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Study on serum Lipoprotein (a) level in preeclamptic Bangladeshi women

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Abstract

It is a case control study which was design to know the association of serum Lipoprotein (a) level in preeclamptic (PE) in women. This study was carried out in department of Obstetrics and Gynecology, Sir Salimullah Medical College Hospital, Mitford, Dhaka.

Total number of subjects was 100. Out of which 50 were cases and 50 were controls. Cases were physically and clinically proved PE patients. Controls were age, parity and gestational age matched. Three ml of blood were collected from each subjects, serum fasting LP(a) level were measured The mean age of study group was 24.49 ± 6.48 years. Serum Lipoprotein(a) level was 51.51 ± 29.38mg/dl Vs 17.40 ± 7.89 mg/dl in cases and controls respectively. This difference was statistically significant ($p<0.001$). Mean serum Lipoprotein(a) level was found to be raised in severe preeclampsia (74.87mg/dl) and lowest in control subject Severe preeclampsia was found to be associated with higher level of lipoprotein (a) than both control ($p<0.01$) and mild preeclamptic ($p<0.01$) subjects. Mild preeclampsia was also found to have higher average serum Lipoprotein (a) than the normal ($P<0.01$) subjects.

Key Words

Lipoprotein(a), Preeclampsia, Bangladeshi women.

Introduction

Preeclampsia (PE) is a hypertensive disorder of pregnancy characterized by generalised inflammatory state and endothelial dysfunction resulting in disseminated microangiopathic disease with vasospasm and hypercoagulation.[1] It is a serious complication of the second half of pregnancy. This disease is a leading cause of foetal growth retardation, infant morbidity, mortality, and maternal death.[9] The world wide incidence of preeclampsia is still high inspite of the significant improvement of the mother and child care over the last decades. All over the world PE is the 3rd leading cause for maternal mortality and the 7th leading cause for the perinatal mortality.[3] In Bangladesh the incidence of PE is very high. It is about 10% to 15% of all deliveries.[8] In this country, only 2.3% women end their pregnancies under medical supervision.[17] and the rest of them have no access to obstetric care. As a result most PE cases remain unrecognized until severe complications, such as eclampsia. Eclampsia accounts for about 16% of maternal mortality in our country and PE is the leading cause of premature termination, intrauterine growth retardation,perinatal mortality and morbidity. Eclampsia is a preventable disease if PE is detected early and treated an early stage.

This clinical condition was first discovered over 100 years ago, but still it pathology remains obscure. The pathogenesis of preeclampsia continues to be a challenge. Several lines of evidence suggests that preeclampsia is a multietiologic syndrome with heterogeneous biologic pathways.[13] Among them genetic predisposition immunologic, circulatory, uterine vascular changes and endothelial dysfunction are important. The most accepted theory about etiology of PE is endothelial dysfunction.[9] The causes of endothelial injury are multifactorial.[15] In preeclampsia, characteristics pathological lesion in the uteroplacental bed is a necrotizing arteriopathy consisting of fibrinoid necrosis, accumulation of foam cells or lipid laden macrophages in the decidua, fibroblast proliferation and a perivascular infiltrate-"acute atherosis" causing reduced placental perfusion. The similarity between leisons of preeclampsia and atherosclerosis has led to speculations of common pathophysiological pathway .Until now the most accepted etiopathogenesis of pre-eclampsia is endothelial injury and most recently by several authors Lipoprotein(a) has been linked to vascular endothelial cell injury in PE and its consequences[18] Lipoprotein (a) [Lp(a)] , a circulating lipoprotein particle,is formed by attachment of carrier protein, apolipoprotein (a) apo(a), to a low density lipoprotein (LDL) like particle. The

gene coding for apo(a) has been localized to the long arm of chromosome 6 (q26-27), close to plasminogen gene.[12] It has been found to be enhance blood coagulation by competeting with plasminogen for its binding site on fibrin clots and endothelial cells. This action is believed to be mediated by structural homology (>90%) between apolipoprotein (a) and plasminogen. The activation of plasminogen to form plasmin is the essential step for the lysis of fibrin by plasminogen.[4] Many studies have demonstrated the elevated Lp(a) levels are associated with atherogenesis and myocardial infraction.[1] Both vitro and vivo data indicate that Lp(a) is involved in the thrombotic and atherosclerotic processes that lead to reduced blood flow.[4] This action might be associated with the action of Lp(a) on fibrinolysis, the accumulation of Lp(a) within the lesions and the function of endothelial cells.[17] Lp(a), circulating lipoprotien, is accepted as an independent risk factor for premature coronary heart disease and atherosclerotic lesions has supplemented early in this Lp(a). There is increased risk of coronary heart disease if Lp(a) concentration is above 30mg/dl.[17]

Normal gestation is associated with a progressive rise in Lp(a) and this association might contribute to pre-eclampsia in some individuals.[17] Lp(a) were elevated in the women at risk in developing IUGR very early preterem delivery (<30 weeks of gestation) and foetal or neonatal loss [2]. In as recent review, there is a additive risk for atherosclerotic disease in women with past history of preeclampsia was estimated to be increased seven fold.[14] Women who previously had eclampsia/ preeclampsia have a two to six fold higher risk of dying from ischemic heart disease than women who only developed hypertension during pregnancy.[6]

Husby et. al.[8] reported two sisters with very high levels of Lp(a), both with a history of severe preeclampsia.

Materials and Methods

This case control study. carried out in the Department of Obstetrics and Gynecology of Sir Salimullah Medical College Hospital, Mitford, Dhaka, Bangladesh. The study was conducted in 100 pregnant women. Among them 50 diagnosod preeclamptic women were enrolled as cases. Cases were divided in to two groups:

Mild PE was diagnosed by BP with >140/90 mm of Hg or < 160/110 mm of Hg with proteinuria of 2 random clean catch urine specimen with 2+ or more on reagent strip.

Severe PE was diagnosed by BP >160/110 mm of Hg with proteinuria of 3+ or more in dipstick test.

Controls were normotensive pregnant women uncomplicated by pregnancy-induced hypertension and proteinurea care was taken to select, equal number of subjects in each group having similar age, and comparable gestational age and to represent the same social stratum. Any subject with diabetes mellitus, chronic renal failure, preexisting hyperlipidaemia, essential hypertension was excluded. Aims and objectives of study were to investigate the association of Lp(a) in pre eclampsia .

Results

Total one hundred subjects were studied, among them 50 were cases and 50 were controls. Cases were admitted in Obstetric and Gynaecoloty Department Sir Salimullah Medical College Hospital, Mitford, clinically diagnosed as preeclampsia either mild or severe PE. Controls were age, parity and gestational age matched. They were uncomplicated by pregnancy-induced hypertension and proteinurea. Care was taken to select, equal number of subjects in each group having similar age, and comparable gestational age and to represent the same social stratum.

The mean age of study group was 24.49 ± 6.48 ; maximum cases were in 3rd decade of life. (Table 1) Lipoprotein(a)l level was 51.51±29.38mg/dl Vs 17.40±7.89 mg/dl in cases and controls respectively. This difference was statistically significant (p<.001). With the higher level of preeclampsia mean Lipoprotein(a) level tends to be higher. Mean serum Lipoprotein(a) level was found to be highest in severe preeclamsia group (74.87 mg/dl) and lowest in control subject. One way ANOVA reveals highly significant statis tical difference of serum Lipoprotein (a) level between the difference level of preeclamsia (F 3.236 P <.01).

Table I Baseline characteristics of study patients

	Group	
	Study group	**Control group**
Primi	31(62%)	18(36%)
Multi	19(38%)	32(64%)
Age (years)	25.54 + 8.8	23.44 + 4.17

All the data are expressesd as mean+SD and percent

Table I shows the distribution of the respondents by age and obstetric history. Among the preeclamtic women majority of the subject and among control subjects were primi gravid. Odds Ratio demonstrated around three times more risk of developing pre eclampsia among the primi gravid women then their multi gravid counter part.

Table II: Comparison of 24 hour total urinary protein between mild preeclampsia& severe preeclampsia

Parameter	Group		p value
	Mild PE (Mean + SD)	**Severe PE (Mean + SD)**	
Urinary Protein gm/24hr	2.06 + 5.36	4.39 + 1.55	p<0.046

p value < 0.05 is significant

Table II compares the level of 24 hour urinary protein between types of pre eclamsia. Average protein content was 2.33gm/24hour urine higher among subject with severe preeclamsia then the women with mild preeclamsia.

Table- III. Distribution of Lipoprotein(a) (mg/dl) in cases & control.

Parameter	Group		p value
	Study group Mean + SD	Control group Mean + SD	
Lipoprotein (a)	51.51 + 29.38	17.40 + 7.89	p <.001

p value < 0.05 is significant

The table above showing mean lipoprotein(a) level in study groups. The mean value was 51.51±29.38 mg/dl and 17.40±7.89 mg/dl for cases and controls respectively there was a statistically significant difference of mean lipoprotein(a) level between cases and controls (p<0.001).

Table IV: Distribution of Lipoprotein (a) (mg/dl) level according to level of preeclampsia

Level of preeclampsia	N	*Lp(a) level (Mean ± SD)	p value
Normal	50	17.40±7.89	F 3.236 P 0 .001
Mild	29	34.58±6.27	
Severe	21	74.87±32.74	

* Lipoprotein(a) level (mg/dl)
P <0.05 was significant

Table IV shows mean serum Lipoprotein (a) level was found to be highest in severe preeclamsia group (74.87 mg/dl) and lowest in control subject.

Table V: Comparison of Lipoprotein(a) (mg/dl) level among different level of preeclampsia

Type of preeclampsia			Mean Difference	Std. Error	pvalue
Normal	Vs	Mild	-17.18	3.79	0.001
Normal	Vs	Severe	-57.46	4.22	0.001
Mild	Vs	Severe	-40.28	4.65	0.001

P <0.05 was significant

In Table V Post hoc (Hochberg) multiple comparison was also performed to explore the nature of difference of Lipoprotein(a) (mg/dl) level among different level of preeclampsia. Severe preeclampsia was found to be associated with higher level of Lipoprotein(a) then both control (P<0.01) and mild preeclamptic (P<0.01) subjects. Mild preeclampsia was also found to have higher average serum Lipoprotein(a) than the normal (P<0.01) subjects.

Discussion

The precise aetiology of preeclampsia is still obscure. Ness & Robert suggested preeclampsia as a multietiologic syndrome with heterogeneous biologic pathways.[13] In search of causal mechanism, researcher's world wide had been pondering several pathways and attempting to indict various factors. Several postulations has already been made by various authors, until now the most accepted etiopathogenesis of preeclampsia is endothelial injury and most recently by several authors Lipoprotein (a) has been linked to vascular endothelial cell injury in PE and its consequences.[18] Abnormal lipid metabolism has been proposed as a pathogenic factor of preeclampsia; however its role is still unclear.[11]

Present endeavour studied the relationship between maternal plasma Lipoprotein (a) concentrations and risk of preeclampsia. A total of 50 preeclamptic patients and 50 normotensive control subjects were included in this study, conducted at department of Obstetric and Gynaecology, Sir Salimullah Medical College Hospital, Mitford, Dhaka over January 2006 to December 2006.

Both cases and controls were recently admitted patients, diagnosed recently and having no complication or co-morbidity. Due emphasis were put on the selection of controls particularly the matching of background features which seems to have confounding potential on the hypothesis. A disparity of age up to two years was accepted between cases and controls.

Background features and demographic information were meticulously assessed to elucidate any bias and to control as well. Most subjects in both the group were of 3rd decade In the present investigation lipid profile has not been assessed due to inadequate logistic support and time constrain. However, many authors pronounced dyslipidemia of having etiologic importance.

There are studies which have shown elevated Lp(a) levels in preeclampsia and the association of severity of disease and level of Lp(a).[2,4,21,22] Wang et al described small cohort study a statistically significant difference of Lp(a) concentrations in third trimester of women with preeclampsia compared to women with normal pregnancies.[21] The study included only 18 mild and 8 severe preeclamptic patients, 24 normal pregnant women. They measured the highest levels in women with severe preeclampsia and intermediate levels in mild preeclamtic patients.

Bar et. al.[4] conducted a cross sectional study which included 16 women with preeclampsia, 35 normotensive pregnant women and 18 healthy nonpregnant.Plasma concentrations of Lp(a) were significantly higher in women with preeclampsia thah normotensive pregnant women.

Van Pampus et.al.[20] observed statistically significant higher concentration of Lp(a) in 40 women with a history of

severe preeclampsia in comparasion with women who had a hisroy of preeclampsia with HELLP syndrome.

Aksoy et. al.[2] described in case control study a statistically significant difference in Lp(a) in 13 severe preeclamtic and 15 mild PE and 15 healthy pregnant women.

This study also showed similar results in accordance with other previous reports Multivariate analysis, considering most confounders, Triglyceride & HDL in particular, might have been considered for unbiased result after controlling necessary intervening variables. As Lipoprotein (a) itself is a derivative of body lipid, it should have been given due attention.

There has been wide range of disagreement regarding serum Lipoprotein(a) level nd development of preeclampsia among pregnant women. Varied study setting and diverse sample structure might have contributed to such dissimilarity in study findings. Consensus regarding the role of Lipoprotein(a) in preeclampsia and its consequence is important. Hence, large-scale, multi-centred study with larger logistic support is hereby recommended.

Conclusion

In the present study serum Lipoprotein (a) level was found to be significantly higher in preeclamptic patient then controls. It signifies strong association of Lp(a) with preeclampsia in our Bangladeshi women. Higher the severity of preeclampsia serum lipoprotein(a) tends to be higher. Severe preeclampsia was found to be associated with higher level of lipoprotein (a) than both control and mild preeclamptic subjects. We included a small number of subjects – only 50 cases and 50 controls. It is difficult to draw conclusion. We recommend further large-scale studies to establish the association of lipoprotein (a) with preeclampsia in our country.

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