

A STUDY ON ALTERATION OF SERUM LIPID PROFILE IN GESTATIONAL PROTEINURIC HYPERTENSIONEvelyn Thomas¹**HOW TO CITE THIS ARTICLE:**

Evelyn Thomas. "A Study on Alteration of Serum Lipid Profile in Gestational Proteinuric Hypertension". Journal of Evolution of Medical and Dental Sciences 2015; Vol. 4, Issue 68, August 24; Page: 11797-11803, DOI: 10.14260/jemds/2015/1701

ABSTRACT: BACKGROUND: Changes in lipid metabolism occurs in normal pregnancy during third trimester. This dyslipidemia indicative of insulin resistance is accentuated with Pre-eclampsia and Eclampsia. It contributes to both the pathogenesis of pre-eclampsia and to the risk of later-life cardiovascular disease in these patients. I have attempted to study the alterations in lipid profile in normal pregnancy, pre-eclampsia and eclampsia. **MATERIALS AND METHODS:** This study was conducted in Govt. Medical College for a period of 6 months. 25 normotensive non- pregnant women, 25 normal pregnant women, 25 pre eclampsia patients and 25 eclampsia patients were selected All the antenatal were in third trimester. Serum lipid profile was determined. Data analysis was done by excel sheet and SPSS software. **RESULTS:** Serum Triglycerides, VLDL, Total Cholesterol, LDL Cholesterol and HDL Cholesterol were significantly elevated in last trimester of normal pregnancy when compared to normal non-pregnant women. Also a significant increase in serum triglycerides and VLDL were seen in pre-eclampsia when compared to that of normal pregnancy. Also a significant decrease in HDL Cholesterol levels were seen in eclampsia when compared to normal pregnancy. **CONCLUSION:** Dyslipidemia suggestive of an exaggerated insulin resistance was found in pre eclampsia and eclampsia. Early interventions like prevention of obesity, exercise and balanced diet can reduce the risk of future cardiovascular morbidity and mortality in these patients. **KEYWORDS:** Triglycerides, Pre-eclampsia, Eclampsia, Cholesterol, Insulin resistance, Normal pregnancy.

INTRODUCTION: Normal pregnancy is associated with changes in lipid metabolism that ensure a continuous supply of nutrients to the growing fetus. Early and mid-pregnancy are characterized by increased hepatic production of triglycerides and their enhanced removal from the circulation resulting in an increased deposition of fat in maternal adipose tissue.¹ the increased estrogen, progesterone and insulin favour lipid deposition and inhibits lipolysis.

In late pregnancy there is a state of net breakdown or mobilization of adipose lipid depots. All lipid and lipoprotein components of blood are significantly elevated by the end of third trimester.²It may be due to over production of lipoproteins by the liver or from impaired delipidation of plasma lipoprotein triglyceride by lipoprotein lipase present in peripheral tissue. Gestational insulin resistance is the most important cause for decrease in the adipose tissue lipoprotein lipase activity and increase in hormone-sensitive lipase activity during third trimester. The net effect of these two mechanisms will be an increase in circulating triglycerides. In late pregnancy, human placental lactogen also promotes lipolysis and fat mobilization.

The maternal cholesterol levels increase during term. A moderate and significant increase in plasma total and LDL cholesterol has been reported at term.³ But HDL cholesterol only increases slightly in normal pregnancy.⁴ LDL cholesterol is more influenced by the combined effect of increased estrogen and progesterone. Estrogens also increase plasma HDL levels.

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Marked dyslipidemia occurs with pre-eclampsia and eclampsia. This contributes to the endothelial cell dysfunction. Mean plasma triglyceride concentration increases about two fold on average in women with pre-eclampsia relative to women with normal pregnancy, reflected in the markedly increased concentrations of very low density lipoprotein.^{5,6} Also the hypertriglyceridemia of pre-eclampsia is accompanied by a decrease in HDL cholesterol relative to normal pregnancy.⁷

However, total cholesterol and LDL cholesterol levels are generally not altered during pre-eclampsia.

The changes in total cholesterol, LDL Cholesterol and HDL Cholesterol levels found in eclampsia are almost similar to that of pre-eclampsia. However, decreased triglyceride and VLDL levels are seen in eclamptic pregnancy, compared to pre-eclamptic pregnancy.

The hypertriglyceridemia shifts the spectrum of LDL subclasses towards predominance of smaller, denser, potentially atherogenic LDL particles. It is more so in women with pre-eclampsia.

The small dense LDL is susceptible to oxidation and once oxidized, it promotes formation of foam cells (lipid-laden macrophages), which initiate endothelial dysfunction.

An exaggerated insulin resistance is observed in pre-eclampsia causing further suppression of lipoprotein lipase, than in normal gestation. So there is further increase in circulating triglycerides.⁵ increased concentrations of human placental lactogen promote lipolytic activity in maternal adipocytes.

In pre-eclampsia, the serum estrogen level is believed to fall down. Thus HDL level is explained by hypoestrogenemia, insulin resistance and hypertriglyceridemia.

As the eclampsia is commonly associated with hepatic damage, the de novo synthesis of triglycerides in liver is inhibited leading to a relative decrease in triglycerides and VLDL.

Lipid abnormalities indicative of insulin resistance are accentuated with established pre-eclampsia. Also studies have shown that exaggerated hyperinsulinemia relative to normal pregnancy is well described in pre-eclampsia.

The presence of hyperinsulinemia in non-pregnant women years after a pre-eclamptic pregnancy indicates that these women may be at increased risk for later life conditions associated with insulin resistance like type 2 diabetes mellitus, hypertension, dyslipidemia and coronary heart disease. Also there are indications that a supraphysiological rise in plasma lipids serves as a marker of "prelipemia" in the same way that gestational diabetes is a marker for pre-diabetes. So identification of these women who display these risk markers, that is, dyslipidemia, allow for early interventions like prevention of obesity, exercise and balanced diet to diminish or delay future cardiovascular morbidity and mortality.

METHODOLOGY: The study was performed in patients admitted in Obstetrics and Gynaecology wards, in labour room, in eclampsia room and the non-pregnant normotensive women were selected from female staff working in the same Medical College. The study was conducted for a period of 6 months from July to December. The study was approved by Institutional Ethics Committee.

Four study groups (sample size 25 in each group) were selected with prior written informed consent. They were normotensive non-pregnant women, normal pregnant women, pre-eclampsia patients and eclampsia patients.

All subjects were of same age group 18 to 35 years and of similar socioeconomic class and dietary habits. Women with history of any acute or chronic illnesses or any cardiac, renal or hepatic dysfunction or having dyslipidemia were excluded from the study.

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The pre-eclampsia group includes antenatal patients having hypertension ($\geq 140/90$ mmHg) for the first time during pregnancy and minimal proteinuria (1+ dipstick in random urine samples). The eclampsia group includes pre-eclampsia patients with convulsions and /or coma that cannot be attributed to other causes. It includes antepartum eclampsia, intrapartum eclampsia and postpartum eclampsia within 48 hrs. of delivery. All antenatals were in the third trimester.

Blood samples for lipid profile were obtained after 8 to 12 hours fasting. Triglycerides, Total cholesterol and HDL cholesterol levels in the serum were estimated using the reagent kits. LDL Cholesterol and VLDL Cholesterol were calculated using the Friedewald's equation.

Statistical analysis was done to compare the lipid levels in normal pregnancy with that of normal non-pregnant women and those of pre-eclampsia patients and eclampsia patients with that of normal pregnant women. Comparison of these lipid values were done using unpaired 't' test.

RESULTS:

Table 1: Comparison of Baseline Parameters of Normal Non pregnant Women and Normal Pregnant Women.

	Normal Non Pregnant		Normal Pregnant		
	Mean	SD	Mean	SD	p value
Triglycerides (mg/dl)	99.52	13.62	199.56	41.93	0.001
Total Cholesterol (mg/dl)	187.28	28.77	247.16	39.67	0.001
VLDL (mg/dl)	19.8	2.78	39.64	8.19	0.001
LDL-C (mg/dl)	118.16	29.22	150.96	35.37	0.002
HDL-C (mg/dl)	49.28	9.27	57.12	11.25	0.012

Table 1

Table 2: Comparison of Baseline Parameters of Normal Pregnant Women with Pre-Eclampsia Patients and Eclampsia Patients.

	Normal Pregnant		Preeclampsia			Eclampsia		
	Mean	SD	Mean	SD	p value	Mean	SD	p value
Triglycerides (mg/dl)	199.56	41.93	235.84	50.56	0.008	205.92	76.17	0.771
Total Cholesterol (mg/dl)	247.16	39.67	236.92	38.43	0.770	219.52	60.57	0.02
VLDL (mg/dl)	39.64	8.19	47	10.04	0.007	41.08	15.06	0.770
LDL-C (mg/dl)	150.96	35.37	134.04	40.92	0.08	131.32	55.06	0.06
HDL-C (mg/dl)	57.12	11.25	53.4	10.41	0.33	48.04	9.855	0.007

Table 2

SBP- Systolic Blood Pressure.

DBP-Diastolic Blood Pressure.

VLDL- Very Low Density Lipoprotein.

LDL- Low Density Lipoprotein.

HDL-High Density Lipoprotein.

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The mean values of serum triglycerides ($p=0.001$), VLDL ($p=0.001$), total cholesterol ($p=0.001$), LDL cholesterol ($p=0.002$) and HDL cholesterol ($p=0.012$) in normal pregnant women are significantly elevated when compared to that of normal non-pregnant women.

The mean serum triglyceride ($p=0.008$) and VLDL levels ($p=0.007$) are significantly elevated in pre-eclampsia patients when compared to normal pregnant women. Though the mean serum cholesterol levels in preeclampsia were almost the same as in normal pregnancy, the mean serum total cholesterol levels ($p=0.02$) in eclampsia were seen to decrease significantly when compared to normal pregnancy.

The mean serum LDL cholesterol levels in pre-eclampsia and eclampsia were almost similar when compared to normal pregnant women. A statistically significant decrease in mean HDL-Cholesterol levels ($p=0.007$) was found in eclampsia when compared to normal pregnancy. The mean HDL-C levels in pre-eclampsia, though not statistically significant, is found to be decreased when compared to normal pregnancy.

DISCUSSION: The maternal plasma lipids are significantly elevated during pregnancy. Women who develop pre-eclampsia and eclampsia experience even more dramatic lipid changes. The dyslipidemia associated with pre-eclampsia may adversely affect maternal endothelial homeostasis and vascular function.

The mean serum triglyceride levels of normal pregnant women in the third trimester in the present study is significantly higher than in normal women. Potter and Nestel² demonstrated a threefold increase in plasma triglycerides during the last trimester of pregnancy. Qureshi et al.⁸ and Jayanta De et al.⁹ also obtained similar results. The significant elevation in fasting triglycerides by late gestation could be attributed mainly to decreased adipose tissue lipoprotein lipase activity and an increased hormone-sensitive lipase activity in maternal adipocytes during the last third of pregnancy due to insulin resistance.

The decreased activity of lipoprotein lipase is responsible for the decreased catabolism of triglycerides at the adipose tissue level. The increased activity of hormone sensitive lipase causes increased release of free fatty acids and glycerol from adipocytes. Much of the glycerol and free fatty acids released from the fat are taken up by the liver and re-esterified for synthesis of very low density lipoprotein triglycerides. Another principal modulator of this hypertriglyceridemia could be estrogen, as pregnancy is associated with elevated estrogen levels. Estrogen induces hepatic synthesis of endogenous triglycerides which is carried by VLDL.

The mean VLDL level in normal pregnant women of third trimester is significantly higher than in non-pregnant controls in this study. This is consistent with the findings of Jayanta De et al,⁹ who showed significantly increased levels of VLDL in third trimester of normal pregnancy. Serum hypertriglyceridemia might be related to enhanced entry of VLDL from liver into the circulation, which carries endogenous triglycerides.

The mean levels of total cholesterol, LDL cholesterol and HDL cholesterol in normal pregnant women are found to be significantly higher than the corresponding values in normal non-pregnant women in the present study. Russel De Alvarez et al.¹⁰ and Dakov et al.¹¹ showed similar results. As estrogen induces HDL, rise in HDL can be explained by the hyperestrogenemia during pregnancy. But the increase in mean LDL value can only be explained by the combined effect of estrogen and progesterone.

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The mean serum triglyceride levels in pre-eclamptic patients are significantly higher than the mean serum triglyceride value in normal pregnant women of third trimester. This rise was similar to that reported by few studies.^{4,6} This significant hypertriglyceridemia in pre-eclampsia could be due to the heightened gestational insulin resistance seen during the third trimester. Also there may be decreased VLDL and LDL receptor expression in placentas of women with pre-eclampsia.

Thus there is decreased clearance of triglycerides from plasma along with increased production leading to hypertriglyceridemia. Due to the increase in the lipolytic activity in maternal adipose tissue; free fatty acids and glycerol are released. This is taken up by liver and re-esterified for synthesis of VLDL triglycerides. Despite the low estrogen levels found in pre-eclampsia and eclampsia, their exaggerated insulin resistance during third trimester is mainly responsible for the markedly elevated triglyceride levels.

The mean serum triglyceride concentration in eclampsia is found to be more than the mean triglyceride concentration of found in normal pregnant women of third trimester. But this rise is not statistically significant as seen in pre-eclampsia. The increased and aggravated hepatic damage in eclampsia which may lead to decreased synthesis of VLDL triglycerides. This could be the probable reason for a less dramatic increase in serum triglycerides in eclampsia.

The serum VLDL levels are also found to be significantly elevated in pre-eclampsia when compared to normal gestation. This finding in the present study is similar to that reported by N sattar et al.¹² and Wetzksa B et al.¹³ Due to the increased lipolytic activity by heightened insulin resistance occurring in preeclampsia, there is overproduction of VLDL by liver.

The mean serum VLDL level in eclampsia is higher than the mean serum VLDL level seen in normal pregnancy. But this rise is not significant statistically as found in pre-eclampsia. As mentioned earlier, hepatic damage may be the cause for decreased VLDL synthesis.

The total cholesterol and LDL cholesterol levels in pre-eclampsia are statistically similar to the values of total cholesterol and LDL cholesterol seen in third trimester of normal pregnancy. These results coincided with those obtained by N sattar et al.¹²

The mean serum LDL Cholesterol in eclampsia is almost similar to the mean serum LDL Cholesterol level seen in third trimester of normal pregnancy. But the mean serum total cholesterol in eclampsia is significantly lower than the mean serum total cholesterol value in third trimester of normal pregnant women. Murakami M et al.¹⁴ showed that in toxemia of pregnancy the serum total cholesterol level decreased significantly than normal pregnancy third trimester.

The mean serum HDL cholesterol levels in preeclampsia and eclampsia are found to be decreased when compared to normal pregnancy. But the decrease was statistically significant only in the case of eclampsia. These results were found to be similar to that shown by some reporters.^{12,15}

This decrease in HDL cholesterol could be due to hypoestrogenemia and increased triglycerides due to exaggerated insulin resistance in the third trimester. Decreased HDL could result from hypertriglyceridemia since the two are metabolically linked. Increased triglycerides leading to low HDL cholesterol is due to actions of Cholesteryl Ester Transfer Protein.

Thus normal pregnancy is associated with increased levels of cholesterol and triglycerides in plasma in the last trimester. In our study, we observed a relatively higher serum triglyceride and lower HDL cholesterol levels in pre-eclampsia and eclampsia in third trimester when compared to that of normal pregnancy. Lipid abnormalities characteristic of insulin resistance are accentuated in women with pre-eclampsia and eclampsia.

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Elevated triglycerides are found to cause oxidative stress and vascular dysfunction in several ways. One important mechanism is by formation of small dense LDL which contributes to the endothelial dysfunction. Thus exaggerated insulin resistance leading to high triglycerides and low HDL cholesterol promotes oxidative stress leading to endothelial dysfunction in pre-eclampsia and eclampsia.

Reports have even shown that women with a history of pre-eclamptic pregnancy have an increased risk for pre-eclampsia in subsequent pregnancies.⁵ Also patients who have had a history of pre-eclamptic pregnancy were shown to have increased risk for diseases associated with insulin resistance, example, type 2 diabetes mellitus, coronary heart disease and dyslipidemia. Insulin resistance is one of the leading causes for later-life cardiovascular disease in women with history of pre-eclamptic pregnancy. Regular exercise, prevention of obesity before pregnancy and excess weight gain after delivery, along with lifestyle counseling and regular health checkups are some of the strategies recommended in pre-eclampsia and eclampsia patients with hypertension.

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