Changes in Lipid Profile in Preeclampsia

Sanzida Nahid[1], Nahid Parveen [2], Shahnaj Begum [3],

ABSTRACT

Background & objective: Preeclampsia is an age-old pregnancy-specific disorder. Numerous theories and ideas have been advanced on its etiology, pathophysiology, and complications, but commendable progress in preventing this long-standing disorder has not yet been made. The relationship between altered blood lipid levels and preeclampsia is currently a topic of discussion. The present study was to ascertain whether serum lipid levels are associated with preeclampsia.

Methods: The present case-control study was carried out at the Department of Obstetrics & Gynaecology, Dhaka Medical College Hospital and Department of Obstetrics & Gynaecology, BSMMU, Dhaka over a period of one year between January 2011 to December 2011. Pregnant women in their 3rd trimester with preeclampsia were included as cases, while normal pregnant women at term without preeclampsia were included as controls. An equal number of cases (n = 75) and controls (n = 75) were selected consecutively. While the exposure variable was preeclampsia, the outcome variable was dyslipidaemia, which was defined as either total cholesterol:HDL ratio >4.5 or triglyceride:HDL ratio > 3.5.

Result: The cases and the controls were almost identical in terms of age. The gestational age was also comparable between groups. The preeclamptic patients were predominantly primigravidae (57.3%) and overweight or obese (85.3%). Past history of PET was found in 12% cases as opposed to none in the controls. The prevalences of elevated serum total cholesterol (TC), LDL-C, and triglycerides (Tg) were considerably higher in the case group than those in the control group, although the differences were not statistically significant. However, the prevalence of low HDL-C was significantly higher in the former group than that in the latter group (56% vs. 14.7%, p < 0.001). The incidences of raised total cholesterol and HDL ratio > 4.5 and raised triglyceride and HDL ratio > 3.5 were observed to be significantly higher in the case group than those in the control group (p< 0.001 and p < 0.001 respectively). The likelihood of having raised TC:HDL ratio was estimated to be 10.1 (95% CI = 4.2 - 23.9) times higher and that of raised TG:HDL ratio was 3.7(95% CI = 1.9 - 7.4) times higher in the case group than those in the control group.

Conclusion: The total cholesterol:HDL ratio and triglyceride:HDL ratio increase significantly in preeclamptic women compared to that in normal pregnant women. However, the alteration is presumably caused by a significant lowering of HDL cholesterol, the total cholesterol and triglyceride do not experience any significant change.

Keywords: Preeclampsia, lipid profile, total cholesterol:HDL, triglyceride:HDL, etc.

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INTRODUCTION:

Preeclampsia is a pregnancy-specific, multi-system disorder that presents a major health problem for both mothers and their babies. It is a major cause of maternal mortality, especially in developing countries.[1,2] Nearly 7-10% of pregnancies are complicated with preeclampsia with higher rates in women with preexisting hypertension, diabetes mellitus or previous history of preeclampsia, although mechanisms underlying preeclampsia are not well understood.[3] Around 11% of maternal death is attributed to preeclampsia in Bangladesh.[4] Preeclampsia is defined

Author's information:

[1] **Dr. Sanzida Nahid,** *MS (Obstetrics & Gynecology), Assistant Professor, Sir Salimullah Medical College & Mitford Hospital, Dhaka.*

[2] **Dr. Nahid Parveen,** *MS (Obstetrics & Gynaecology), Assistant Professor, Sylhet MAG Osmani Medical College, Sylhet.*

[3] **Dr. Shahnaj Begum,** *MS (Obstetrics & Gynecology), Assistant Professor, Sheikh Hasina National Institute of Burn and Plastic Surgery, Dhaka.*

Correspondence: **Dr. Sanzida Nahid,** *Mobile: 01778901206, E-mail: sanzida.mithun@gmail.com*

as a pregnancy-specific syndrome observed usually after the 20th week of gestation with systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg accompanied by significant proteinuria with or without oedema. During preeclampsia, the oxidative, coagulative, & vasomotor balance are altered due to increased sensitivity to angiotensin II associated with reduced synthesis of vasodilator prostaglandins, sympathetic nervous system hyperactivity, hyperlipidemia associated with lipo-peroxide synthesis and incomplete implantation of cytotrophoblast in maternal spiral arteries. Women with preeclampsia, are at increased risk of abruptio placentae, acute renal failure, cerebrovascular and cardiovascular complications, and maternal death.[5] Preeclampsia is not only the cause of maternal mortality but it is a leading cause of premature delivery and foetal growth retardation. It is associated with increased lipid peroxidation in the maternal circulation and in the placenta.[6] The majority of adverse pregnancy outcomes occur in women who develop severe gestational hypertension or pre-eclampsia prior to 3 weeks of gestation or preexisting vascular disease.[7]

Despite much active research for years, the exact aetiology of this fatal disorder remains unknown. Many theories and concepts have been put forward regarding its aetiology, pathogenesis, and complications but commendable success has not so far been achieved to prevent this age-old disorder. The association between the alteration of serum lipids and morbidity, and mortality in preeclampsia is presently a talked-about issue. In a study conducted in Peruvian women, HDL-cholesterol concentration was 9% lower in preeclamptic patients than that in normal pregnant women.[8] De et al[9] also reported a significant decrease in HDL-C in preeclamptic and eclamptic pregnant women. Several studies, on the other hand, showed that the most dramatic change in the lipid profile in normal pregnancy is serum hypertriglyceridaemia, which may be as high as 2 - 3 folds in the third trimester compared to the levels in non-pregnant women.[9-11] Increased Tg found in pregnancy-induced hypertension is likely to be deposited in predisposed vessels, such as the uterine spiral arteries, and contribute to endothelial dysfunction.[12] However, much controversy prevails

with regard to changes in total cholesterol. While Hubel and his associates[13] have found a significant increase in total cholesterol levels in preeclampsia, De et al[9] did not observe any alteration in total cholesterol levels in the same condition. As different researchers put forward different opinions about changes in serum lipids during preeclampsia, it is difficult to generalize the findings to reference populations. The present study was designed to evaluate the alteration in lipid profiles in preeclamptic women compared to that in normal pregnant women.

METHODS:

This cross-sectional study was carried out in the Department of Obstetrics & Gynaecology, Dhaka Medical College Hospital, and Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital over a period of 1 year from January 2011 to December 2011. Ethical clearance was taken from the Institutional Review Board of BSMMU. Pregnant women in their 3rd trimester with preeclampsia were included as cases, while normal pregnant women at term without preeclampsia were included as controls. A case of preeclampsia was defined as a pregnancy-specific syndrome (systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg accompanied by significant proteinuria with or without oedema) observed after the 20th week of gestation, while a control was defined as a pregnant woman at term with systolic and diastolic blood pressures < 140 and < 90 mmHg respectively with trace or absence of proteinuria. A total of 75 cases and 75 controls were consecutively included in the study. However, pregnant women with diabetes mellitus, cardiac diseases, renal insufficiency, pyelonephritis, hepatitis, smoking habit, known hyper or hypothyroidism, SLE, or twin pregnancy were excluded from the study. While the exposure variable was preeclampsia, the outcome variable was dyslipidaemia, which was defined as either total cholesterol:HDL ratio > 4.5 or triglyceride:HDL ratio > 3.5. Data were processed and analyzed using SPSS (Statistical Package for Social Sciences) version 16.0. The test statistics used to analyse the data were descriptive statistics, Chi-square (χ^2) Probability Test, and Odds Ratio (OR) with its 95%

confidence interval (CI). The level of significance was set at 0.05 and a p-value < 0.05 was considered significant.

RESULTS:

Table I shows the distribution of demographic characteristics between the study groups. Out of 75 cases, 72% were between 20 - 30 years, followed by 22.7% < 20 years and 5.3% > 30 years old. In the control group, 84% were 20 - 30 years, 13.3% were below 20 years and 2.7% were > 30 years old. The cases and controls were almost similar in terms of age (p = 0.169). The majority of the cases (84%) and controls (78.1 %) belonged to lower social classes (p = 0.352). The proportion of overweight and obese subjects was significantly higher in the case group (85.3%) than that in the control group (69.3%) (p = 0.019).

Majorities of the case and control groups had gestational age below 37 weeks (p = 0.500). Approximately 58% of the cases and 34.7% of controls were primigravida and the rest of the respective groups were multigravida. Of the 75 cases, 65% had severe proteinuria (+++) and the rest 35% had mild proteinuria. Some 12% of the cases had a past history of preeclampsia as opposed to none of the control group (p = 0.002) (Table II). The prevalence of elevated serum TC, LDL-C and Tg were considerably higher in the case group than those in the control group, although the differences were not statistically significant (p = 0.185, p = 0.311, and p = 0.275 respectively). However, the prevalence of low HDL-C was significantly higher in the former group than that in the latter group (56% vs. 14.7%, p < 0.001) (Table III).

Table IV explains the association of preeclampsia with total cholesterol:HDL (TC:HDL) ratio and triglyceride:HDL (Tg:HDL) ratio. The incidences of raised total cholesterol:HDL ratio > 4.5 and raised triglyceride:HDL ratio > 3.5 were observed to be significantly higher in the case group than those in the control group (p < 0.00.1 and p < 0.001 respectively). The likelihood of having raised TC:HDL ratio was estimated to be 10.1(95% CI= 4.2 -23.9) times higher and that of raised Tg:HDL ratio was 3.7(95% CI= 1.9 - 7.4) times higher in the case group than those in the control group.

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Table I: Comparison of demographic characteristics between groups

Demographic characteristics	Group		p-value
	Case (n=75)	Control (n=75)	
Age (years)#			
< 20	17(22.7)	10(13.3)	
20-30	54(72.0)	63(84.0)	
> 30	4(5.3)	2(2.7)	
Mean ±SD	22.9 ± 4.1	23.8 ± 3.7	0.169
Socioeconomic status*			
Lower class	63(84.0)	57(78.1)	0.352
Middle class	12(16.0)	16(21.9)	
BMI (kg/m2)			
< 25 (Normal)	11(14.7)	23(30.7)	
≥25 (Overweight & Obese)	64(85.3)	52(69.3)	0.019
Mean ± SD	28.3 ± 3.3	26.1 ± 2.4	

#Data were analysed using **Student's t-Test** and were presented as **mean ± SD**; *data were analysed using **Chi-square** (χ^2) **Test**. Figures in the parentheses indicate corresponding percentages.

Table II: Distribution of cases & controls by obstetric characteristics

Obstetric characteristics	Group		p-value
	Case (n=75)	Control (n=75)	
Gestational age (weeks)*			
< 37 (preterm)	73(97.3)	72(96.0)	0.500
≥37 (term)	2(2.7)	3(4.0)	
Gravida*			
Primigravida	43(57.3)	26(34.7)	0.001
Multigravida	32(42.7)	49(65.3)	
Past history of preeclampsia#	9(12.0)	0(0.0)	0.002

*Data were analysed using **Chi-square** (χ^2) **Test**; #**Fisher's Exact Test** was done to analyze the data. Figures in the parentheses indicate corresponding percentages.

Table III: Association between serum lipids and preeclampsia

Lipid profile#	Group		p-value
	Case (n=75)	Control (n=75)	
Total cholesterol			
Normal (< 200 mg/dl)	40(53.3)	48(64.0)	0.185
Raised (≥200 mg/dl)	35(46.7)	27(36.0)	
Triglyceride			
Normal (< 150 mg/dl)	44(58.7)	50(66.7)	0.311
Raised (≥150 mg/dl)	31(41.3)	25(33.3)	
LDL			
Normal (<130 mg/dl)	51(68.0)	57(76.0)	0.275
Raised (≥130 mg/dl)	24(32.0)	18(24.0)	
HDL			
Low (<40 mg/dl)	42(56.0)	11(14.7)	< 0.001
Normal (≥40 mg/dl)	33(44.0)	64(85.3)	

#Data were analysed using **Chi-square** (χ^2) Test. Figures in the parentheses indicate the corresponding percentage;

Table IV: Association between preeclampsia and dyslipidaemia				
Dyslipidaemia	**Group**		**OR (95% CI of OR)**	**p-value**
	Case (n=75)	Control (n=75)		
Total cholesterol: HDL[#]				
> 4.5	67(89.3)	34(45.3)	10.1(4.2 -23.9)	< 0.001
≥ 4.5	8(10.7)	41(54.7)		
Triglyceride: HDL[#]				
> 3.5	48(64.0)	24(32.0)	3.7(1.9 - 7.4)	< 0.001
≤ 3.5	27(36.0)	51(68.0)		

#Data were analysed using **Chi-square** (χ^2) Test. Figures in the parentheses indicate the corresponding percentage;

DISCUSSION:

Although preeclampsia is an age-old disorder of pregnancy, its exact aetiology is still a mystery. Many theories and concepts have been put forward regarding its etiology and pathogenesis; of them, the association between preeclampsia and dyslipidemia is a recent one. It has become a much-talked-about issue in the medical community. Many studies have been conducted on the changes in different lipids in the serum during pregnancy. Several of them have documented the association between preeclampsia & dyslipidemia. Reduced HDL,[14] increased triglycerols,[8] LDL cholesterol[15], & small dense LDL,[13] have consistently been reported in the preeclamptic population.

In the present study, the cases and the controls were almost identical in terms of age and gestational age. Overweight/obesity was significantly more common in the case group than that in the control group. Preeclamptic patients were primigravida and had a significant history of past preeclampsia. More than half (56%) of the preeclamptic women had low HDL cholesterol compared to 14.7% of the normal pregnant women (p < 0.001). The prevalence of raised serum total cholesterol, serum LDL and serum triglycerides were considerably higher in the former group than those in the latter group, although the differences were not statistically significant. Our data are in line with previous studies reporting the existence of abnormal lipid metabolism in women with a history of preeclampsia.[16-18] In preeclampsia the levels of serum TC, LDL-C, Tg are reported to be higher and the HDL-C levels lower as compared to normal pregnancy,[19,20] although serum TC was not higher in Satter et al's[13] study. This hyperlipidemia is associated with vascular dysfunction and endothelial damage as observed in pre-eclampsia.[21,22]

Manten and associates[23] conducted a study on 70 pregnant women. Of them, 30 had preeclampsia (10 with severe and 20 with mild preeclampsia), 20 were healthy pregnant controls, and the rest were healthy non-pregnant controls. Data on cholesterol, HDL-C, and Tg were available for three groups except for severe preeclampsia. There were significantly higher serum TC, HDL-C, and Tg in the preeclamptic women compared to the healthy pregnant and non-pregnant controls. These findings are more or less consistent with our findings, where TC, LDL-C, & Tg all increased & HDL-C reduced in preeclampsia compared to those found in healthy pregnant controls, although the differences between the groups were not statistically significant, except in the case of HDL-C. Manten[23] also did not find any statistical differences in the serum concentrations of TC, HDL-C, and Tg between the mild preeclampsia group and the healthy pregnant controls. This might be explained by the fact that their patients had only mild pre-eclampsia. But in our study two-thirds of the preeclampsia were of severe degree (proteinuria +++).

Increased plasma levels of Tg and LDL-C together with reduced HDL-C has been reported in two studies on preeclamptic woman a few months after delivery.[16,17] The lipid profile observed during the symptomatic phase of pre-eclampsia might persist as a portent similarity with the atherogenic lipid phenotype.[24] This lipid profile, characterized by hypertriglyceridemia, predominance of small, dense LDL, and increased susceptibility to LDL oxidation is strongly associated with and constitutes a major risk factor for the development of atherosclerosis.[24-27] The atherogenic lipid phenotype is not exclusive of atherosclerosis but may be found in other dyslipidaemic conditions, such as diabetes mellitus and familial dyslipidaemias.[24] The expression of this lipid pattern is to a large extent genetically determined,[24] which further supports the existence of common aetiologic links between preeclampsia and atherosclerosis.

Dorothy and associates[2] reported 9% lower HDL-C levels in women with preeclampsia than that in

control. De[9] also reported a significant decrease in HDL-C in preeclamptic pregnant women. The findings of the present study are, therefore, almost consistent with those of other investigators. Dyslipidemia is considered atherogenic and it increases the risk of coronary heart disease.[28]

In the present study, a decrease in the level of HDL cholesterol was observed although other components of lipids did not experience any significant deviation from the normal level. The study demonstrated an elevation of total cholesterol:HDL ratio and triglyceride:HDL ratio in the case group than that in the control group, although elevation is apparently due to a significant lowering of HDL in the preeclamptic population. Studies relating to changes in total cholesterol:HDL ratio and Triglyceride:HDL ratio in preeclamptic populations are rare. Kokia and associates[16] showed a slight decrease in TC:HDL-C during normal pregnancy but increased significantly in both preeclampsia and eclampsia.

An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular diseases and has a direct effect on endothelial dysfunction. Normal human pregnancy results in a pronounced physiologic hyperlipidemia involving a gestational rise in blood triglycerides and cholesterol. Women with preeclampsia display additional alterations in blood lipids, reflecting a disordered lipid and lipoprotein metabolism.[8] The association between dyslipidemia and the risk of preeclampsia is biologically plausible and compatible with what is known about the pathophysiology of preeclampsia. At least 3 hypothesized mechanisms for the dyslipidemia and preeclampsia association have been described. First, elevated plasma lipids may induce endothelial dysfunction secondary to oxidative stress. This hypothesis is supported by the Tg accumulation in endothelial cells leading to decreased release of prostacyclin.[29] The second possible mechanism is the pathologic process of preeclampsia via dysregulation of lipoprotein lipase release resulting in a dyslipidaemic lipid profile.[30] A third possible mechanism may be via the metabolic characteristics of the 'insulin resistance syndrome', namely hyperinsulinemia.[31] However, as very few

studies have so far been conducted, the alteration of TC:HDL-C ratio and TG:HDL-C ratio in preeclampsia is yet to be established.

CONCLUSION:

The study concluded that cholesterol:HDL ratio and triglyceride:HDL ratio were significantly altered in the preeclamptic women compared to those in normal pregnant women. However, this alteration was due to a significant lowering of HDL-C, the TC and Tg did not experience any significant change. Therefore, the chance of developing dyslipidemia in preeclamptic women seems to be due to the lowering of HDL-C, the protective cholesterol.

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