

STUDY OF SERUM LIPID AND LIPOROTEIN IN PRE-ECLAMPSIA WITH SPECIAL REFERENCE TO PARITY

FARAH KHALIQ, USHA SINGHAL*, ZAKIA ARSHAD AND M. MOBARAK HOSSAIN

*Departments of Physiology and Obst. & Gynaecology,
J. N. Medical College,
A.M.U., Aligarh - 202 002*

(Received on April 15, 1999)

Abstract : A cross sectional study was done to determine serum lipid and lipoprotein cholesterol in pre-eclamptic women in their third trimester, taking normal pregnant women in third trimester as controls. The values were compared in patients of different parity. It was observed that serum triglycerides (TG), cholesterol (Chol), LDL-c, VLDL-c, phospholipids (PL) and total lipids (TL) were significantly raised, while HDL-c, was significantly lower in pre-eclampsia compared to normal pregnancy. TG and VLDL-c were found to be increased significantly with parity.

Key words : lipid
pre-eclampsia

lipoproteins
parity

INTRODUCTION

Human pregnancy is associated with numerous physiological, biochemical and anatomical alterations. Increase in circulating steroids, formation of placenta presence of rapidly developing and apparently well tolerated allograft i.e. foetus are characteristics of normal pregnancy. As a result serial alterations occur in serum lipid levels of a mother. Increase in serum triglycerides cholesterol and to a lesser extent phospholipids have been reported (1-3).

Pre-eclampsia is a pregnancy specific disorder characterized by hypertension,

proteinuria oedema and activation of haemostatic system. The pathogenesis of pre-eclampsia remains obscure. Insufficient placentation has been implicated as the underlying cause of the disease (4). In the development of maternal manifestation of pre-eclampsia the dysfunction of vascular endothelial cells is considered to play a major role (5).

This study is undertaken to determine the concentrations of various lipids and lipoproteins in the serum of patients with pre-eclampsia and its correlation to changes occurring with increase in parity of women. Statistical analysis is done from point of view of normal and complicated pregnancies.

*Corresponding Author

METHODS

Forty pre-eclamptic and twenty normal pregnant women in third trimester of pregnancy were selected from Gynae & Obstet. inpatient Department of J.N. Medical College, Aligarh Muslim University, Aligarh between July 96 and September 97. The pre-eclamptic women constituted the study group, while the normal 20 were controls for comparison. In the study group 16 women were primiparous, 12 were second para and 12 had three or more pregnancies.

While in the control group 10 were primiparous, 5 second para and 5 with three or more pregnancies. Exclusion criteria were associated cardiac, hepatic, renal disease, a metabolic disorder like diabetes mellitus, lipid disorders and past history of hypertension. Both the study and control groups were between 20 and 40 years of age, having singleton pregnancy and were not on any medication except for Vitamins, Iron and Calcium.

Previously healthy normotensive women were considered to have pre-eclampsia if their blood pressure after 20 weeks of gestation was raised to 140/90 mmHg or more or had a mean blood pressure (diastolic + 1/3 rd pulse pressure) of more than 110 mmHg. These increase in blood pressure (B.P.) had to be present on at least two occasions 6 hours apart and proteinuria of more than 300 mg/day or 100 mg/dl.

Intracubital venous blood was collected early morning on empty stomach, with the patient in supine position for at least ten minutes. Fresh serum was used for the

analysis. The concentration of triglycerides (TG) in serum was measured by GPO-PAP method (6) cholesterol (Chol) was estimated by one step method of Wybenga and Pillegi (7). High density lipoprotein cholesterol (HDL-c) was determined by phosphotungstate/Mg²⁺ precipitation method (8), phospholipids (PL) by precipitation method (9) and total lipids (TL) by phosphovanillin method (10, 11). The values of low density lipoprotein cholesterol (LDL-c) and very low density lipoprotein cholesterol (VLDL-c) was derived by using Friedwald formula (12).

Data analysis:

Values were presented as mean \pm S.D. lipid and lipoprotein levels were compared between the different sets by Student 't' test. The corresponding value of 'P' was obtained from the standard table of critical 't' values at the appropriate degree of freedom. Statistical significance was considered as $P < 0.05$.

RESULTS

It was observed that serum TG, Chol, LDL-c, VLDL-c, PL and TL were significantly raised, while the HDL-c level was significantly lower in pre-eclampsia as compared to normal pregnancy (Table I).

The subjects were grouped according to parity into two, primiparous and multiparous women, it was observed that TG and VLDL-c increased significantly with the parity (Table II). The lipid levels when compared in the subgroups of multiparous

TABLE I: Serum lipid/lipoprotein in normal and pre-eclamptic pregnancies.

	Normal pregnancy (n=20)	Pre-eclamptic pregnancy (n=40)
Triglyceride (mg/dl)	196.62±35.06	260.83±77.35**
Cholesterol (mg/100 ml)	187.66±31.87	220.95±45.38*
H.D.L.-c (mg/100 ml)	53.77±10.45	44.17±11.89*
L.D.L.-c (mg/100 ml)	94.61±28.23	124.61±40.38*
V.L.D.L.-c (mg/100 ml)	39.31±7.01	52.16±15.46**
Phosplolipids (mg/100 ml)	226.99±23.26	251.44±32.83*
Total lipids (mg/100 ml)	456.11±60.65	519.46±86.37*

*P<.01; **P<.001

TABLE II: Serum lipid/lipoprotein in normal and primiparous and multiparous women.

	Primiparous normal PET	Multiparous (n=10) (n=16)	(n=10) (n=24)
TG (mg/dl)	Normal PET	174.58±31.36 209.11±68.93	218.65±22.47* 295.31±59.11**
Chol. (mg/100 ml)	Normal PET	176.98±30.52 212.39±45.21	198.34±29.52 226.66±44.59
HDL-c (mg/100 ml)	Normal PET	56.43±10.95 47.27±15.45	51.11±9.17 42.10±7.36
LDL-c (mg/100 ml)	Normal PET	85.63±27.48 123.29±43.77	103.60±26.03 125.49±37.93
VLDL-c (mg/100 ml)	Normal PET	34.91±3.27 41.82±13.78	43.72±4.49* 59.22±11.83**
PL (mg/100 ml)	Normal PET	219.19±22.28 245.04±33	234.78±21.55 255.45±32.55
TL (mg/100 ml)	Normal PET	435.78±58.08 503.16±86.05	476.43±56.18 530.32±48.86

*P<.01; **P<.001

TABLE III: Serum lipid/lipoprotein in multiparous women having pre-eclampsia.

	Para-2 (n=12)	Para-3 or more (n=12)
TG	272.31±57.55	318.32±51.16*
Chol.	221.44±48.55	231.88±39.57
HDL-c	44.16±9.41	40.04±3.35
LDL-c	122.81±42.90	128.17±31.99
VLDL-c	54.45±11.5	63.99±10*
PL	251.64±35.44	259.27±28.88
TL	520.39±92.39	540.26±75.30

*P<.05

women, it was observed that TG & VLDL-c increased significantly in the group of pre-eclamptic women having third or more pregnancy as compared to those having second pregnancy ($P < 0.5$). There was no significant change in other lipid levels (Table III).

DISCUSSION

Plasma cholesterol and triglyceride concentration were reported to be increased markedly during normal pregnancy (13, 14). The increase in plasma cholesterol was amplified by parity. The pattern achieved in the present study is similar expect that the rise in total cholesterol in normal pregnancy was not related to parity and the level was not significantly high in multiparous pregnancy. This difference may be attributed to the time of collection of samples. In the above study/studies, there was a wide range and sample were collected between 8 to 40 weeks of pregnancy. Another variation in this study was that the collection of samples was not in fasting state and the samples collected during labour were also included. All these samples pooled together constituted the controlled mean value. While in the present study only samples above 28 weeks of pregnancy were taken and were collected in fasting state.

LDL-c, VLDL-c, PL and TL were significantly increased in pre-eclamptic pregnancy in comparison to normal pregnancy. These results are in line with the studies done previously (13, 15). They showed that with severity of hypertension

in pre-eclampsia, there is increase in plasma TG concentration which was reflected mainly as an increase in VLDL-c. While others (16, 17, 18) have reported increase which was not always significant. This may be attributed to the inclusion of patients having diabetes and other similar systemic illness in their study.

In the present study TG and VLDL-c show significant increase with parity of patients, while cholesterol remains unchanged. It was reported earlier that the level of cholesterol also showed an upward significant change (13). The possible explanation for this variation has been disused earlier.

Extensive ultrastructural endothelial injury was observed in both placental & non-placental blood vessels from pre-eclamptic women but not in normotensive women (22). The injury appeared to affect the endothelial mitochondria suggests a possible metabolic link in the pathophysiology. There is no direct evidence of the increase of lipids & lipoproteins in the pathogenesis of pre-eclampsia, but evidence is accumulating that free radicals may be important in its pathogenesis as these are increased in pre-eclamptic women (23). Although all the major classes of biomolecules may be attacked by free radicals but lipids are probably the most susceptible ones. The lipid peroxides formed as a result of oxidative destruction of PUFA's are known to injure the cell membrane. This may contribute to endothelial dysfunction in pre-eclampsia but the direct role of lipids in causing endothelial dysfunction is yet to be determined.

REFERENCES

1. Knopp RH, Bergelin RO, Whal PW, Walden CE, Chapman M, Irvin S. Population based lipoprotein lipid reference values for pregnant women compared to non pregnant women classified by sex hormone usage. *Am J Obstet & Gynaecol* 1982; 143: 626-637.
2. Piechota W, Staszewski A. Reference ranges of lipids and apolipoproteins in pregnancy. *Eur J Obstet & Gynaecol Reprod Med* 1992; 45: 27-35.
3. Jimenez SM, Pocovi M, Raman Cajal J, Romero MA, Martinez H, Grande F. Longitudinal study of plasma lipids and lipoprotein cholesterol in normal pregnancy and puerperium. *Gynecol & Obstet Invest* 1988; 25: 158-164.
4. Redman CWG. Immunology of the placenta. *Clin Obstet Gynaecol* 1986; 13: 469-499.
5. Roberts JM, Taylor RN, Musci TJ, Rodgers GM, Hubel CA, Mc Laughlin MK. Pre-eclampsia: An endothelial cell disorder. *Am J Obstet Gynaecol* 1989; 161: 1200-1204.
6. Werner M, Gabrielson DG, Eastman G. Ultramicro determination of serum triglyceride by bioluminescent assay. *Clin Chem* 1981; 27: 268-272.
7. Wybenga DR et al. Direct manual determination of serum total cholesterol with a single stable reagent. *Clin Chem* 1970; 16: 980-984.
8. Bustein et al. Gen analytical techniques & principles Chap I, Sec A: In A Manual of lab techniques. *National Institute of Nutrition ICMR Hyderabad*. Raghurameelu N., Madhuan Nair K, Katyanasurgaram S. Edition 1983: 1-15.
9. Henry RJ, Canon DC, Winkelman JW. Clinical Chemistry principles and techniques, Harper & Rowe IInd edition, 1974; 843.
10. Annino JS, Clinical Chemistry Principles & Procedures 4th edition, 1976; 268.
11. Frings CS, Fendley TW. Improved determination of total serum lipids by the sulphophospho-vanillin reaction. *Clin Chem* 1972; 18: 673-674.
12. Friedwald WT, Levy RI, Friedreichson DS. Estimation of concentration of low density lipoprotein cholesterol in plasma without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499-502.
13. Potter JM, Nestel PJ. The hyperlipidemia of pregnancy in normal and complicated human pregnancy. *Am J Obstet & Gynaecol* 1979; 133: 165-170.
14. De Alvarez RR, Gaiser DF, Simkins DM, Smith EK, Bratvold GE. Serial Studies of lipids in normal human pregnancy. *Am J Obstet & Gynaecol* 1959; 77: 743.
15. Bjorg L, Drevon CA, Endresen MJ, Henriksen T. Fatty acid pattern of esterified and free fatty acids in sera of women with normal and pre-eclamptic pregnancy. *Br J of Obstet & Gynae* 1995; 102: 530-537.
16. Boyd EM. Lipemia of pregnancy. *J Clin Invest* 1934; 13: 347-351.
17. De Alvarez RR, Bratvold GE. Serum lipids in pre-eclampsia-eclampsia. *Am J Obstet & Gynaecol* 1961; 81: 1140-1148.
18. Konttinen A, Pyorala T, Carpen E. Serum lipid pattern in normal pregnancy and pre-eclampsia. *Br J Obstet & Gynaecol* 1964; 71: 453-458.
19. Shanklin DR, Sibai BM. Ultrastructural aspects of pre-eclampsia. Placental bed and uterine boundary vessels. *Am J Obstet & Gynaecol* 1989; 161: 735-341.
20. Hubel CA, Roberts JM, Taylor RN et al. Lipid peroxidation in pregnancy: new perspectives on pre-eclampsia. *Am J Obstet Gynecol* 1989; 161: 1025-1034.