IMPACT OF LIPID PROFILE ON THE SEVERITY OF PREECLAMPSIA AND MATERNAL MORBIDITY: A CASE CONTROL STUDY

Nishi Roshini Kondakasseril[1], Roshini[2], Andrews Mekkattukunnel[3]

[1]Associate Professor, Department of Obstetrics & Gynaecology, Government Medical College, Trichur.
[2]Senior Resident, Department of Obstetrics & Gynaecology, Government Medical College, Trichur.
[3]Professor, Department of Medicine, Government Medical College, Trichur.

ABSTRACT

Preeclampsia is a pregnancy-specific disease associated with significant maternal and perinatal mortality and morbidity. Abnormalities in lipid profile have been reported as a feature of the disease. Our aim was to detect the serum lipid profile abnormalities in primigravid women with preeclampsia and its impact on severity of the disease and maternal morbidity.

MATERIALS AND METHODS

A prospective case-control study was conducted with pregnant subjects presenting to the Obstetric Unit of Government Medical College, Thrissur during the period of 1st June 2013 to 31st May 2014. Study group included 100 primigravidae with preeclampsia between 18 and 40 years of age with singleton pregnancy with gestational age between 24 weeks to term. Control group consisted of 100 matched normotensive pregnant primigravidae. Multipara, multiple gestations, pre-existing hypertension, ischaemic heart disease, chronic renal failure, diabetes mellitus, women taking any drugs which may influence lipid profile were excluded. Assessment of fasting serum lipid profile (12 hrs. fasting) levels of both study and control group was done using fully automated random clinical biochemistry analysers- Erba Manheim XL–640. Women with preeclampsia were grouped into mild and severe preeclampsia. Comparison of fasting serum lipid profile between those with mild and severe preeclampsia was made. Serum fasting serum lipid profile was analysed in women with complications like abruption, HELLP and eclampsia. Their demographic and clinical characteristics were used to generate a database for analysis.

STATISTICAL ANALYSIS

Data was analysed using Epi info version 7. The data is presented descriptively, providing the number of women, mean with standard deviation. The differences between study group and controls were analysed using t-test for continuous variables. A p value of <0.05 was considered significant.

RESULTS

The age of the study group was 23.52±3.29 years and of the controls 23.21±3.78 years. Serum Cholesterol (224.99±47.68 mg), Triglycerides (232.33±63.39 mg), LDL–C (123.30±38.45 mg), VLDL–C 46.47±12.68 mg) were significantly increased ($p<0.001$) in women with preeclampsia compared to normotensives. There was no statistically significant difference in serum HDL-C levels between the two groups. Among women with preeclampsia, 46% had mild disease and 54% had severe disease. In women with severe preeclampsia, serum cholesterol (245.65±45.88 mg), Triglycerides (262.78±54.96 mg), LDL–C (140.85±39.42 mg), VLDL–C (52.56±10.99 mg) were significantly increased ($p<0.001$) and HDL–C (52.24±6.69 mg) was significantly decreased (p-0.011). Nine women had complications and in those with maternal complications Serum Cholesterol (272.22±38.41 mg), Triglycerides (275.11±34.12 mg), LDL–C (168.09±30.24 mg), VLDL–C (55.02±6.82 mg) were significantly increased ($p<0.05$) and HDL–C (49.11±4.106 mg) was significantly decreased (p-0.002).

CONCLUSIONS

Serum lipid profile may be used as an indicator to detect the development of preeclampsia and for prognostication regarding the severity and maternal outcome; dyslipidaemia being a significant risk factor for coronary artery disease, this may help to institute life style modifications and pharmacological interventions to reduce mortality and morbidity in later life.

KEYWORDS

Lipid Profile, Preeclampsia, Pregnancy, Proteinuria, Hypertension.

HOW TO CITE THIS ARTICLE: Kondakasseril NR, Roshini, Mekkattukunnel A. Impact of lipid profile on the severity of preeclampsia and maternal morbidity: A case control study. J. Evid. Based Med. Healthc. 2016; 3(47), 2337-2341. DOI: 10.18410/jebmh/2016/516

Financial or Other, Competing Interest: None.
Submission 19-05-2016, Peer Review 29-05-2016,
Acceptance 03-06-2016, Published 11-06-2016.
Corresponding Author:
Dr. Nishi Roshini Kondakasseril,
Mekkattukunnel House, VRA 108, Chakkoth Lane,
Poonkunnam-680002, Trichur, Kerala, South India.
E-mail: nishiroshini@gmail.com
DOI: 10.18410/jebmh/2016/516

INTRODUCTION: Hypertensive disorders complicate 5 to 10 per cent of all pregnancies.[1] Preeclampsia is a pregnancy-specific disease characterised by the new onset of hypertension and proteinuria occurring from 20 weeks of gestation onward.[2,3] It is more frequent in nulliparous young women.[2] Endothelial dysfunction in the placental vasculature is considered in the aetiology and pathogenesis of the disease.[4]

Preeclampsia is linked to oxidative stress within the placenta.[5] Increased production of lipid peroxides, thromboxane and/or cytokines trigger vascular and organ dysfunction in pre-eclampsia.[5] Cardiovascular research has shown that serum lipids have a direct effect on endothelial function and abnormal serum lipid profiles are associated with endothelial dysfunction. Maternal predisposition to pre-eclampsia may be due to the altered lipid profile, but findings reported are inconsistent.

OBJECTIVES: The present study was designed to investigate the alteration in serum lipid profile including Total Cholesterol, High-Density Lipoprotein (HDL)-Cholesterol, Low-Density Lipoprotein (LDL)-Cholesterol, Very Low Density Lipoprotein (VLDL) And Triglycerides in pre-eclamptic and normal pregnant women and the impact on severity of preeclampsia and maternal morbidity.

Settings and Design: This is a case-control study conducted in the Department Of Obstetrics and Gynaecology, Government Medical College, Thrissur after approval by the Ethical Committee. 100 primigravid women between the age group of 18-40 years with gestational age between 24 weeks to term admitted with preeclampsia in the Department of Obstetrics and Gynaecology, Government Medical College, Thrissur during 1st June 2013 to 31st May 2014 were selected. Multiparous women, multiple gestations, pre-existing hypertension, ischaemic heart disease, chronic renal failure, diabetes mellitus, women taking any drugs which may influence lipid profile were excluded from the study. The control group consisted of 100 matched normotensive pregnant women with similar inclusion and exclusion criteria.

Preeclampsia is defined as high blood pressure (≥140/90 mm of Hg noted for the first time during pregnancy on ≥2 occasions at least 6 or more hours apart) after 20 weeks of gestation with proteinuria (excretion of ≥300 mg protein/24 hours or ≥ +1 by dipstick or protein-creatinine ratio ≥ 0.3 in a random urine sample). Preeclampsia is classified into mild or severe disease. Severe preeclampsia is defined by the presence of one or more of the following like blood pressure >160/110 mmHg, severe proteinuria (≥5 g/24-hr. urine or proteinuria ≥ 3+) or there is evidence of multiorgan involvement such as pulmonary oedema, seizures, oliguria (<500 mL/24-hr. period), thrombocytopenia (platelet count <100,000/mm^3), abnormal liver enzymes AST/ALT (twice the normal: Normal=10 – 40 IU/L), persistent epigastric or right upper quadrant pain, persistent severe central nervous system symptoms (altered mental status, headaches, blurred vision, or blindness) or elevated serum creatinine level (> 1.1) or presence of obvious foetal growth restriction.

Cases were also screened for coagulation abnormalities using bleeding time (BT) and clotting time (CT). BT > 2'30" and CT>7' were considered as evidence of coagulopathy and was further confirmed by prothrombin time, and activated partial thromboplastin time.

Maternal complications like HELLP syndrome (Haemolysis, Elevated Liver Enzymes, Low platelet count), abruption, eclampsia (Antepartum /intrapartum/ postpartum), disseminated intravascular coagulation (DIC), renal failure, pulmonary oedema, PPH (Post-Partum Haemorrhage), cerebral haemorrhage, if any were noted. HELLP Syndrome was diagnosed if at least two of the following abnormalities were present like abnormal peripheral blood smear (burr cells, schistocytes), elevated bilirubin (> 1.2 mg/dL), increased LDH (> twice the upper limit of normal for the laboratory), elevated transaminases (ALT or AST ≥ twice the upper limit of normal for the laboratory) and low platelet count (<100,000/mm^3).

Abnormalities Of Triglycerides, Total Cholesterol, Low-Density Lipoprotein (LDL)-Cholesterol And High-Density Lipoprotein (HDL)-Cholesterol were defined as levels ≥150 mg/dL, ≥200 mg/dL, ≥100 mg/dL and <40 mg/dL, respectively. Abnormal lipid profile for each subject was defined as abnormality in any one of the four parameters in the panel.

METHOD OF STATISTICAL ANALYSIS: The Excel and Epi info version 7 software packages were used for data entry and analysis. The results are shown as (Mean± standard deviation) for continuous variables. Number and percentage for discrete variables are presented in tables and charts. Normality of the data was tested using Shapiro-Wilks test. Proportions were compared using Chi-square (x2) test of significance. The student 't' test was used to determine whether there was a statistical difference between groups. A "p" value of less than 0.05 was accepted as indicating statistical significance.

OBSERVATIONS AND RESULTS: The [mean±SD] age of the study group was 23.52±3.29 years and of the control 23.21±3.78 years. There was no difference in age between the two groups. The [mean ±SD] BMI in first trimester of the study group was 22.62±2.587 kg/m^2 and of the controls 22.45±2.038 kg/m^2. (BMI=Weight in kg/Height in m^2). There was no statistical difference in BMI between the two groups. The maternal demographic features are shown in Table 1.

Characteristics (Mean with SD*)	Preeclampsia	Controls	T value	P value
Age	23.52(3.291)	23.21(3.780)	0.6185	0.501
Gestational age	36.14(2.767)	39.07(1.037)	9.9156	0.295
Height	154.57(5.205)	155.20(4.367)	0.860	0.355
Weight	54.51(5.684)	54.07(5.252)	0.860	0.355
BMI	22.62(2.587)	22.45(2.038)	0.860	0.355
Pulse	83.99(5.821)	81.41(5.170)	10.981	0.001

Table 1: Maternal Features of Preeclampsia and Controls

*SD Standard deviation.

All the subjects in study group had albumin (Proteinuria) in the urine which ranges from 1+ to 4+. Albumin (Proteinuria) was absent in urine of control groups. In the study group mean proteinuria was 0.63 mg/24 hours.

The mean of lipid profile of cases and controls are given in Table 2. Serum cholesterol, Triglyceride, LDL – C, VLDL – C were significantly elevated in the cases (p <0.001). The [mean ± SD] serum HDL-C level in study subjects was 55.22±12.745 mg/ dl and in controls was 56.65±11.212 mg/dl. There is no statistical difference in serum HDL-C levels between the two groups.

Parameters (Mean with SD)	Preeclampsia	Controls	T value	P value
Cholesterol	224.99(47.68)	185.95(40.07)	39.291	<0.001
Triglyceride	232.33(63.39)	177.10(24.56)	66.004	<0.001
LDL-C†	123.30(38.45)	93.88(32.09)	34.51	<0.001
VLDL-C‡	46.47(12.68)	35.42(4.91)	66.00	<0.001
HDL-C•	55.22(12.75)	56.65(11.21}	0.710	0.401

Table 2: Maternal mean of Lipid Profile in Preeclampsia and Controls

*SD Standard deviation, †LDL-C Low Density Lipoprotein Cholesterol, ‡ VLDL-C Very Low Density Lipoprotein Cholesterol, •HDL –C High Density Lipoprotein.

Among 100 women with preeclampsia, 46(46%) had mild disease and 54(54%) had severe preeclampsia. Lipid profile in mild and severe pre-eclampsia is shown in Table 3. In severe preeclampsia, there was statistically significant increase in serum total cholesterol, TG, LDL-C and VLDL-C (p<0.001). There is a statistically significant decrease in serum HDL-C levels in severe pre-eclampsia (p-0.011).

Parameters (Mean with SD*)	Mild pre-eclampsia (n- 46)	Severe pre-eclampsia (n- 54)	T value	P value
Cholesterol	200.74(37.55)	245.65(45.88)	28.053	<0.001
Triglyceride	196.59(53.53)	262.78(54.96)	36.90	<0.001
LDL†	102.70 (24.872)	140.85(39.424)	32.14	<0.001
VLDL‡	39.32(10.705)	52.56(10.992)	36.90	<0.001
HDL•	58.72(16.778)	52.24(6.690)	28.05	0.011

Table 3: Lipid Profile and Severity of Preeclampsia

*SD Standard deviation, †LDL-C Low Density Lipoprotein Cholesterol, ‡ VLDL-C Very Low Density Lipoprotein Cholesterol, •HDL –C High Density Lipoprotein.

The maternal complications noted in our cases (n=9/100) were abruption with DIC in 1, HELLP syndrome in 5 and eclampsia in 3 women. Association of maternal complications with lipid profile is shown in Table 4.

Parameter (Mean with SD*)	No maternal complications	Maternal complications	T value	P value
Cholesterol	220.32±46.096	272.22±38.41	3-793	0.002
Triglycerides	228.10±64.154	275.11±34.12	2.16	0.003
LDL-C†	118.87±36.394	168.09±30.24	4.56	<0.001
VLDL-C‡	45.62±12.830	55.02±6.82	3.56	0.004
HDL-C•	55.82±13.156	49.11±4.11	3.45	0.002

Table 4: Lipid Profile in Pre-eclampsia with and without Maternal Complications

*SD Standard deviation, †LDL-C Low Density Lipoprotein Cholesterol, ‡ VLDL-C Very Low Density Lipoprotein Cholesterol, •HDL –C High Density Lipoprotein.

In the presence of maternal complications compared to women without complications, the mean serum cholesterol, TG, VLDL-C, LDL-C were high. The mean serum HDL-C value in those with maternal complications was decreased significantly (p-0.002).

Lipid profiles in various maternal complications are shown in table 5.

Complications	Cholesterol	Triglycerides	LDL -C	HDL-C	VLDL-C
None (n=91)	220.32	228.10	118.88	55.82	45.62
Abruption with DIC* (n=1)	290.00	280.00	187.00	47.00	56.00
HELLP Syndrome† (n=5)	250.00	263.20	149.16	48.20	52.64
Eclampsia (n=3)	303.33	293.33	193.33	51.33	58.67

Table 5: Lipid Profile in Preeclampsia with Maternal Complications

*DIC Disseminated intravascular coagulation, †HELLP syndrome Haemolysis Elevated Liver Enzyme Low Platelet count.

DISCUSSION: Placenta uses cholesterol for the synthesis of steroid hormones and fatty acids for the synthesis of the cell membrane. High-density lipoprotein (HDL) cholesterol under the influence of oestrogen increases from the 12th week and remains high throughout the gestational period.[6] The LDL-cholesterol, very low-density lipoprotein (VLDL) and triglycerides levels progressively increase in the second trimester.[6] In Preeclampsia, there is stimulation of system of inflammation and endothelial functions beyond the physiological limits of normal pregnancy.[7] In the modification of endothelial function and structure, lipids have important role. Free radical formation is promoted by hypercholesterolaemia.[7] Elevated triglyceride has a prothrombotic activity. TG shift the of LDL-C towards smaller denser, more atherogenic LDL particles.[7] LDL especially oxidised LDL increases vascular sensitivity and inhibits endothelial-dependent vasodilatation.[7]

In our study, we have observed that there was significant increase in serum total cholesterol, mean triglycerides, LDL-cholesterol, VLDL-cholesterol of the preeclampsia compared to normotensive women. Study by Pradnya Phalak et al reported significant rise in Serum Total cholesterol, Triglycerides, LDL Cholesterol and a significant decrease in HDL Cholesterol in pre-eclampsia group as compared to normal healthy pregnant women[8]. Preeclampsia was associated with elevated total cholesterol, non-HDL-C, and triglyceride levels, regardless of gestational age at the time of blood sampling, and with lower levels of HDL-C in the third trimester in a meta-analysis[9]. Maternal HDL-C levels during the third trimester of pregnancy are lower in preeclampsia women compared with normotensive pregnant women.[9]

There was no statistically significant difference in serum HDL-C levels between the two groups of women with and without preeclampsia in our study. In a study done by Wakatsuki A et al., the levels of HDL-C did not differ significantly between pre-eclamptic women and normal pregnant women which correlated with our study.[8]

The mean serum total cholesterol levels, Triglycerides, LDL-cholesterol and VLDL-cholesterol level significantly increased with increasing severity of preeclampsia. VLDL levels were also found increased in pre-eclampsia in the studies conducted by Kokio et al., and Teichmann et al., this is probably due to increased VLDL lipoproteins which accumulate over the maternal vascular endothelium, particularly those of uterine and renal vessels.[10] In severe preeclampsia with the development of maternal complications, the mean serum total cholesterol levels, Triglycerides, LDL-cholesterol and VLDL-cholesterol level further significantly increased. Maternal triglyceride concentrations in pregnancy were positively associated with the risk of GDM, preeclampsia among Chinese population.[3]

We found that there was a statistically significant decrease in HDL-C in women with severe form of the disease and in women with maternal complications.

The existence of maternal predisposing factors seems to be essential to explain why some pregnant women develop preeclampsia and why others do not. Preliminary evidence suggests that abnormal lipid metabolism could be one of these factors. Lipid alterations may promote oxidative stress in preeclampsia and may have an important role in the pathogenesis of preeclampsia. Women with a history of preeclampsia appear to have an increased risk of hypertension and coronary heart disease (CHD) in later life.[9] Generally, the earlier preeclampsia is diagnosed during the index pregnancy, the greater the likelihood of recurrence. So preeclampsia has to be predicted as early as possible to prevent maternal and foetal mortality and morbidity.

As lipids (lipid profile) are the indicators of endothelial dysfunction or oxidative stress in preeclampsia. They can be used as a predictor of preeclampsia. Abnormal lipid profiles were correlated with the severity of the disease and life threatening maternal complications. Lipid profile may be made use in monitoring the progress of the established preeclampsia. Thus, this can be used for prediction as well as risk stratification. Future studies with longterm followup of women with preeclampsia may help to identify the role of dyslipidaemia in recurrence of preeclampsia in future pregnancies and the development of stroke and coronary artery disease in later life. This may help to institute life style modifications and pharmacological interventions to reduce mortality and morbidity.

CONCLUSIONS: Our results suggest that dyslipidaemia, a marker of oxidative stress in pregnancy, is independently and significantly associated with an increased risk of preeclampsia, severity of the disease and increased the risk of maternal complications. Our findings highlighted the importance of abnormal maternal lipid metabolism in causing short-term and longterm adverse maternal outcomes.

REFERENCES

1. Wolde Z, Segni H, Woldie M. Hypertensive disorders of pregnancy in Jimma University Specialized Hospital. Ethiop J Health Sci 2011;21(3):147–154. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?

2. Al-Jameil N, Aziz Khan F, Fareed Khan M, et al. A Brief overview of preeclampsia. J Clin Med Res 2014;6(1):1-7. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?
3. Jin WY, Lin S, Hou RL, et al. Associations between maternal lipid profile and pregnancy complications and perinatal outcomes: a population-based study from China. BMC Pregnancy and Child birth 2016;16(1):60. Available from: http://dx.doi.org/10.1186/s12884-016-0852-9.
4. Siddiqui I. Maternal serum lipids in women with pre-eclampsia. Ann Med Heal Sci Res 2014;4(4):638–641.
5. Abubakar A, Mabrouk M, Girei AB, et al. Lipid profiles and platelets counts of pre-eclamptic women in selected rural areas of northern Nigeria. Webmed Central Physiology 2011;2(8):WMC002121.
6. Oliveira D, Pereira J, Rúben Fernandes. Metabolic alterations in pregnant women: gestational diabetes. J Pediatr Endocrinol Metab 2012;25(1-9):835–842.
7. Patel GJT, Patel PK, Priyanka G. Estimation of lipid profile in subjects of preeclampsia. J Obstet Gynaecol India 2011;61(4):399-403.
8. Pradnya Phalak, Tilak M. Study of lipid profile in pre-eclampsia. Indian Journal of Basic & Applied Medical Research 2012;5(2):405-409.
9. Spracklen CN, Smith CJ, Saftlas AF, et al. Systematic reviews and meta- and pooled analyses maternal hyperlipidaemia and the risk of preeclampsia: a meta-analysis. Am J Epidemiol 2014;180(4):346-358.
10. Agarwal V, Gupta BK, Vishnu A, et al. Association of lipid profile and uric acid with pre-eclampsia of third trimester in Nullipara women. J Clin Diagn Res 2014;8(7):4-7.