Association of Lipid Profile with Preeclampsia

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Abstract

Background: Preeclampsia is a pregnancy specific disorder characterized by hypertension and proteinuria after 20 weeks of gestation. Abnormal lipid profile is known to be associated with development of symptoms of preeclampsia. Obective of the study includes evaluating the association oflipid profile with preeclampsia.

Materials and methods: This case control study was carried out in the Department of Obstetrics & Gynecology, Bangabandhu Sheikh Mujib Medical University (BSMMU) Dhaka, between 1st October 2017 and 30th September 2018. 46 pregnant women clinically diagnosed as preeclampsia were selected as cases (Group I) and equal number of age, parity and gestational age group matched apparently healthy normotensive pregnant women were selected as control (Group II) for the study. Fasting blood sample were collected and estimated for serum lipid profile. Demographic data and lipid profile were analyzed by using student t-test and chi square test, a p-value of <0.05 was considered significant. Odds ratio with 95% Confidence Interval was calculated to assess the risk. Pearson's correlation coefficient test and Spearman's rank correlation coefficient test were done to assess the correlation.

Results: Mean total cholesterol in preeclampsia group was 245.2±59.9 mg/dl and normal pregnancy group was 192.5±32.5 mg/dl. Mean HDL-C in preeclampsia group was 50.9±11.3 mg/dl and in normal pregnancy group was 50.3±11.1m g/dl. Mean LDL-C in preeclampsia group was 141.1±54.1 mg/dl and normal pregnancy was 100.9±31.8 mg/dl. Mean triglycerides in preeclampsia group was 272.5±84.8 mg/dl and in normal pregnancy group was 178.9±48.2 mg/dl. Total cholesterol, LDL-C and triglycerides, all were increased in preeclampsia as compared to normal pregnancy. These were statistically significant (p<0.05) but no significant difference was noted in HDL-C level between the two groups (p>0.05). Significant positive correlation between blood pressure and levels of total cholesterol, LDL-C and triglycerideswas revealed by Pearson's correlation test. Spearman's rank correlation coefficient test also revealed positive correlation of total cholesterol and triglycerides with the severity of preeclampsia.

Conclusion: Dyslipidemia is significantly evident in preeclampsia and may play an important pathological role. Estimating serum lipid profile is a simple screening test, helps to recognize dyslipidemia in early second trimester of pregnancy who are at risk of preeclampsia.

Key words: Dyslipidemia; Lipid Profile; Preeclampsia.

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Introduction

Preeclampsia is a common medical complication of pregnancy. It's incidence has continued to increase worldwide. Annually it accounts for about 50,000 deaths worldwide. Incidence of preeclampsia is about 2% to 8% of all pregnancies. Between 10% and 15% of maternal deaths occur due to preeclampsia and eclampsia.[1] According to various reports, the incidence of preeclampsia is between 1.8% and 16.7% in the developing countries.[2] In Bangladesh 20% of all maternal death occurs due to preeclampsia and eclampsia and it is the second most common cause of maternal death.[3]

Preeclampsia is a hypertensive disorder in pregnancy, which is characterized by the occurrence of new onset of persistent hypertension with a new onset of proteinuria or in absence of proteinuria presence of new onset end organ damage, usually after 20 weeks of gestation.[4]

Preeclampsia may cause maternal mortality and serious morbidity like stroke, convulsion, cerebral and pulmonary oedema, renal and hepatic failure, abruptio placenta or disseminated intravascular coagulation. It also causes fetal and neonatal complication such as intrauterine growth restriction, stillbirth and iatrogenic prematurity.[5]

As preeclampsia is the 3rd common cause of maternal death in the world, the search for causative factor and pathogenesis has therefore been a major focus of obstetrical investigations.[6] The specific etiology and pathophysiology of preeclampsia are still unknown in spite of several decade studies. It is one of the major causes of maternal mortality in developed and developing countries. To avoid complications, it is very important for early diagnosis of preeclampsia.

Preeclampsia constitutes a multifactorial disease that involves genetic, metabolic, immunological and environmental factors.It includes the presence of endothelial dysfunction that develops before the onset of clinical symptoms. Many efforts have been made in recent years to define pathophysiological factors and to identify possible screening methods.[7] Several theories, including inadequate placental implantation, immune response and angiotensinogen II sensitivity have been proposed. Placental hypoxia and/or ischemia, excessive oxidative stress and endothelial cell dysfunction have been implicated.[8]

Lipid profile changes during pregnancy occur because of physiological adaptation to the state of pregnancy. There are increases in the blood concentration of cholesterol and triglycerides to supply the developing fetus.[9] An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular disease 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.[10] Altered lipid synthesis leading to a decrease in PGI_2: TXA_2 ratio is also supposed to be an important way of pathogenesis in pregnancy induced hypertension.[11]

In normal pregnancy, plasma lipids are at the atherogenic levels, even more so in preeclampsia.[12] The preeclamptic women had disturbed lipid profile due to abnormal lipid metabolism. Increased triglycerides levels, delayed triglycerides clearance and high blood pressure are the reasons for development of preeclampsia.[13] The principal modulator of hypertriglyceridemia is estrogen which is also associated with hyperestrogenemia during pregnancy. About 83% of dyslipidemic women developed gestational hypertension, preeclampsia, eclampsia and also developed significant level of perinatal complications like preterm (18.05%) labor, IUGR (15.28%) and IUD (13.39%).[14]

The present study was designed to determine the levels of lipid profile in serum samples of pregnant women diagnosed with preeclampsia without any history of previous PE and comparing them with those of the control group to verify the possible association between lipid profile and PE.

Materials and methods

This case control study was carried out in the Department of Obstetrics & Gynecology, Bangabandhu Sheikh Mujib Medical University, Dhaka between 1st October 2017 and 30th October, 2018. Ethical clearance for the study was taken from the institutional review board, BSMMU. A total of 92 singleton pregnant women between 18 and 36 years of age attending Out patient Department and admitted in the Department of Obstetrics and Gynecology, BSMMU at their second and third trimester (>20-40 weeks) were included in this study. Out of which 46 with preeclampsia considered as case (Group I) and another 46 without preeclampsia were considered as control of the study (Group II). Pregnant women with chronic hypertension, Pregnancy Induced Hypertension (PIH) without proteinuria, DM, GDM, Multiple pregnancy, maternal history of taking antithyroid drug, previous history of any thyroid disorder, thyroid surgery, chronic renal disease, chronic liver disease were excluded from this study. Purposive sampling was done according to the availability of the participants, who had voluntarily joined this study. The purpose and procedures of study were discussed with the participants and informed written consent was obtained. An interviewer administered questionnaire was used for data collection. Detailed socio-demographic data, obstetric history, menstrual history, LMP to calculate the gestational age, family history and medical history were recorded in a predesigned data sheet. Then physical examination, anthropometric measurements (Height, weight) were taken and obstetric examination was performed and recorded. After 10 minutes of rest, BP was measured following standard procedure for systolic (SBP) and diastolic (DBP). When blood

pressure was found elevated on initial assessment, the measurement was repeated at least 4 to 6 hours apart to confirm hypertension. The subjects with blood pressure ≥140/90 mm of Hg on two occasions were evaluated for presence of urinary protein by Dipstick method to establish the diagnosis of preeclampsia. When proteinuria found > 1+ in collected urine sample, then the diagnosis of preeclampsia was established and they were selected as cases. The subjects who were found normotensive were selected as control. After selecting cases and controls 5ml of ante-cubital venous blood sample was collected from each subject with all aseptic precaution after an overnight fasting. Following parameters were measured in all blood samples collected from the study subjects: Serum Total cholesterol, Serum HDL, Serum LDL, Serum Triglycerides. Statistical analysis of the results was obtained by using Windows based computer software devised with Statistical Packages for Social Sciences (SPSS-22).

Results

Table I Distribution of the study patients by fasting serum lipid profile (n=92)

Lipid profile (mg/dl)	Group-I (n=46)		Group-II (n=46)		OR (95% CI)	p value
	n	%	n	%		
Total Cholesterol						
>200	36	78.3	15	32.6	7.44 (2.67 to 21.28)	0.001^{s}
≤200 (normal)	10	21.7	31	67.4		
HDL-C						
<40	7	15.2	6	13.0	1.20 (0.32 to 4.49)	0.765^{ns}
≥40 (normal)	39	84.8	40	87.0		
LDL-C						
≥130	26	56.5	7	15.2	9.66 (3.13 to 31.03)	0.001^{s}
< 130 (normal)	15	32.6	39	84.8		
Triglycerides						
≥150	44	95.7	34	73.9	7.76 (1.49 to 54.05)	0.003^{s}
<150 (normal)	2	4.3	12	26.1		

Table I shows 78.3% patients had total cholesterol ≥200 mg/dl in group I and 32.6% in group II (OR 7.44). In HDL-C, 84.8% patients found ≥40 mg/dl in group I and 87.0% in group II (OR 1.20). In LDL-C, 56.5% patients were found ≥130 mg/dl in group I and 15.2% in group II (OR 9.66). Triglycerides, 95.7% was found ≥150 mg/dl in group I and 73.9% in group II (OR 7.76). p values of total cholesterol, LDL-C and triglycerides were statistically significant (p<0.05).

Table II Results of lipid profile in study subjects (n=92)

Lipid profile (mg/dl)	Group-I (n=46) Mean±SD	Group-II (n=46) Mean±SD	p value
Total Cholesterol	245.2 ±59.9	192.5 ±32.5	0.001^{s}
HDL-C	50.9 ±11.3	50.3 ±11.1	0.798^{ns}
LDL-C	141.1 ±54.1	100.9 ±31.8	0.001^{s}
Triglycerides	272.5 ±84.8	178.9± 48.2	0.001s

s=significant,
ns=not significant.

Table II shows the mean TC was found 245.2±59.9 mg/dl in group I and 192.5±32.5 mg/dl in group II. Mean HDL-C found 50.9±11.3 mg/dl in group I and 50.3±11.1 mg/dl in group II. The mean LDL-C was found 141.1±54.1 mg/dl in group I and 100.9±31.8 mg/dl in group II and mean TG was found 272.5±84.8 mg/dl in group I & 178.9±48.2 mg/dl in group II. The differences of total cholesterol, LDL-C and TG were statistically significant (p<0.05) between two groups.

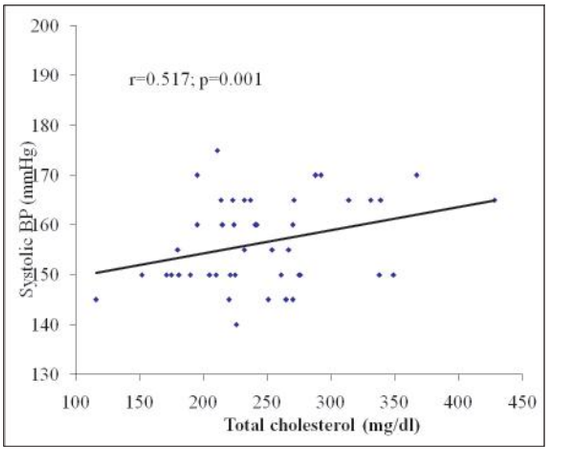

Figure 1 Scatter diagram showing positive Pearson's correlation (r=0.517, p=0.001) between total cholesterol and systolic BP in preeclamptic group

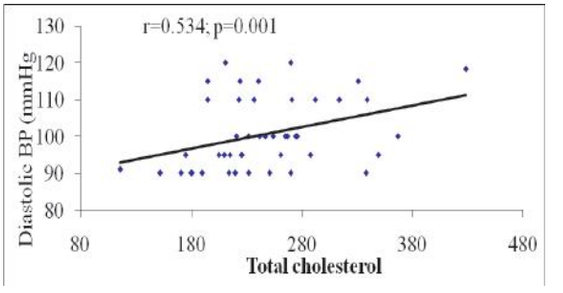

Figure 2 Scatter diagram showing positive Pearson's correlation (r=0.534, p=0.001) between total cholesterol and diastolic BP in preeclamptic group

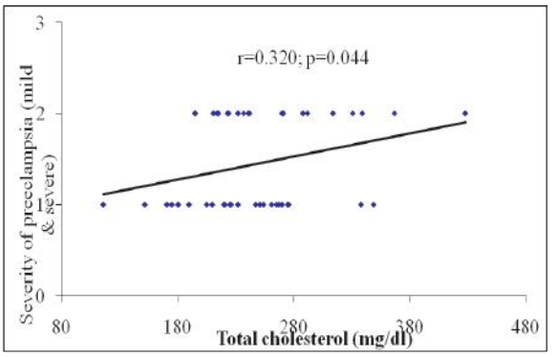

Figure 3 Scatter diagram showing positive Spearman's correlation coefficient (r=0.320, p=0.044) between total cholesterol and Severity of preeclampsia

Discussion

This study observed 78.3% patients had Total Cholesterol (TC) >200mg/dl in group I and 32.6% in group II which indicates>200mg/dl had OR 7.44 (95% C.I, 2.67 to 21.28) times significantly increase to develop preeclampsia. The mean TC was found 245.2±59.9 mg/dl in group I and 192.5±32.5 mg/dl in group II, which was significantly ($p<0.05$) higher in group I. It was observed in this study that 84.8% patients had HDL-C ≥ 40mg/dl in group I and 87.0% in group II. The mean HDL-C was found 50.9±11.3 mg/dl in group I and 50.3±11.1 mg/dl in group II, which was almost alike ($p>0.05$) between two groups. Regarding the LDL-C level, 56.5% patients had LDL-C ≥ 130mg/dl in group I and 15.2% in group II which indicates that LDL-C ≥ 130mg/dl had OR 9.66 (95% C.I, 3.13 to 31.03) times significantly increase to develop preeclampsia. The mean LDL was found 141.1±54.1 mg/dl in group I and 100.9±31.8 mg/dl in group II, which is significantly ($p<0.05$) higher in group I. Similarly about Triglyceride (TG), 95.7% patients had ≥ 150mg/dl in group I and 73.9% in group II which indicates ≥ 150mg/dl had 7.76 (95% C.I, 1.49 to 54.05) times significantly increase to develop preeclampsia. The mean triglyceride was found 272.5±84.8 mg/dl in group I and 178.9±48.2 mg/dl in group II, which is significantly ($p<0.05$) higher in group I.

Thathagari and Kumar conducted a study and observed that higher mean of TC (198.5±18.91), HDL-C (50.63±9.35), LDL-C (84.5±16.16) and TG (74.92±11.95) mg/dl in preeclampsia compared to normal pregnancy, which was statistically significant.[15] Among all parameters the differences in TC levels the two groups were very high and HDL-C levels were less. Another study was done by Gohil and colleagues which presented the concentration of TC (232.0±2.9 vs 219.1±3.1), LDL-C (135.8±4.1 vs 115.7±3.4) and TG (270±2.1 vs 215.2±1.9) mg/dl were found to be significantly increased in preeclamptic females as compared to normal pregnant females. HDL-C level was significantly lower between two groups (42.1±1.9 vs 60.3±1.2) mg/dl.[16]

Another similar study conducted by Das et al. showed that in preeclamptic group mean TG 212.75±50.29 mg/dl was increased significantly ($p<0.02$) as compared to normotensive pregnant women 185.60±40.67 mg/dl.[17] Other parameters were not significantly changed TC (202.1±37.37 vs 192.35±42.86), LDL-C (113.87±26.21vs 111.63±41.20) mg/dl between preeclamptic and normal pregnancy group respectively.

The preeclamptic patients in Kalar and colleague's study presented significantly higher serum concentrations of TG (254±0.45 vs 116.59), LDL-C (132.95±32.26 vs 99.36±17.75) mg/dl which were statistically significant in preeclamptic as compared to normal controls ($p<0.06$).[18] They also showed significant lower mean concentration of HDL-C (36.92±7.70 vs 51±5.46) mg/dl in preeclamptic women indicating a risk factor as compared to controls. Total cholesterol (179.53±7.24 vs 182.44±6.89) mg/dl were not statistically significant between cases and controls. Regarding the association between serum lipid profile level with mild and severe preeclampsia group it was observed that the mean total cholesterol was found 228.92±53.28 mg/dl in mild preeclampsia and 266.45±62.71 mg/dl severe preeclampsia. The mean triglycerides was found 222.38±38.38 mg/dl in mild preeclampsia and 337.70±84.67 mg/dl severe preeclampsia. The differences of total cholesterol and triglycerides were significantly ($p<0.05$) higher in severe preeclampsia group, however HDL-C (51±10.5 vs 50.90±12.51) mg/dl and LDL-C (144.27±61.53 vs 135.53±39.44) mg/dl were not significant between mild and severe preeclampsia. Ahmed and colleagues conducted a study which showed mean level of total cholesterol 229.47±12.61 mg/dl, LDL-C 152.13±11.03 mg/dl and TG, 210.57±14.09 mg/dl

in severe preeclamptic patients was significantly higher comparative as mild preeclamptic patients.[19] Mean HDL-C was lower in severe PE women than mild PE women.In this study we observed that there was positive significant correlation among systolic BP with total cholesterol (r=0.517, p=0.001), LDL (r=0.385, p=0.001) and triglyceride (r=0.658, p=0.001) in preeclampsia group. Similarly, there was positive significant correlation was also found among diastolic BP with total cholesterol (r=0.534, p=0.001), LDL-C (r=0.371, p=0.001) and triglycerides (r=0.669, p=0.001) in preeclampsia group. Kashinakunti and colleagues did a similar study which showed positive correlation between the systolic blood pressure and triglycerides (r=0.721) and also between diastolic blood pressure and triglycerides (r=0.583).[20] Another study conducted by Winkler and colleagues showed positive correlation between triglycerides and diastolic blood pressure (r=0.631, p<0.001) and negative correlation between DBL and LDL-C (r= -0.50; p=0.002).[12]

Limitation

The present study was conducted within a short period of time. The study population was selected from one selected hospital, so that the results of the study may not be reflect the exact picture of the country. Other predictors of preeclampsia (Placenta growth factor, C-reactive protein and uterine artery mean resistance index) were not observed and their association was not determined with lipid profile.Small sample size with purposive sampling was also a limitation of the present study.

Conclusion

This study concluded that dyslipidemia is significantly evident in preeclampsia and plays an important pathological role. There is elevation of serum lipids among preeclamptic womenin comparison to normal pregnancy. There is also increase in cholesterol, LDL, triglyceride from mild to severe preeclampsia significantly.

Recommendation

Further longitudinal studies with larger sample size with multicentric approach and long duration are needed to establish the actual relationship of dyslipidemia with preeclampsia. This will strengthen the outcome of this study result.

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Contribution of authors

RA-Conception, acquisition of data, drafting & final approval.
NH-Acquisition of data, data analysis, drafting & final approval.
NH-Interpretation of data, critical revision & final approval.
NK-Data analysis, drafting & final approval.
FI-Interpretation of data, critical revision & final approval.
TH-data analysis, critical revision & final approval.
RHS-Design, acquisition of data, drafting & final approval.

Disclosure

All the authors declared no competing interests.

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