Lipoprotein (a) level in pre-eclampsia patients

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Abstract

This study was carried in BSMMU from July 2001 to June 2003. During the study period, 60 pregnant women were studied. Thirty patients were preeclamptic and thirty were normal healthy pregnant women served as control. Serum lipoprotein(a) was found significantly higher in preeclamptic women 56.63±22.6 mg/dl and found within limit in normal healthy pregnant women, 12.89±4.59mg/dl. Result is statistically highly significant (P<0.001). Mean Systolic Blood Pressure was 163.33±29.63 mmHg and 117.00±11.19mmHg in case and control and Diastolic Blood Pressure was 108.53±14.54 mmHg and 76.00±6.87mmHg respectively in case and control group. Result was highly significant as P <0.001. The mean (±SD) serum lipoprotein(a) concentration in normal pregnancies and preeclampsia were found to be 12.91±4.94 and 56.65±22.62. Moderate Proteinuria was found in 77.5% and severe proteinuria in 22.2% cases of preeclampsia respectively. Regardless of mechanism and pathophysiology of preeclampsia, we found high serum level of lipoprotein (a) in preeclampsia patients. These high levels of lipoprotein (a) significantly correlated with blood pressure and proteinuria.

Introduction

Preeclampsia in hypertension associated with proteinuria ≥ 300mg in 24 hours urine or Igm/L in any random sample of urine and with or without oedema occurring primarily in nulliparous women after the 2nd half of gestation and most frequently near term. Sometimes this turn into essential hypertension[1]. Preeclampsia occurs in about 5 to 15 percent of the general population[2].

Characteristic features of severe preeclampsia[3]- 1) Blood pressure greater than 164mmHg. 2) Proteinuria exceeding 2gm in a 24- hours, 3) Creatinine (>1.2mg/df), 4) Oliguria <500 ml 24 hours, 5) Cerebral or visual disturbance, Epigastric pain, 7) Elevated liver enzyme, 8) Platelet count <100, 000/mm^3, 9) Retinal haemorrhage, exudate or papilledema, 10), Pulmonary oedema.

Genetic factors seems to be important in the aetiology of preeclampsia[4] preeclampsia is postulated to be caused by insufficient causing a compromised placental circulation[5].

Preeclampsia is a serious complication of the second half of pregnancy that occurs with a frequency of upto 15 percent[2].

Altered coaguability may be important in the pathogenesis of preeclampsia. This study has been designed to measure and analyze the concentrations of lipoprotein (a) level in maternal serum, to find out its significance in the pathogenesis of preeclampsia.

Aims and Objective

General Objectives:
Lipoprotein (a) level are elevated in preeclampsia patients and associated with severity of the disease. On the basis of the above hypothesis; a case control study with the aim to determine the role of lipoprotein (a) in the pathogenesis of preeclampsia was done.

Specific Objectives:
a) To determine the level of serum lipoprotein(a) in preeclampsia patients.
b) To determine the association of raised lipoprotein(a) with the severity of preeclampsia
c) To evaluate; its usefulness in screening for preeclampsia.

Materials and Methods

This is a case control prospective, consecutive, cross sectional observational study. Study period is July 2001 to June 2003.

Study Subjects
This study included 60 pregnant women, selected consecutively from among the patients attending the Department of Obstetrics and Gynecology, BSMMU and DMCH, during the study period. The

women were divided into two group: (a) case (n=30) and (b) control (n=30).

Inclusion criteria:

- Preeclampsia patient means hypertension with proteinuria with or without oedema appearing in pregnant patient after 20 weeks of pregnancy.
- Hypertension means systolic blood pressure >140 mm of Hg and diastolic blood > 90 mm of Hg on two occasion at least 6 hours apart.
- Proteinuria may be defined as ≥ 300 mg albumin in urine in 24 hours urine or 1 gm/L of urine in any sample.
- Mild proteinuria : e.g. +albumin,
- Moderate proteinuria : e.g. ++ albumin
- Severe proteinuria: e.g. +++ albumin
- Preeclampsia is of two degree mild and severe depending on diastolic blood pressure.
- Mild preeclampsia that is diastolic blood pressure is <110 mm of Hg.
- Severe preeclampsia that is diastolic blood is > 110 mm of Hg.

a) For case
   1. Pregnant women, 28 to 42 weeks gestation
   2. Hypertension and Proteinuria present
   3. Body weight 45 to 80 kg
b) For control
   1. Pregnant women, 28 to 42 weeks gestation
   2. No hypertension or Proteinuria present
   3. Body weight 45 to 80kg.

Age:

- Age ranging from 18 to 30 years in control and 18 to 32 years in case group.
- Age range of control group is 23.40 ±3.04 years and case group 23.73±4.33 year as similar age group of case and control will be easier to compare and above mentioned age group of pregnant patient is available and beyond these age group are not available. If available they had other disease associated.

Height: Height ranged from 144 to 155 cm in control group and from 132 to 165 cm in case group.

Gravida: Gravidity of the patients were recorded.

Blood pressure: (both systolic and diastolic) were measured in a supine position.

Exclusion criteria:

a. Patients with known renal disease
b. Patients with diabetes mellitus
c. Diagnosed patients of hepatic dysfunction
d. Patients in labour
e. Patients using diuretics

Procedure of proteinuria detection: Urinary protein that is proteinuria is detected by dip stick method.

Sample collection for serum lipoprotein(a) detection: For lipoprotein(a) from each subject (both case and control), 5 ml of venous blood was collected in the morning in fasting state, using sterile disposable plastic syringe, by antecubital venipuncture, taking full aseptic precaution and poured into a clean dry glass test tube. Serum from 30 normal and 30 preeclampsia patients were prepared at BSMMU and DMCH and kept under -40°C at BIRDEM until analyzed for serum Lp(a) level by special lipoprotein assay kit.

Serum Lp(a) levels were assayed by Nephelometer agglutination measurement using special Lp(a) assay kit. This method is based on Ag-Ab reaction.

All relevant collected data were complied on a master chart first, then organized by using scientific calculator and statistical analysis was done by using computer based software SPSS. Here Chi-square and unpaired Student's 't' test were done to find out probability value.

Observations & Results

Table I: Comparison of clinical biochemical parameter between control and case

Parameter	Control (n=30) Mean±SD	Case n=30 Mean±SD	P value[a]
Age (years)	23.40±3.04	23.73±4.33	0.731[NS]
Height (cm)	149.80±2.81	148.07±4.89	0.422[NS]
Weight (kg)	55.87±5.82	57.17±9.82	0.000[*]
Gestation age (week)	37.67±3.00	34.10±3.52	0.000[*]
Systolic blood pressure (mmHg)	117.00±11.19	163.33±29.63	0.000[*]
Diastolic blood pressure (mmHg)	76.00±6.87	108.53±14.54	0.000[*]
Serum lipoprotein (a)	12.91±4.94	56.65±22.62	0.000[*]

Unpaired student's 't' test, [NS]Not significant,*Significant at P<0.001

Table II: Status of proteinuria in the study subject

Proteinuira	Control (n=30) No. (%)	Case (n=30) No. (%)	P value[a]
Moderate	0	21(77.5)	<0.000[*]
Severe	0	9(22.5)	
Nil	30(100.0)	0	

[a]Chi-square test, *Significant at P<0.001

Table III: Status of oedema in the study subject

Oedema	Control (n=30) No. (%)	Case (n=30) No. (%)	P value[a]
Mild	20(66.67)	1(3.33)	
Moderate	0	19(63.33)	
Severe	0	10(33.34)	<0.000*
Absent	10(33.33)	0	

[a]Chi-square test, *Significant at P<0.001

Table IV: Relationship between serum lipoprotein(a) and systolic blood pressure

Group	n	r Value	P value
Control	30	+0.031	0.870[NS]
Case	30	0.0192	0.309[NS]

[NS] Not significant

Table-V: Relationship between serum lipoprotein(a) and diastolic blood pressure

Group	n	r Value	P value
Control	30	+0.129	0.498[NS]
Case	30	0.197	0.296[NS]

[NS] Not significant

Table VI: Status of parity in the study subjects

Parity	Control (n=30) No. (%)	Case (n=30) No. (%)	P value[a]
0	8 (26.7)	19 (63.3)	
1	12 (40.0)	4 (13.3)	
2	7 (23.3)	3 (10.0)	0.053[NS]
3	2 (6.7)	1 (3.3)	
≥ 4	1 (2.3)	3 (10.0)	

Unpaired student's 't' test, [NS] Not significant

Discussion

The present study dealt with a significant number (n=30) of preeclampsia case where high serum lipoprotein (a) level, i.e. more than 30mgld, which has been set as a cut -Off level, associated with increased of thrombosis and atherosclerosis.[7] None of the normal pregnant women had lipoprotein level more than 30 mg/dl.

In a study on pregnant women showed serum lipoprotein. (a) level as 7.8 mg/dl in control (normal pregnancy), 15.77 mg/dl in women with mild preeclampsia and 82.69mg/dl in women with severe preeclampsia.[2] In our study the serum liproprotein(a) level was 12.91 ±4.94mg/dl in normal pregnancy and 56.65±22.62mg/dl in preeclamptic women.

A rise in blood pressure is the most important clinical criteria to preeclampsia. The result of correlative analysis between serum lipoprotein (a) and their corresponding systolic and diastolic blood, pressure among preeclampsia cases as well as among total study population suggested the significance of high serum lipoprotein (a) in the pathogenesis of preeclampsia. The direct relation between serum lipoprotein (a) and blood pressure obtained in this study corroborate with the hypothesis that increased serum lipoprotein (a) leads to preeclampsia. Among, with rise of systolic and diastolic blood pressure, there is also of serum lipoprotein (a). So, there is direct correlation between severity of preeclampsia and serum lipoprotein(a) level. So, high serum lipoprotein (a) is associated with severity of preeclampsia. Though statistical result do not necessarily reflect, that occurs in vivo the finding in this study indicate a significant role of increased serum lipoprotein(a) in preeclampsia.

Conclusion: From the results of this study, it appears that raised level of serum lipoprotein(a) occur in pregnant patients with preeclampsia. At this time, we do not know the exact mechanism of high serum level of lipoprotein(a). Moreover, this study did not show why this high level of lipoprotein(a) play central role to the pathophysiology of preeclampsia. Regardless of we mechanism and pathophysiology of preeclampsia, found high serum level of lipoprotein (a) in preeclampsia patients. These high levels of lipoprotein (a) significantly correlated with blood pressure and proteinuria. Further prospective studies are needed to determine whether a rise in serum lipoprotein(a) can be used as an early predictor of the disease.

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