A TERTIARY CARE CENTRE BASED STUDY ON SERUM LIPID LEVELS IN HEALTHY NON-PREGNANT WOMEN, NORMAL PREGNANCY AND IN PREECLAMPSIA

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ABSTRACT

BACKGROUND

Preeclampsia is more prevalent in the first pregnancy and is associated with very high maternal and foetal morbidity and mortality. Although, the exact cause of preeclampsia is still unknown, the basic pathology lies in the endothelial cell dysfunction and intense vasospasm. Dyslipidaemia is believed to play a key role in altering the microenvironment around endothelium.

So, the objective is to study the serum lipid levels in healthy non-pregnant women, normal pregnancy and in preeclampsia.

MATERIALS AND METHODS

Fasting serum lipid levels were estimated in 40 healthy non-pregnant women (Group-1), 40 normotensive primigravida (Group-2) and in 40 preeclamptic primigravida in their third trimester (Group-3). Serum lipid levels were estimated using fully automated analyser. Data was analysed using SPSS Version 18 software. P value < 0.05 was considered as statistically significant.

RESULTS

Compared with normal pregnancy, in preeclampsia, the level of serum total cholesterol, triglycerides, VLDL and LDL were significantly increased and HDL was decreased significantly. In normal pregnant women, serum total cholesterol, triglycerides, HDL, VLDL and LDL levels were significantly high compared to healthy non-pregnant women.

CONCLUSION

Dyslipidaemia in pregnancy may be associated with increased risk of developing preeclampsia. Screening of the above parameters may help in developing strategies for prevention and better management of preeclampsia.

KEY WORDS

Preeclampsia; Dyslipidaemia; Endothelial Cell.

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BACKGROUND

Preeclampsia affects about 0.4% to 2.8% of all pregnancies in developed countries. The most serious outcomes occur in developing countries. It is associated with proteinuria, pathological oedema, coagulation abnormalities and reduced uteroplacental blood flow and intrauterine growth retardation.[1] Endothelial cell dysfunction is the most important event in the pathogenesis of preeclampsia and lipids have a role on this event. Modification in lipid metabolism during pregnancy may be one of the causes for preeclampsia. Lipid peroxidase and cytokines increase secondary to an increase in the levels of plasma lipids. Disturbance of endothelial cells results in vasoconstriction throughout the body.[2],[3] In this context it is postulated that estimation of serum lipid levels is important in pregnancy, so that it can be used as an effective screening test for diagnosis of preeclampsia.

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Objective

To study the serum total cholesterol, triglycerides, HDL, VLDL and LDL levels in healthy non-pregnant women, normal pregnancy and in preeclampsia.

MATERIALS AND METHODS

Study Design

Present study was a cross-sectional comparative study conducted for a period of 1 year from July 2015 to June 2016 in obstetric OPD and antenatal wards of Institute of Maternal and Child Health, Government Medical College, Kozhikode. The study was approved by Institutional Ethics Committee.

Study Group

Three study groups were selected according to inclusion and exclusion criteria. Statistical sample size was taken as 40 subjects in each group. Sample size was taken as convenience, since the duration of the study was few months. The patients were selected by convenience and the sample size estimation was also done at convenience.

Inclusion Criteria

Study Group 1

Healthy non-pregnant women in the age group of 18 - 30 years.

Study Group 2
Normotensive age matched primigravida with gestational age between 34 - 40 weeks.

Study Group 3
Preeclamptic age matched primigravida with gestational age between 34 - 40 weeks with blood pressure ≥ 140/90 mmHg in more than two occasions and proteinuria of at least 1+ in dipstick testing.

Exclusion Criteria
Any history of chronic hypertension, diabetes, kidney disease, liver disease, coagulation disorders or multiple pregnancies. Prior informed consent was taken from all. A detailed history was taken from all subjects that include age, gravida, parity and history of hypertension, dyslipidaemia, cardiac illness, renal disease, hepatic dysfunction or any other acute or chronic illness. Details of drug intake was also noted. Blood pressure recording along with a detailed physical examination was done. Urine protein was detected using dipstick method.

Statistical Analysis
The present study was designed as a comparative study and statistical analysis has been done to determine the differences between 3 groups. Data was analysed using Statistical Package for Social Sciences [SPSS] version 18. Results were expressed as Mean + SD. Mean differences between the groups were analysed using ANOVA. The p-value of < 0.05 was taken as the level of significance.

From the above three groups of subjects under aseptic precautions, blood was collected by venous puncture using disposable syringes and needles. Samples for lipid profile were obtained after 8 to 12 hours fasting. 2 mL of blood was drawn. Serum lipid profile was estimated using fully automated analyser- Clinical chemistry analyser- XL-300 (ERBA-TRANSASIA).

RESULTS

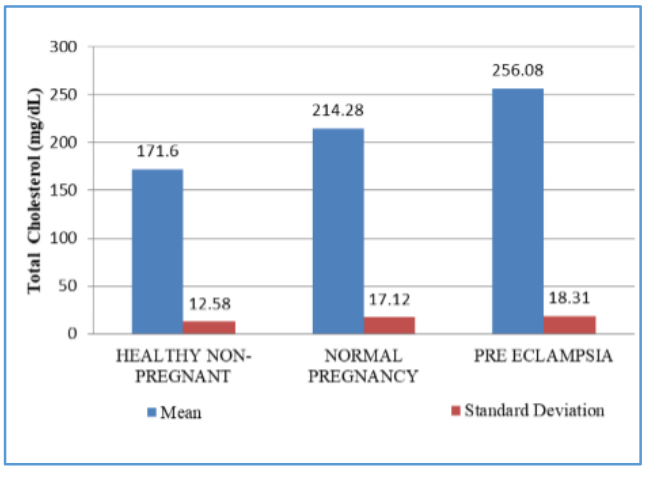

Figure 1. Comparison of Serum Total Cholesterol Levels (mg/dL), p= 0.000 (Highly Significant)

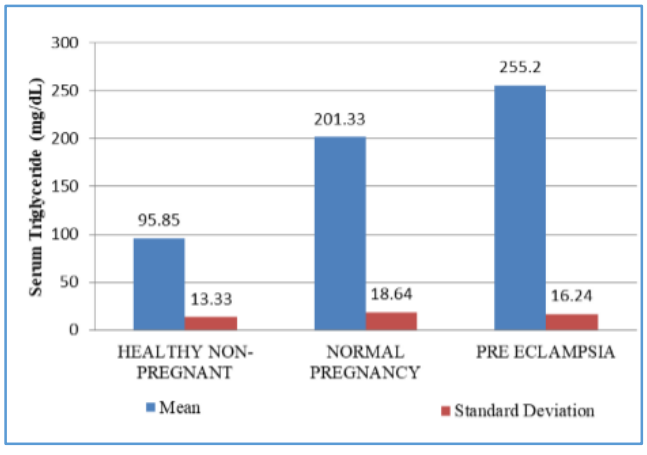

Figure 2. Comparison of Serum Triglyceride Levels (mg/dL), p= 0.000 (Highly Significant)

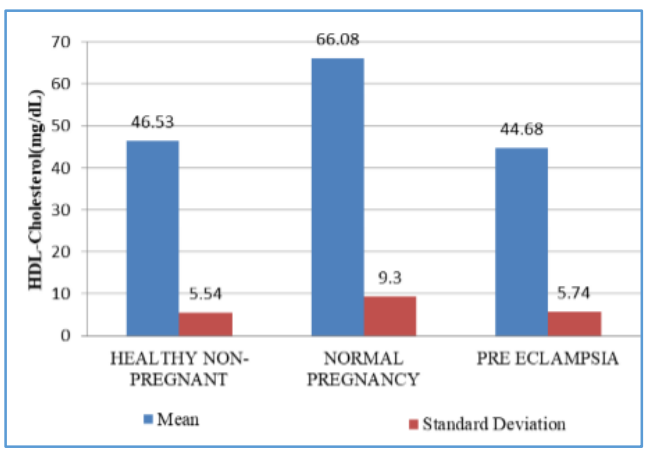

Figure 3. Comparison of Serum HDL - Cholesterol Levels (mg/dL), p= 0.000 (Highly Significant)

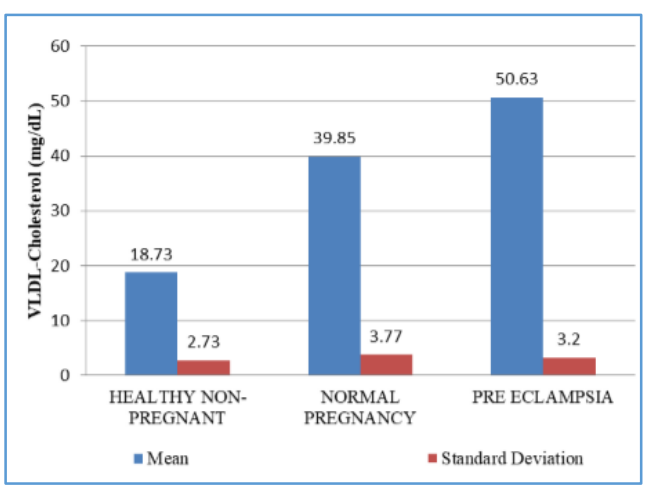

Figure 4. Comparison of Serum VLDL - Cholesterol Levels (mg/dL), p= 0.000 (Highly Significant)

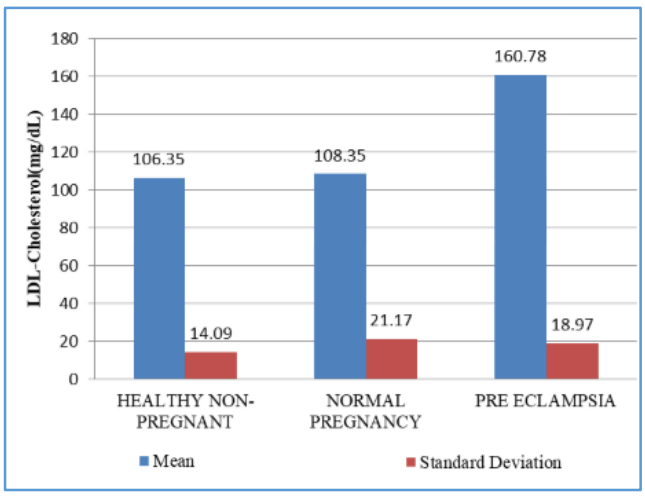

Figure 5. Comparison of Serum LDL - Cholesterol Levels (mg/dL), p= 0.000 (Highly Significant)

*The mean serum LDL-cholesterol level is increased in normal pregnancy when compared to healthy non-pregnant women. But the increase is not statistically significant as p=1.00. When compared to normal pregnancy, the LDL-C level is significantly increased in preeclampsia with p-value=0.000.

DISCUSSION

The serum total cholesterol values were significantly higher in normal pregnant group when compared to healthy young women. Preeclampsia group showed the maximum values when compared to other two groups. The differences among the groups were statistically significant. It is known that a high concentration of oestrogen and progesterone occurs as normal pregnancy advances and is highest in third trimester.[4] Desoye et al stated that the hepatic effects of estradiol and progesterone in normal pregnancy may also be responsible for these changes.[5],[6] The mechanisms responsible for increased cholesterol include increased lipolytic and decreased lipoprotein lipase activities in adipose tissue.[7] In normal pregnancies lipolysis increases, but in preeclamptic patients this increase is significantly higher.[8] Hypercholesterolaemia observed may result in excessive lipid peroxidation and generation of free radicals. There is also increased oxygen demand to meet the bodily functions in pregnancy, which can also act as a contributory factor for the oxidative stress that results in the formation of free radicals. Thus, hypercholesterolaemia may promote oxidative stress, leading to endothelial cell dysfunction in preeclampsia.[9]

The most marked change observed in the serum lipid profile was hypertriglyceridaemia. Levels were two-to-three folds higher in the third trimester of normal pregnancy compared with the levels of non-pregnant women. Significant modulators of lipoproteins during pregnancy include oestrogen, lipoprotein lipase and insulin.[10] The principle modulator of this hypertriglyceridaemia is oestrogen. Normal pregnancy is associated with hyperoestrogenaemia.[11] Oestrogen inhibits hepatic lipid oxidation. This may cause increased delivery of free fatty acids for biosynthesis of endogenous triglycerides in liver.[12] Lowering of lipoprotein lipase in normal pregnancy may be another reason for increase in serum TG levels.[13] Insulin resistance and hyperinsulinaemia found in pregnancy may also be responsible for the hypertriglyceridaemia in normal pregnancy.[14]

Increase in the level of triglycerides in preeclampsia is probably not associated with hyperoestrogenaemia. The levels of oestrogen were found to decrease in preeclampsia. The increase in level of triglycerides in preeclampsia is probably as a consequence of competition between chylomicron and VLDL cholesterol for the enzyme lipoprotein lipase. Classically, chylomicron clearance occurs in two sequential steps: (a) Triglyceride hydrolysis by the lipoprotein lipase, (b) Uptake of the chylomicron remnants by the liver. Delay in the second step leads to accumulation of remnants in plasma. This is responsible for the atherogenic risk of hypertriglyceridaemia.[15] Elevation in triglyceride levels in preeclampsia is likely to be deposited in predisposed vessels, such as uterine spiral arteries and contributes to the endothelial cell dysfunction directly. Indirectly, through the generation of small dense low-density lipoprotein cholesterol also can cause endothelial dysfunction.[16]

The mean level of HDL in normal pregnant women was significantly higher than in healthy young women. The mean value was significantly decreased in preeclampsia. Oestrogen may be responsible for the induction of HDL.[17] The increase in HDL in normotensive pregnant women can be explained by hyperoestrogenaemia.[12] In preeclampsia, the oestrogen level decreases, so reduced HDL may be due to hypooestrogenaemia. The decrease in HDL may also be due to exaggerated insulin resistance seen in preeclampsia.[18] This reduced HDL level may also contribute to the reduced prostacyclin level seen in preeclampsia.[19] The effects of HDL on prostacyclin synthesis are mediated via up-regulation of cyclooxygenase-2 expression.[20] Prostacyclin is an important regulator of vascular homeostasis.[21] Lower serum HDL level may also reduce antioxidative protection due to paraoxonase-1 on other lipoproteins.[22] Paraoxonase-1 is the enzyme responsible for HDLs antioxidant function. It is closely bound to the HDL particle.[23]

The rise in VLDL in normal pregnancy may be due to hypertriglyceridaemia. Increased triglycerides leads to enhanced entry of VLDL, as endogenous triglycerides are carried into circulation by VLDL from the liver.[13] The rise in triglyceride-rich VLDL particles during pregnancy is dependent more on an increased rate of synthesis caused by oestrogens.[24] Increased VLDL in preeclampsia may be explained by heightened insulin resistance, which leads to increased inhibition of lipolytic activity. It will result in overproduction of VLDL in liver.[25] Increased VLDL lipoproteins accumulate in the maternal vascular endothelium of uterine and renal vessels.[21]

The mean serum LDL is increased in normal pregnancy compared to healthy young women. But the increase is not statistically significant in our study. In preeclamptic patients, the value obtained is significantly higher than other two groups. The increase of LDL in normal pregnant women could be secondary to increased conversion of abundant VLDL. In preeclampsia, increase in LDL level may be due to decreased level of oestrogen.[26] The greatest effect of oestrogen on LDL metabolism was to increase the fractional catabolic rate of LDL particles.[27] It was indicated that small dense LDL had a greater capacity to stimulate thromboxane synthesis and release by endothelial cells, thereby causing vaso-constriction.[28]

Small dense LDL are also more susceptible to oxidative modifications. It leads to formation of peroxides that inhibit endothelium-derived relaxation factor and also leads to foam cell formation in decidua.[17],[29] Study by Uboh et al supports this hypothesis, as they observed increased levels of free radical products of lipid peroxidation (Malondialdehyde) in preeclamptic condition compared to normotensive pregnant women and healthy non-pregnant women.[30] Oxidised LDL impairs endothelial function by expression of adhesion molecules, inhibition of endothelial prostacyclin synthesis, increased endothelin production and release and increased platelet aggregability.[31]

CONCLUSION

In our study, preeclampsia is associated with decreased HDL and increased serum total cholesterol, triglycerides, VLDL and LDL levels in their third trimester. These factors are found to cause endothelial dysfunction in several ways. Endothelial cell dysfunction is said to be an important factor in the aetiopathogenesis of preeclampsia. Women with a history of preeclampsia are reported to be associated with increased risk of cardiovascular disease, hypertension, ischaemic heart attack, venous thromboembolism and death. These findings confirm the possible association between hypertension during pregnancy and future cardiovascular disease.[32] In order to implement preventive healthcare protocols, it is important to identify risk factors for preeclampsia. So, changes in the serum levels of above parameters can be used as an effective marker in the early diagnosis of preeclampsia. Also, it may prevent the possible risk of developing cardiovascular disease in future.

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