiovascular risk in preeclampsia patients. These women should be counseled regarding possible health hazards and motivated to adopt healthy lifestyles and to seek periodic checkups, in order to detect cardiovascular disease in its early stages, before irreparable damage or even death ensues.

Conclusion

In our study, increased serum Lp(a) level and lipid profile abnormalities (raised TG & VLDL, decreased HDL) correlating with blood pressure have been observed among preeclamptic women. Early detection of abnormalities in these parameters may aid in early detection and better management of preeclampsia, which is important to improve the maternal and fetal outcome in these cases.

Study Limitation

This research was conducted only on a small size of population.

References

1. Ekambaram Padmini, Munuswamy Usha Rani. Lipid Profile Alterations and Oxidative Stress in Patients with Preeclampsia: Role of Black Tea Extract on Disease Management. Turk J Med Sci 2011;41(5):761-768.
2. Pradnya Phalak, Mona Tilak. Study of Lipid Profile in Pre-Eclampsia. Indian Journal of Basic & Applied Medical Research December 2012;2(5):405-409.
3. NAF Islam, MAR Chowdhury, GM Kibria, S Akhter. Study of Serum Lipid Profile in Pre-Eclampsia and Eclampsia. Faridpur Med. Coll. J. 2010;5(2):56-59.
4. Lima VJ, Andrade CR, Ruschi G, Sass N. Serum Lipid Levels in Pregnancies Complicated by Preeclampsia. Sao Paulo Med J. 2011;129(2):73-76.
5. Stefan Kiechl, Johann Willeit. The Mysteries of Lipoprotein (a) and Cardiovascular Disease Revisited. Journal of the American College of Cardiology. May 2010;55(19):2168–70.
6. Vibha. C, C.S. Muralidhara Krishna, K.L. Mahadevappa. Lipids & Lipoprotein (a) [Lp(a)] In Pregnancy Induced Hypertension. International Journal of Basic Medical Science. July 2011;2(2):73-77.
7. Murat Yasar Isildak, Sembol Turkmen Yildirmak, Serkan Dogan, Mustafa Cakmak, Ekrem Ozakin. Serum Homocysteine and Lipoprotein(a) Levels in Preeclamptic Pregnants. Trakya Univ Tip Fak Derg. 2009;26(3):208-213.
8. MG van Pampus, MMW Koopman, H Wolf, HR Buller, MH Prins, A van den Ende. Lipoprotein (a) Concentrations in Patients with a History of Severe Preeclampsia; A Case Control Study. Thrombosis and Haemostasis 1999;82:10-13.
9. Uzma Iftikhar, Azhar Iqbal, Shazia Shakoor. Relationship between Leptin and Lipids during Pre-Eclampsia. J Pak Med Assoc. June 2010;60(6):432-435.
10. Angela E. Fanshawe, Michael Ibrahim. The Current Status of Lipoprotein (a) in Pregnancy: A Literature Review. Journal of Cardiology. 2013;61:99–106.
11. Saila Parvin, Latifa Samsuddin, Ahammed Ali, Shafiqul Alam Chowdhury, Ibrahim Siddique. Lipoprotein (a) Level in Pre-Eclampsia Patients. Bangladesh Med Res Counc Bull. 2010;36:97-99.
12. Musleh Uddin Kalar, Nabila Kalar, Farah Mansoor, Abdul Rehman Malik, Todd Lessley, Susanne Kreimer et al. Preeclampsia and Lipid Levels – A Case Control Study. International Journal of Collaborative Research on Internal Medicine & Public Health. 2012;4(10):1738-1745.
13. Gohil J. T., Patel P. K., Gupta Priyanka. Estimation of Lipid Profile in Subjects of Preeclampsia. The Journal of Obstetrics and Gynecology of India. July–August 2011;61(4):399–403.
14. Jayanta De, Ananda Kumar Mukhopadhyay, Pradip Kumar Saha. Study of Serum Lipid Profile in Pregnancy Induced Hypertension. Indian Journal of Clinical Biochemistry. 2006;21(2):165-168.
15. B Demir, S Demir, Y Atamer, S Guven, A Atamer, Y Kocyigit et al. Serum Levels of Lipids, Lipoproteins and Paraoxonase Activity in Pre-eclampsia. The Journal of International Medical Research. 2011;39:1427-1431.