Preeclampsia and Lipid levels – a case control study

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Abstract

Introduction: Pre-eclampsia occurs in 3-5% of pregnancies and is an important cause of fetal and maternal morbidity and mortality worldwide. The most important feature in preeclampsia is hypertension which is due to vasospastic phenomenon in kidney, uterus, placenta and brain.

Objective: The objective of this study was to compare the mean lipid levels in preeclamptic and normal pregnancy.

Methods: This was a case control study and participants were selected on the basis of non-probability convenient sampling. Patients had singleton pregnancies, diagnosed as having pre-eclampsia according to the guidelines of Royal College of Obstetricians and Gynecologists. Pregnancy with preexisting hypertension, renal disease and gestational diabetes were excluded. Normotensive women with singleton pregnancies without any medical complication were taken as controls. Lipid profile was determined by enzymatic colorimetric method. Independent Sample *t*-test was used to compare BP and lipid levels between preeclamptic and control group, *p* value <0.05 was considered statistically significant. The study protocol was approved by ethical review committee.

Results: Mean triglycerides levels were (254 mg/dl ± 0.45 versus 116.59 ± 4.9) statistically significantly higher in preeclamptic as compared to normal controls ($p<0.05$). Mean HDL-C levels were (36.92 mg/dl ± 7.70 versus 51 ± 5.46) statistically significantly higher in preeclamptic as compared to normal controls ($p<0.05$). Mean LDL-C levels were (132.95 mg/dl

± 32.26 versus 99.36 ± 17.75) statistically significantly higher in preeclamptic as compared to normal controls (p<0.05).

Conclusion: Preeclamptic women had deranged lipid profile as compared to normal pregnant women.

Keywords: preeclampsia, lipid profile, hypertension, cholesterol, triglycerides, HDL-C, LDL-C

Introduction

Pre-eclampsia occurs in about 3-5% of pregnancies and is an important cause of fetal and maternal morbidity and mortality world wide.[1] Pre-eclampsia occurs during second and third trimester of pregnancy and it is more common in nulliparous women. It is characterized by blood pressure of 140/90 mm Hg or rise in systolic blood pressure of more than 30 mmHg or diastolic blood pressure of more than 15 mmHg after 20 weeks of gestation, in conjugation with proteinuria ≥300 mg/24 hours or greater or equal to 1+ or 100 mg/dl by dipstick response.[2,3]

The association of alteration of serum lipid profile in preeclampsia is well documented. An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular diseases and has a direct effect on endothelial dysfunction. The most important feature in preeclampsia is hypertension which is supposed to be due to vasospastic phenomenon in kidney, uterus, placenta and brain.[4] Altered lipid synthesis leading to decrease in PGI2:TXA2 ratio is also supposed to be an important way of pathogenesis in pregnancy induced hypertension.[5] Thus abnormal lipid metabolism seems important in the pathogenesis of preeclampsia. Pre-eclampsia and related disorders are known to affect function of various organs involved in lipid and lipoprotein metabolism. Several studies have shown that endothelial dysfunction is related to hyperlipidemia.[5] Significantly elevated plasma concentration of triglycerides (TG), phospholipids and total lipids and decreased high density lipoprotein – cholesterol (HDL-C) concentrations were found in women with pre-eclampsia in comparison to normal pregnancy.[6,7] In this context, the present study has been undertaken to compare the changes in lipid profile in normal pregnancy and preeclampsia. Preeclampsia tends to threaten maternal health and fetal viability adding to maternal and neonatal mortality and morbidity. As frequency of preeclampsia in developing countries is high where pregnant women have been found to utilize diets with lesser amounts of essential minerals and vitamins and the consequences of preeclampsia are alarming, there is a need for patients' education in recognizing the preventive measures of preeclampsia. It is hypothesized that lipid levels are deranged in preeclampsia but negligible studies have been conducted at Jinnah Postgraduate Medical Center. There is a need to explore these factors in our area. Hence the objective of this study was to compare the mean serum level of lipids in preeclamptic and normal pregnancy.

Materials & Methods

Study design and study cases

This study was conducted at the department of gynecology and obstetrics, Jinnah Postgraduate Medical Center in Pakistan from January till April 2012. The sample size software used for this study was openepi, confidence interval 95%, power 80%, group 1(cases) mean = 108.43 SD = 6.6, variance = 43.56, group 2 (controls) mean = 117.93 SD = 12.56, variance = 157.75. Sample size of group 1= 18, group 2 = 18, total sample size = 36. A total of 44 subjects were recruited to avoid the chances of type ii error. This was a case control study in which 22 cases and 22 controls were recruited and the sampling technique was non probability convenient sampling. Patients recruited in this study had singleton pregnancies diagnosed as having preeclampsia according to the Royal College of Obstetricians and Gynecologists, guideline no.10 (a),[8] when they presented with "Blood Pressure >140/90 mmHg on 2 separate occasions 4 hours apart in association with proteinuria >0.3gm in 24 hours." Pregnant women were diagnosed as having dyslipidaemia according to American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and prevention of Atherosclerosis[9] (Table 1). Normotensive women with singleton pregnancies without any previous history of hospitalization or any medical complication were taken as control. A detailed general physical examination was conducted and history was taken. The arterial blood pressure in the brachial artery was measured by using a simple mercury sphygmomanometer on right arm in a comfortable sitting position after 10 minutes of rest. Blood pressure was measured using both palpatory and auscultatory methods. The reported values represent the mean of two readings taken at 5 minutes interval. The blood samples were collected under strict aseptic measures. Each sample was labeled with patient's name and identification number. Samples were analyzed in one run at the end of the study. Lipid profile was determined by enzymatic colorimetric method. All the subjects included in the study were primigravidas with same maternal age, gestational age, height and weight. Pregnancy with preexisting hypertension, renal disease even without functional impairment diabetes preexisting or gestational and multiple pregnancies were excluded. Pregnant women of age ranging between 18-32 years and gestational age between 28-38 weeks were selected. All the subjects were briefed about the nature of the study and an informed consent was taken.

Statistical Analysis

Mean and standard deviation were calculated for preeclamptic and control groups. Descriptive statistics were calculated and data was presented as mean ± standard deviation. Systolic BP, Diastolic BP and lipid levels between preeclamptic and control group were analyzed using independent sample *t*-test and *p*-value <0.05 was considered statistically significant. All analyses were performed using statistical package for social sciences version 16 (SPSS, Inc., Chicago, IL, USA).

Study Limitation

Although the research has reached its aims, there was a limitation that needs to be mentioned. Due to time limit this research was conducted only on a small size of population who attended the department.

Ethical Considerations

The study protocol was approved by ethical review committee. Written informed consent was taken from the participants before their enrolment in this study. The participants' involvement in this study was voluntary and no financial incentives were provided to any study participant.

Results

Mean age was 29 years and mean gestational age was 36 weeks in preeclamptic and controls (Table 2). In preeclamptic mean systolic BP was 154 ± 0.55 mm Hg, in controls mean systolic BP was 116 ± 0.63 mm Hg. In preeclamptic mean diastolic BP was 102 ± 0.73 mm Hg, in controls mean diastolic BP was 69 ± 0.90 mm Hg. Mean Systolic and diastolic BP were statistically significantly higher in preeclamptic as compared to controls ($p<0.05$). Mean cholesterol levels were within normal range in preeclamptic and controls (179.53 mg/dL ± 7.24 versus 182.44 mg/dL ± 6.89) and were not statistically significant in preeclamptic as compared to controls ($p>0.05$). Mean HDL-C, levels were (36.92 mg/dL ± 7.70 versus 51 mg/dL ± 5.46) statistically significantly lower in preeclamptic as compared to normal controls ($p<0.05$). Mean LDL-C levels were (132.95 mg/dL ± 32.26 versus 99.36 mg/dL ± 17.75) statistically significantly higher in preeclamptic as compared to normal controls ($p<0.05$). Mean triglycerides levels were (254 mg/dL ± 0.45 versus 116.59 mg/dL ± 4.9) statistically significantly higher in preeclamptic as compared to normal controls ($p<0.05$). (Table 3)

Discussion

Hypertensive disorders during pregnancies, especially preeclampsia, are a pregnancy-specific disorder that affects 3-5%[10,11,12] of pregnant women worldwide. Preeclampsia is one of the most frequently encountered medical complications of pregnancy. Classically, the condition presents with new-onset hypertension and proteinuria after 20 weeks of gestation.[13] In developing countries where access to healthcare is limited, preeclampsia is a leading cause of maternal mortality, causing an estimated 60,000 maternal deaths worldwide per year. Furthermore, preeclampsia is the third biggest cause of maternal mortality in the United States and accounts for 20% of maternal deaths.[13] This prospective case control study is designed to evaluate blood serum levels cholesterol, lipoproteins, and triglycerides of pregnant preeclamptic women as lipid levels change substantially during gestation. The preeclamptic patients in our study presented significantly higher serum concentrations of triglycerides, LDL-C and lower serum concentrations of HDL-C in preeclamptic women indicating a risk factor as compared to controls. Although it is still unclear whether hypertriglyceridemia becomes a risk factor for preeclampsia or whether there is any causal association between them, high triglyceride levels seem to increase the risk of placental vascular disorders,[14] which trigger endothelial dysfunction, atherosclerosis and thrombosis.[15] The development of atherosclerosis in the placental spiral arteries of preeclamptic women indicates that elevated levels of triglycerides are involved in this disorder.[16] The principle modulator of this hypertriglyceridemia is estrogen as pregnancy is

associated with hyperoestrogenaemia. Estrogen induces hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL. This process may be modulated by hyperinsulinism found in pregnancy.[17] Moreover, this hypertriglyceridemia may be associated with hypercoagulability.[18] Hypertriglyceridemia could also be involved in the pathogenesis of hypertensive disorders during pregnancy.[19] Ray et al reported that women with elevated triglycerides had twice the risk of preeclampsia, studies that adjusted for confounders (age, BMI and parity) indicated that the risk was four times higher, compared with women with normal triglycerides.[20] It was also suggested that triglyceride assessment between 28 and 32 weeks could be predictive of preeclampsia.[21] Several other investigators have reported that hypertriglyceridemia could be involved in the pathogenesis of hypertensive disorders during pregnancy.[22-24]

In order to implement preventive healthcare protocols, it is important to identify risk factors for preeclampsia, these include nulliparity, multifetal gestations, previous history of preeclampsia, obesity, diabetes mellitus, high blood pressure, edema and proteinuria, age >35 years and smoking. These endanger both mother and child during second half of pregnancy. Women having elevated cholesterol and blood pressure before pregnancy are more at risk and should be followed more closely by their obstetrician. Although the exact etiology and genetics are not fully understood but preventive measures should be taken, women should receive adequate counseling to urge them to adopt healthier habits and lifestyles and to seek periodic checkups, in order to detect diseases in its early stages, before irreparable damage or even death. Interventional studies are needed to determine whether pre-pregnancy weight reduction and dietary modification can lower the risk of pre-eclampsia. In a systematic review of the literature, Bellamy et al reported that women with a history of preeclampsia presented increased risk of cardiovascular disease (Relative Risk, RR = 3.7), hypertension (RR = 2.16), ischemic heart attack (RR = 1.81), venous thromboembolism (RR = 1.79) and death (RR = 1.49).[25] These findings confirm the possible association between hypertension during pregnancy and future cardiovascular disease. In order to execute preventive healthcare protocols, it is important to recognize patients who are at risk of increasing cardiovascular diseases. Enhanced understanding of lipid metabolism, abnormalities and how these changes relate with the endothelial dysfunction of preeclampsia is fundamental from a public health perspective.

Conclusion

Preeclamptic women had deranged lipid profile due to abnormal lipid metabolism. Increased triglyceride levels and delayed triglycerides clearance and high blood pressure are the grounds for the development of preeclampsia. This relationship 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. Future studies on hypertriglyceridemia and preeclampsia associations might prove valuable information in understanding its pathophysiology and the development of preventive and therapeutic strategies that allow close vigilance and easy referral for the pregnant women at risk that subsequently improves health of the community.

Recommendations

Women with blood pressure greater than 140/90 mmHg with or without proteinuria should be referred to a day assessment or obstetric unit. Antiplatelet therapy, in particular, low dose (<75 mg) aspirin, reduces the risk of pre-eclampsia by around 15% for women at both low and high risk. There appears to be a similar reduction in the risk of perinatal death. Magnesium sulfate is recommended for the treatment of women with eclampsia in preference.

Conflict of Interest The authors declare that they have no competing interests.

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Table 1: American Association of Clinical Endocrinologists' Guidelines for Management of Dyslipidemia and prevention of Atherosclerosis [9]
Optimal/Near-Optimal, Borderline, and High-Risk Serum Lipid Concentrations

Lipid	Optimal/near-optimal serum concentration	Borderline serum concentration	High-risk/very high-risk serum concentration
TC, mg/dL	<200	200-239	≥240
HDL-C, mg/dL	≥60 (negative risk factor)	50-59	<50
LDL-C, mg/dL	<100 optimal (100-129 near-optimal)	130-159	160-189 high ≥190 very high
TG, mg/dL	<150	150-199	200-499 high ≥500 very high

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides.

Table 2: Demographic and Clinical Characteristics of Controls and Pre-eclamptic subjects

Variables	Preeclamptic Mean ± SD or %	Controls Mean ± SD or %
Age (years)	29	29
Ethnicity		
Sindhi	45.5%	54.5%
Punjabi	31.8%	27.3%
Pathans	22.7%	18.2%
BMI	22 .94 ± 0.67	22.92 ± 0.61
Gestational age (weeks)	36	36

Abbreviations: BMI: Body Mass Index

Table 3: BP & Lipid profile of cases and controls

Clinical Parameters	Preeclamptic	Controls	*p* values
Systolic BP	154 ± 0.55	116 ± 0.63	<0.05
Diastolic BP	102 ± 0.73	69 ± 0.90	<0.05
Total Cholesterol, mg/dL	179.53 ± 7.24	182.44 ± 6.89	>0.05
HDL-C, mg/dL	36.92 ± 7.70	51 ± 5.46	<0.05
LDL-C, mg/dL	132.95 ± 32.26	99.36 ± 17.75	<0.05
Triglycerides	254 ± 0.45	116.59 ± 4.9	<0.05

Abbreviations: BP: Blood Pressure