Original Article

LIPIDS & LIPOPROTEIN (A) [LP(A)] IN PREGNANCY INDUCED HYPERTENSION

Vibha.C, C.S. Muralidhara Krishna, K.L.Mahadevappa

ABSTRACT:

The present study was designed to evaluate the lipid profile & Lp(a) in pregnancy induced hypertension(PIH) compared with healthy normal pregnant as control. 60 cases were studied of which 30 were normal healthy pregnant control & 30 were PIH cases of the same trimester. The plasma lipid parameters such as total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) & very low density lipoprotein cholesterol (VLDL-C) were measured along with plasma lipoprotein(a) [Lp(a)]. Blood glucose, blood urea, serum creatinine & urine albumin were also measured. There is a significant elevation in the levels of serum TG & Lp (a) in PIH cases when compared to the control. In the background of increased Lp (a) being a potential risk factor for cardio-vascular diseases the significance of elevated Lp (a) in the PIH needs to be evaluated.

Keywords: Lp (a), PIH.

INTRODUCTION:

Hypertension is the most common medical complication of pregnancy. Of the varying forms of hypertension that can affect pregnancy; pre-eclampsia is the one specific to pregnant woman.. In general, hypertension is said to complicate about 7% of all pregnancies & pre-eclamptic syndrome accounts for approximately 5% of all pregnancies, pre-eclampsia may cause severe maternal disease & premature birth. PIH is diagnosed when BP is > 140/90 mm of Hg or greater, proteinuria of 300mg/24 hr or more or ≥ 1+ dipstick response, generalized edema which usually involves the face & hands & persists after evening. It has been estimated that worldwide, approximately 50,000 women die each year of eclampsia[2]. Changes in the plasma lipids during pregnancy have been recognized described & are thoughts to be done mostly to alterations in hormonal milieu. An increase in resistance to angiotensin, a predominance of lipid metabolism over glucose utilization & an increased synthesis of thyroid & steroid binding protein in liver, fibrinogen & other proteins are characteristic of pregnancy. Plasma lipids & lipoproteins undergo both qualitative & quantitative changes during pregnancy. These changes revert towards normal shortly after delivery[2]. Levels of Lp(a) appears to be lower in the normal pregnancy. Lp(a) a variant of LDL was discovered as an antigen in the blood of certain persons. It carries one copy of a protein apo(a) joined to apo(B)100, by disulphide linkage. Lp(a) a circulating lipoprotein particle has been found to enhance blood coagulation by competing with plasmalogen for its binding sites on fibrin clots & endothelial cells[(4)]. The Lp(a) is a variant of LDL that is highly correlated with atherosclerosis. The hypothesis that Lp(a) levels are elevated in pre-eclampsia & associated with disease is supported by a recent observation of high Lp(a) levels in single family with two cases of severe pre-eclampsia. Lp(a) levels are elevated in pre-eclampsia & associated with severity of disease. It may serve as a marker of pathogenic process. Elevated Lp(a)may influence the fibrinolysis & have unfavorable rate on pregnancy outcome. In this background the present study was undertaken to assess the lipid & lipoprotein (a) levels in pregnancy induced hypertension.

The aim of the present study is to assess & compare the serum lipids & lipoprotein (a) levels in normal pregnant woman & PIH in third trimester of pregnancy.

MATERIALS & METHODS:

The present study was carried out in KIMS, Bangalore. The ethical committee of KIMS, Bangalore approved the study protocol. Informed consent was taken from individual subjects. The study comprised of 60 cases, of which 30 were normal health control and 30 were PIH cases in third trimester. The subjects selected for the present study were attending & admitted to KIMSH,

Bangalore, who were all primigravida aged less than 30 yrs with PIH normal Pregnancy & in third trimester of pregnancy. The diagnosis of PIH was based on the definition of American College of Obstetrics & Gynecologist, systolic blood pressure greater than 140 mm of Hg or a rise of atleast 30 mm of Hg or diastolic blood pressure greater than 90 mm of Hg or a rise of atleast 15 mm of Hg (manifested on two occasion atleast 6 hrs apart) & proteinuria of 300 mg or greater in a 24 hrs urine collection or protein concentration of 1 gm/lt (on two occasion at least 6 hrs apart).

None of the women had received anti hypertensive medication until the study samples were taken. The levels of blood pressure & protinuria were determined at the time of sampling. All subjects with obesity, diabetes mellitus & family history of HT, DM, IHD & any cardiovascular complications were excluded from the study.

5 ml of fasting blood samples was collected, serum was separated by centrifugation & analyzed immediately in auto-analyzer by kit method .urine samples was collected in a clear dry container & was tested immediately by AMES multiple reagent strip.

Lp(a) in serum was estimated by turbidimetric immunoassay. The absorbance was measured at 340nm. 'P' values were calculated using student t-test.

RESULTS:

		Control (n = 30)	Cases (n = 30)
Gestational Age	Age (Yrs) 18 – 24 25 – 28	 24 6	 16 14
	Wks of 28-32 Gestation 34-36	5 25	5 25
Diet Pattern	Veg Mixed	3 27	6 24
BP (Blood Pressure)	Systolic Diastolic	114.13±7.66 74.33±5.58	114.13±7.66 98.13±4.64
Protinuria	Dipstick Method	None	None – 6 Traces – 1 1+ – 23
BMI	Wt in Kg/m2 (p>0.06)	25.75±3.22	26.76± 3.31

Table1: History & BMI of cases & control subjects

Protinuria à Traces = 5 – 20 mg/dl

1^{+} – 30 mg/dl

BMI = Wt in Kg

(Body Mass Index) Ht (m^2)

The means BMI of controls was 25.75 ± 3.22 & study group was 26.76 ± 3.31. The p-value was > 0.06.

Figure. 1

All cases were booked & immunized. Cases in both control & study group were within 30yrs

of age & were primigravida.They were in the third trimester & consisted of both vegetarians & non vegetarians. Pedal edema was absent in control group & other 25 cases had pedal edema. The mean value of systolic blood pressure in control was 114.13 ± 7.66, while in study group, it was 144.4 ±9.80.The mean value of diastolic BP in control group was 74.33 ±5.58 & in study group it was98.13 ±4.64, protinuria was checked by dipstick, it was absent in all control group while in 6 cases of study group urine albumin was absent but in rest of the cases it was present.

Biochemical Parameters	Controls (normal pregnant)	Cases (PIH cases trimester) n=30	Statistical relative P – value
Blood urea	18.66±2.19	18.17±3.73	>0.3
Serum creatinine	0.83 ± 0.12	0.91±0.20	<0.04

Table 2; Biochemical parameters to assess the renal function

Table2; projects the values of the blood urea, serum creatinine in the study & control groups.

The mean value of blood urea in control group is18.66 ±2.19 & in cases, the values were18.17 ±3.73. No significant difference (p>0.3) is found when blood urea in cases is compared to controls. The mean value of serum creatinine are 0.83±0.12 & in cases values were0.91±0.20. The serum creatinine levels were significantly more in cases of PIH when compared to controls (p<0.04)

Biochemical Parameters	Controls (normal pregnant) III trimester n=30	Cases (PIH cases trimester) n=30	Statistical relative P – value
Lp(a)	27 2.9	37.03 ± 3.76	< 0.01
Total Cholesterol	197.28±37.19	192.69±43.26	> 0.4
TG	181.63±14.44	208.56±46.08	<0.02
HDL – C	41.58±8.02	38.27±10.26	>0.05
LDL – C	118.43±37.40	107.13 ± 40.80	>0.1
VLDL – C	36.13 ± 8.42	40.15 ± 11.37	>0.1

Table3: Lipids and LP(a)

Table 3; projects the serum lipid profile &Lp(a) in control and study group.

The mean serum Lp(a) in the PIH cases is 37.03±3.76 & in control is 27±2.9. The serum Lp(a) is significantly elevated (p<0.001) in cases of PIH when compared to control that is normotensive pregnant women. Figure.4

The mean value of TC in cases is 192.69±43.76 & in controls 197.28±37.19. The Serum TC when compared between cases & control showed no significant differences (p>0.02).

The mean value of TG in cases is 208.56±46.68 & in controls is 181.63±41.44. The mean value of HDL-C in cases is 38.27±10.26 & in controls is 41.58±8.02. The mean serum HDL-C is insignificant in cases when compared to controls (p>0.05) while the mean value of VLDC-C & LDL-C when compared between cases & control there was no significant differences (p>0.1).

DISCUSSION :

In the present study an attempt has been made to assess the plasma levels of Lp(a) along with other lipid parameter such as TC, TG, HDL – C, LDL – C, VLDL – C. The lipid profile in our study in characterized by an elevated Lp(a) & TG Concentration. TC, HDL – C, VLDL – C levels remains unchanged. This observation is similar to that of Farah Kaholiz et al 2000[7].

Elevation of Plasma triglyceride in PIH has been reported in several studies. According to sattar et al 1997[8], raised plasma TG may be a potential contribution to endothelial dysfunction which is related to hyperlipidemia. Roberts et al 1989, Kokia et al 1990[9].

An important observation in the present study is elevated levels of Lp (a) in PIH when compared to normotensive pregnancy controls. Findings in our study is similar to that Lp(a) levels are elevated in preeclampsia & associated with severity of the disease[10].

PIH & related disorder are known to affect the function of various organ involved in lipids & lipoprotein metabolism. Uslu et al[11] 1996 have hypothesized that vascular lesions of PIH & arterial lesions of atherosclerosis share a common patho-physiological pathway which involves lipid metabolism. The likely cytotoxic factor that damages endothelial cells in suggested to be Lp (a).

Lp(a) bound to glycosaminoglycans is incorporated into fibronectin in the intimal layers of the arteries. This is known to contribute to foam cell formation. Lp(a) also binds to plasminogen activator & fibrinogen & ultimately resulting endothelial thrombosis[12, 13].

In pregnancy there is a state of of enhanced coagulability & decreased fibrinolytic activity. The presence of fibrin deposits in some origins of patients with PIH suggests a possible role for intravascular coagulation in the patho-physiology of toxemia. Several cross-sectional studies[14, 15, 16] have demonstrated that Lp(a) is a risk factor in cardiovascular disease.

The present study suggest that the measurement of Lp(a) in PIH along with other lipid parameter appears to be of immense value in understanding the pathophysiology of the PIH. In the back ground of the available literature, increased Lp(a) is a potential risk factor for cardiovascular disease, obviously, further studies are needed to establish the usefulness of Lp(a) levels in assessing the risk of cardiovascular disease in PIH.

SUMMARY :

The present study aims to assess the alterations in lipid parameters and Lp (a)

levels in PIH and to understand the pathophysiology of PIH. 30 PIH cases were evaluated with 30 normotensive pregnant cases as controls. The levels of lipid parameters like TC, TG, HDL-C, LDL-C, VLDL-C were measured along with serum Lp (a) levels. Blood urea, serum creatinine and urine albumin were also assayed to assess the kidney function. There is a significant elevation of serum triglycerides and Lp (a) in PIH cases when compared to controls. There was no significant change in other parameters like T. Cholesterol, HDL-C, LDL-C and VLDL-C. The parameters used in our study to assess the renal function were also unaltered. Serum Lipoprotein (a) levels and triglyceride levels are elevated in PIH cases and this finding is in accordance with other studies. The present study aims to assess the alterations in lipid parameters and Lp (a).

Figure. 1

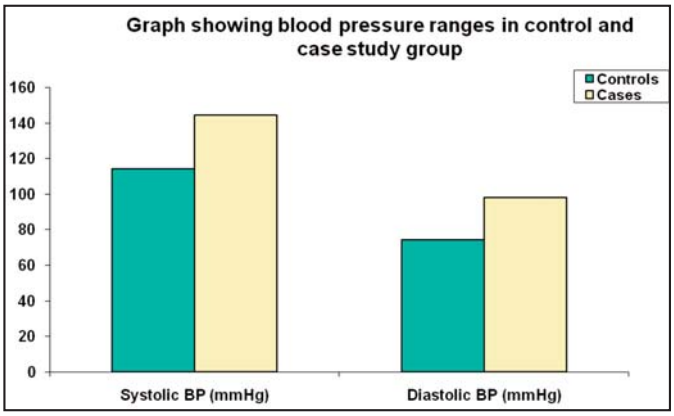


Figure. 2

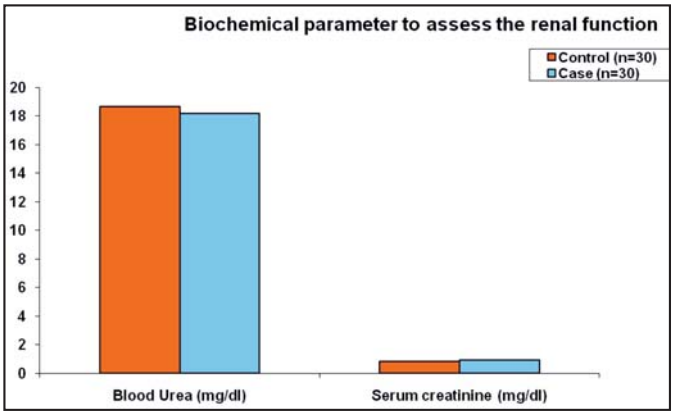


Figure. 3

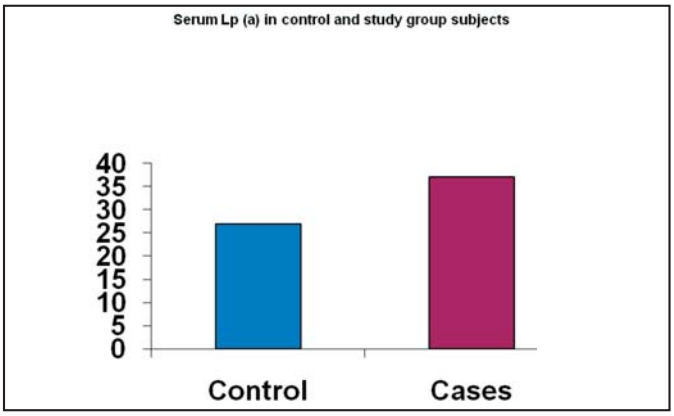
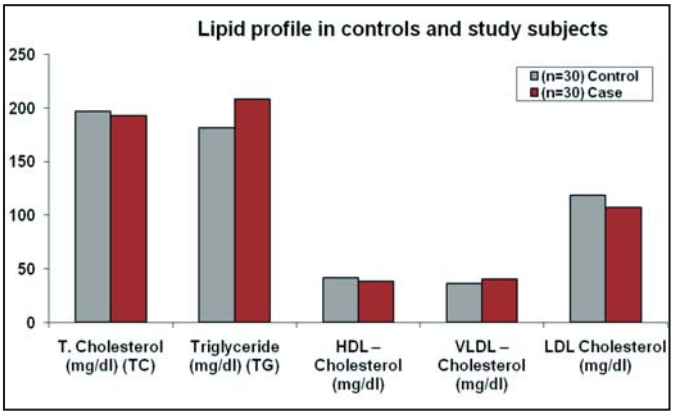


Table 3; projects the serum lipid profile &Lp(a) in control and study group.



REFERENCES:

1. William. F. O'Brian, MD: The prediction of pre eclampsia clinical Obstetrics & Gynecology, 35(2) & 351, June 1992.
2. F. Gary Cunningham, Noreman F Gant, Kenneth, J. Levene Larry C. Gilstrap III, John C Hantha, Kathene Dwenston Hypertensive disorders in pregnancy in Williams Obstetrics, 21st edn, McGraw Hill 568 – 569, 572.
3. Wacl A, Salemet M.D & Dimitrios. S, Mastrogianenis, Md, Ph D, FACo G: Maternal Hyerlipidemia in pregnancy clinical Obstetrics & Gynecology 37(1) 66, Mar 1994
4. Jain Wang Ph D, Shigeko Minero MBBS, Rovert Lahond, MBBS, Brain Trudinper, MD & Xing Li

Wang Ph D: elevated levels of Lp(a) in woman & preclation Am.j Obstetrics & Gynecology 1998:178:146 – 9.

5. SattarN, Clark P, Greer I A, Shepherd J, Packed Cj Lp(a) levels in normal pregnancy & in pregnancy complicated with pre-eclampsia. Atherosclerosis 200 Feb, 148(2) 407-11.
6. American college of Obstetrics & Gynecology, Management of Pre eclampsia. Technical bulletin Washington DC; American college of Obstetrics & Gynecology, 1986.
7. Farat Khalid, Usha Singhal, ziakian Arshad & M. Bobarak Hossain: Study of serum lipid & lipoprotein in preeclampsia with special references to parity. Indian J physical pharmacal 2000: 44(2) 192 – 196.
8. Sattar N, Bendonir A, Shepherd J, Greece I A, Packard C.J : Lipoprotein Sub fraction Concentration in pre eclampsia parallel to atherosclerosis. Obstetrics & Gynecology 1997. Mar, 89(3); 403-8
9. Kokia E, Barkai G, Reichman B, Segal p, Goldman B, Maichiach S (1990); Maternal Serum lipid profile in pregnancies complicated by hypertensive disorders J. perinal Med 18; 473
10. AKSOYH, Kumtipe Y, Akcay F, yildirion A.R, Correlation of p-selection & Lp(a) & other lipid parameters in preeclampsia, clin Exp. Med 2002, May; 2(1): 39- 43.
11. Uslu, T. Uslu, F. Bringal, S. Aydin: Lipoprotein level in patients with pregnancy induced hypertension Arch Gyneal Obstet (1996) 258; 21-24.
12. Steinberg D, Parathasarothys, caren T. E et al (1989): Beyond cholesterol; modification of low density lipoprotein that increase its atherogenecity N.Eng J. Med 320:1915
13. Harpel P.C. Gordon B.R, Parker T.S (1989); Plasma Catalyzed binding on Lp(a) to immobilized fibrinogen & fibrin. Proc Natt. Acad Sci. 86; 3847.
14. Dahlen D.H (1990) Incidence of Lp(a) among population In.Scann.Am.(ed) Lipoprotein(1) Academic press, New York, P151
15. Nachman R1 (1989); Lp(a) modulation of endothelial cell surface fibrinolysis & its potential risk in atherosclerosis. Nature 339:303.
16. Miles L.A, Gless G.M, Levin E, Scanncia. M, Planet (1989); A potential basis for the thermostatic risks associated with Lp(a). Nature 339: 301

Authors :

1. Vibha.C
   Department of Biochemistry,
   Kempegowda Institute of Medical Sciences
2. C.S. Muralidhara Krishna
   Department of Biochemistry,
   Kempegowda Institute of Medical Sciences
3. K.L.Mahadevappa