

PRE-ECLAMPSIA AND LIPID PROFILE

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ABSTRACT

Objectives: The present study was designed to evaluate the role of lipid profile alteration in the development of Pre-eclampsia.

Methodology: We selected 32 pregnant women, 16 healthy pregnant women (mean age 25.56±3.68) as normal and 16 already diagnosed preeclamptic women (mean age 24.65±4.25) as study group. Serum lipid profile (total lipids, cholesterol, triglycerides, HDL-cholesterol and LDL-cholesterol) of thirty two women with Pre-eclampsia (n=16), normotensive women (n=16) were monitored.

Results: The serum triglyceride concentrations increased significantly (232.18±106.41 vs. 113.12±21.3, P<0.01) while Serum HDL-cholesterol concentrations decreased significantly (39.75±11.99 vs. 51.18±06.09, P<0.01) in preeclamptic group as compared to normal pregnant women.

Conclusion: Lipid metabolism plays a key role in the pathophysiology of Pre-eclampsia. Increased triglycerides levels along with decreased HDL-cholesterol levels and delayed triglycerides clearance and high blood pressure are associated with development of preeclampsia.

KEY WORDS: Preeclampsia, High Density Lipoproteins, Triglycerides, Low Density Lipoproteins.

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INTRODUCTION

Pre-eclampsia, / eclampsia is one of the most common complications of pregnancy. It is a cause of high morbidity for both mother and fetus, especially in developing countries.¹ Pre-eclampsia is characterized by hypertension, proteinuria, and edema. Without intervention, Pre-eclampsia progresses to eclampsia, which is characterized by malignant hypertension and epileptiform convulsions requiring emergency caesarian section.² The prevalence, com-

plications as well as correlation of maternal and fetal outcome in a community of Pakistani women, showed high incidence of pre-eclampsia, 19%.³ Pre-eclampsia most commonly occurs during the last trimester of pregnancy when it arises in the early 2nd trimester 14-20 weeks.³ The risk of developing pre-eclampsia appears to be greater in women who have family history of essential hypertension, and there may also be a relationship between risk of pre-eclampsia and the metabolic syndrome.² Pre-eclampsia is associated with substantial risks. For the fetus, these include intrauterine growth restriction, death and prematurity with attendant complications where as the mother is at risk of seizures (eclampsia), renal failure, pulmonary edema, stroke, and death.⁴ Pre-eclampsia is a syndrome, which affects virtually all maternal organ systems.⁵ Despite considerable research, the cause or causes of pre-eclampsia remain unclear and there are no clinically useful screening tests to identify women in whom it will develop.⁴ Early pregnancy dyslipidemia is associated with an increased risk of Pre-eclampsia.⁵ Women with a history

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of pre-eclampsia have significant differences in lipid parameters and an increased susceptibility to lipoprotein oxidation when compared with women who had normal pregnancy.⁶ Disorders of lipoprotein metabolism are reported to be a major cause of hypertension and proteinuria in Pre-eclampsia.⁶

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. The present study was designed to investigate the alteration in lipid profile (Cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol and total lipids) in normal and preeclamptic women.

PATIENTS AND METHODS

This study was approved by the Institutional Ethical Committee, and verbal informed consent was obtained. A total of thirty-two subjects were included in the present study, selected from Obstetrics and Gynae wards of the Holy Family Hospital and Civil Hospital, Karachi. These subjects were divided into two groups:

1. 16 Pre-eclamptic patients [Pre-eclampsia was defined as the occurrence after 20 weeks of gestation, a diastolic BP 90mmHg or more on 2 occasions at least 4 hour apart, and proteinuria of 0.3g/1 or more in a 24 hour urine collection period]⁷ in third trimester³ (mean age 24.65 ± 4.25).
2. 16 healthy pregnant women as normal controls of matching age (mean age 25.56 ± 3.68). None was known to have chronic hypertension or renal or any other metabolic disease.

Excluding Criteria: All maternal or fetal abnormal pregnancies (except pre eclampsia) were excluded.

Peripheral fasting blood specimens were collected from all control and preeclamptic subjects. Blood was always collected before onset of labor. Serum was separated for analysis.

Serum total cholesterol (mg/dl): Serum total cholesterol in Cholesterol was determined after enzymatic hydrolysis and oxidation, indicator

quinoneimine is formed from hydrogen peroxide and 4-aminoantipyrine in the presence of phenol and peroxidase.⁷

HDL-cholesterol (mg/dl): HDL-cholesterol in Chylomicron, very low density lipoproteins, low density lipoproteins, are precipitated by adding of phosphotungstic acid and magnesium ions to the sample. Centrifugation leaves only HDL in the supernatant, their cholesterol content is determined enzymatically.⁷

LDL-cholesterol (mg/dl): LDL-cholesterol in LDL is precipitated by adding polyvinyl sulphate to the sample, their concentration is calculated from the difference between the serum total cholesterol and the cholesterol in the supernatant after centrifugation.⁷

Triglycerides (mg/dl): Triglycerides were determined after enzymatic hydrolysis with lipases. The indicator was a quinoneimine formed from hydrogen peroxide, 4-aminop- henazone and 4-cholorophenol under the under the catalytic influence of peroxidase.⁷

Total lipids (mg/dl): Lipid reacts with sulphuric acid, phosphoric acid, and vanillin to form a pink colored complex⁸ were estimated by standard kit (Merck) methods.⁹ Body Mass Index (BMI) was calculated by dividing body weight (kg) by the square of height (metres).

Statistical analysis: Mean and standard deviation were calculated for both control and Pre-eclamptic groups. Level of significance between control and preeclamptic group were analyzed using student's t test. Data are presented as mean \pm standard deviation. P value < 0.01 was considered statistically significant.

RESULTS

Clinical and laboratory parameters are given in Tables-I and II respectively.

Mean Triglycerides { 232.18 ± 106.41 vs 113.12 ± 21.3 } levels are significantly higher in group of women who had preeclampsia as compare to normal controls ($P < 0.01$) as shown in Table-II. While mean High density lipoprpteins cholesterol { 39.75 ± 11.99 vs 51.18 ± 06.09 } levels were significantly lower in women with preeclampsia than in normal

Table-I: Demographic and Clinical Characteristics of Controls and Pre-eclamptic subjects.

Parameters	Control	Pre-eclampsia
Age (years)	25.56 ± 3.68	24.65 ± 4.25
Primigravida	8	6
Multigravida	8	10
Gestational age (weeks)	32.87 ± 1.45	32.31 ± 1.19
Systolic BP (mmHg)	113.13 ± 10.78	166.25 ± 20.62*
Diastolic BP (mmHg)	86.88 ± 9.46	133.75 ± 15.0*
BMI	27.69 ± 2.47	28.88 ± 2.31

* P<0.01 as compared to normal control.

control subjects (P<0.01) as shown in Table-II. Mean cholesterol {177.5±57.19 vs.183.5±12.88}, Low density lipoprpteins-cholesterol {117.93 ± 12.56 vs.108.43± 06.60} and total lipids {806.12 ± 243.11 vs. 574.93±47.55} levels were not statistically different between preeclamptic and normal subjects as shown in Table-II. The data are shown as mean±standard deviation value.

DISCUSSION

In this study we investigate the role of lipid profile in the occurrence of Pre-eclampsia. There was a positive correlation between Pre-eclampsia and lipid parameters as shown in Table-II.

We observed significantly increased triglycerides and decreased HDL-cholesterol during Pre-eclampsia, which provide evidence of abnormal lipid metabolism. Pre-eclampsia is characteristically associated with hypertriglyceridemia. Increased levels of triglycerides with reduced high density lipoprotein -cholesterol have been observed in our

study as shown in Table-II. These types of higher results also reported by other studies on pre-eclamptic women.^{5,6,10-12}

During the course of normal pregnancy, plasma triglyceride and cholesterol concentrations rise and as pregnancy progresses both become normal. Hormonal variations during pregnancy affect lipid metabolism.⁸ The endogenous female sex hormones have significant effect on serum lipids.¹³ During pregnancy, there is an increase in the hepatic lipase activity and decrease in lipoprotein lipase activity.¹³ Hepatic lipase is responsible for the increased synthesis of the triglycerides at the hepatic level, whereas the decreased activity of lipoprotein lipase is responsible for the decreased catabolism at the adipose tissue level, the net effect of which will be an increase in circulating triglycerides and the second step of uptake of the remnant chylomicrons by the liver is delayed so it leads to accumulation of triglycerides in plasma as observed during present study shown in Table-II.

Another hypothesis is that hypertriglyceridemia is probably consequence of competition between chylomicrons and very low-density lipoprotein cholesterol for the lipoprotein lipase. Classically, chylomicron clearance occurs in two sequential steps: (1) triglycerides hydrolysis by lipoprotein lipase, (2) uptake of the remnant by the liver. Delay in the second step leads to accumulation of remnants in plasma and is generally thought to represent the atherogenic risk of hypertriglyceridemia. The conclusion of another study also indicated that there exists a consistent positive association between elevated maternal TG and the risk of pre-eclampsia.¹²

Table-II: Lipid Profile of Controls and Pre-Eclamptic group.

S #	Investigations	Controls (n=16)	Pre-Eclamptic Subjects (n=16)
1	Cholesterol (mg/dl)	183.5 ± 12.88	177.5 ± 57.19
2	Triglycerides (mg/dl)	113.12 ± 21.3	232.18 ± 106.41*
3	HDL-Cholesterol (mg/dl)	51.18 ± 06.09	39.75 ± 11.99*
4	LDL-Cholesterol (mg/dl)	108.43 ± 06.60	117.93 ± 12.56
5	Total Lipids (mg/dl)	574.93 ± 47.55	806.12 ± 243.11

* P<0.01 as compared to normal control.

On the other hand increased triglycerides play a part to decrease the HDL-cholesterol. HDL particles carry cholesterol from peripheral tissues to liver. Impaired transport of cholesterol from peripheral tissues to the target area of utilization may cause the decrease in HDL-cholesterol in serum. According to Pirzado, et al there is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL cholesterol. This direct correlation may be responsible for low levels of HDL cholesterol.¹⁵ Hypertriglyceridemia, leading to low HDL cholesterol is due mainly to the actions of Cholesteryl Ester Transfer Protein (CETP).

In hypertriglyceridemia there is also a chance to have that larger triglyceride-enriched VLDL (very low density lipoproteins) particles, which do not increase in number therefore LDL number is not increased.

In summary, the findings reported in this article suggest that the women who develop pre-eclampsia had disturbed lipid profile due to abnormal lipid metabolism. Increased triglycerides levels and delayed triglycerides clearance and high blood pressure are the reasons for the development of preeclampsia. This association may be significant in understanding the pathological process of pre-eclampsia and may help in developing strategies for prevention and early diagnosis of pre-eclampsia.

REFERENCES

1. Vanderjagt DJ, Patel RJ, El-Nafaty AU, Melah GS, Crossey MJ, Glew RH. High density lipoprotein and homocysteine levels correlate inversely in preeclamptic women in northern Nigeria. *Acta Obstet Gynecol Scand* 2004;83(6):536-42.
2. Packer CS. Biochemical markers and physiological parameters as indices for identifying patients at risk of developing pre-eclampsia. *J Hypertens* 2005;23(1):45-6.
3. Tariq M, Rehmani H, Tayyab M, Kamal F, Yasmeen N, Sultan F. Clinico-pathological study of pre-eclampsia. *Biomedica* 2000;16:60-5.
4. Caren G, Solomon, Seely EW. Preeclampsia-searching for cause. *New Eng J Med* 2004;350(7):641-2.
5. Enquobahrie DA, Williams MA, Butler CL, Frderick IO, Miller RS, Luthy DA. Maternal plasma lipid concentration in early pregnancy and risk of preeclampsia. *Am J Hypertens* 2004;17(7):574-81.
6. Gractacose E, Casals E, Gomez O, Llubra E, Mercader I, Carach V, et al. Increased susceptibility to low density lipoprotein oxidation in women with a history of pr-eclampsia. *Br J Obstet Gynaecol* 2003;110(4):400-4.
7. Study Group, European Atherosclerosis Society. Strategies for the prevention of Coronary heart disease: A policy statement of European Atherosclerosis Society. *Euro Heart J* 1987;8:77-88.
8. Zollner N, Kirsch K. Colorimetric method for the in vitro determination of serum and tissue total lipids. *Ges Exp Z Med* 1962;135:545.
9. Karim S, Karim S, Begum A, Javeed N. Combined effect of captopril and thiazide diuretic on serum lipid profile in hypertensive women. *J Ayub Med Coll* 2001;13(1):19-21.
10. Winkler K, Wetzka B, Hoffmann MM, Friedrich I, Kinner M, Baumstark MW, et al. Triglyceride-rich lipoproteins are associated with hypertension in preeclampsia. *J Clin Endocr Metab* 2003;88(3):162-1166.
11. Toescu V, Nuttall SL, Martin U, Nightingale P, Kendall MJ, Brydon P, et al. Changes in plasma lipids and markers of oxidative stress in normal pregnancy and pregnancy complicated by diabetes. *Clin Sci* 2004;106(1):93-8.
12. Ray JG, Diamond P, Singh G, Bell CM. Brief overview of maternal triglycerides as a risk factor for pre-eclampsia. *Br J Obstet Gynaecol* 2006;113(4):379-86.
13. Patrizia B, Giancarlo T, Franca E, Loreta P, Salvatore D, Mario M, et al. Lipoprotein metabolism during normal pregnancy. *Am J Obstet Gynecol* 1999;181(2):430-4.
14. Genovefa D, Kolovou MD, Deliana CH. Daskalova MD, Stella A, Iraklianos MD, et al. Postprandial lipemia in hypertension. *J Amer Coll Nutrition* 2003;22(1):80-7.
15. Pirzado ZA, Sangi SA, Malik R. High density lipoprotein cholesterol (HDL) metabolism and its role in the ischemic heart disease. *Pak J Med Res* 1999; 38(1):38-41.