Indian Journal of Clinical Biochemistry, 2006 / 21 (2) 165-168

STUDY OF SERUM LIPID PROFILE IN PREGNANCY INDUCED HYPERTENSION

Jayanta De, *Ananda Kumar Mukhopadhyay and Pradip Kumar Saha

*Departments of Biochemistry and *Physiology, Medical College & Hospital, Kolkata 700073*

ABSTRACT

Four groups of subjects: normal healthy normotensive nonpregnant women (Group A), normal normotensive pregnant women (Group B), women with preeclamptic toxaemia (Group C) and eclamptic women (Group D): with fifty subjects in each group, were investigated for serum lipid profile in the third trimester of pregnancy. There was significant increase in serum triglyceride and VLDL cholesterol level as well as decrease in LDL cholesterol in normal pregnancy, while total cholesterol and HDL cholesterol levels did not show any statistically significant alteration. The preeclampsia (Group C) was associated with a significant rise in triglyceride and VLDL cholesterol and fall in HDL cholesterol concentration, while eclamptic women showed significant fall in HDL cholesterol and rise in LDL cholesterol as compared to normal pregnant women. However, interestingly, elevation of the ratios of total cholesterol : HDL cholesterol and triglyceride : HDL cholesterol as well as diminuition of the ratio of HDL cholesterol : VLDL cholesterol showed statistical significance in pregnancy induced hypertension in both Groups C and D, while eclamptic women showed significant elevation of LDL cholesterol : HDL cholesterol ratio in addition.

KEY WORDS

Blood Lipids, Dyslipidemia, Normal Pregnancy, Pre-eclampsia, Eclampsia, PIH

INTRODUCTION

The association of alteration of serum lipid profile in essential hypertension is well documented. An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular diseases and has a direct effect on endothelial dysfunction. The most important feature in toxaemia of pregnancy is hypertension which is supposed to be due to vasospastic phenomenon in kidney, uterus, placenta and brain (1). Altered lipid synthesis leading to decrease in PGI_2 : TXA_2 ratio is also supposed to be an important way of pathogenesis in pregnancy induced hypertension (2). Thus abnormal lipid metabolism seems important in the pathogenesis of pregnancy induced hypertension (PIH) too. Obviously the association of serum lipid profile with gestational proteinuric hypertension is highly suggested to reflect some new diagnostic tools. Moreover, the hormonal imbalance is a prime factor for the etiopathogenesis of PIH and this endocrinal imbalance is well reflected in alteration of serum lipid profile. Therefore, simple measurement of serum lipid parameters may be of good predictive value in toxaemia of pregnancy, avoiding the costly endocrinal investigations.

Address for Correspondence:

Dr. Jayanta De
Associate Professor, Dept. of Biochemistry,
Medical College & Hospital, Kolkata 700073
E-mail : dejayantade@rediffmail.com

MATERIALS AND METHODS

The study was performed in the Department of Biochemistry of Medical College & Hospital, Kolkata, in collaboration with its Obstetrics Department during the period of 01/06/2004 to 31/12/2004. In total, four groups of subjects were selected for the study, with fifty subjects in each group.

Group A - nonpregnant normotensive normal women; Group B - women having normal uncomplicated pregnancy without hypertension; Group C - women with preeclamptic toxaemia; Group D - toxaemic women with eclampsia.

All the subjects were ranging in age from 18 to 30 years with similar low socio-economic status and dietary habit. They were abstrained from smoking and alcoholism. No subjects from any group were suffering from any acute or chronic illness during the study nor they had any past history of cardiac, renal, hepatic dysfunction or dyslipidaemia. The preeclamptic patients were diagnosed by the presence of persistent hypertension (more than 140/90 mm of Hg), gross

proteinuria (tested by heat test of urine), pathological oedema and hyperuricemia (assayed by coupled uricase method). The eclamptic patients were diagnosed by the additional feature of convulsion or coma. All the subjects of groups B,C & D were in the third trimester. The preeclamptic patients were on salt restricted diet and the eclamptic patients on intravenous glucose drip, in addition to all the supportive therapies.

Blood samples were drawn from all the subjects following a fast of 12 hours and analyzed for Serum Triglycerides (TG), Total cholesterol (TC) and HDL cholesterol (HDL-C) by enzymatic methods with the help of Glaxo kits on ERBA Chem-5 semi auto analyzer. Serum LDL cholesterol (LDL-C) was calculated by Frederickson-Friedwald's formula according to which LDL cholesterol = Total cholesterol - (HDL cholesterol + VLDL cholesterol). VLDL cholesterol (VLDL-C) was calculated as 1/5 of Triglycerides. Data were statistically analyzed by Student's 't' test and significance was expressed in term of 'P' value.

RESULTS AND DISCUSSION

Some previous studies showed that the most dramatic damage in the lipid profile in normal pregnancy is serum hypertriglyceridemia, which may be as high as two to three folds in the third trimester over the levels in nonpregnant women (3). In our study also this observation holds true. Here the serum triglyceride concentration showed very significant ($P<0.001$) increase in the third trimester of normal pregnancy than in the nonpregnant women, the mean value being raised almost two folds. The principle modulator of this hypertriglyceridemia is oestrogen as pregnancy is associated with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous triglycerides, which is carried by VLDL (4). This process may be modulated by hyperinsulinism found in pregnancy (5). Serum triglyceride concentration also rose much more significantly in toxaemia of pregnancy in our study which corroborated with the findings of many workers (6,7). The above mentioned interactions alongwith increased endothelial triglyceride accumulation may result in endothelial cell dysfunction in gestosis (8). Increased TG, found in pregnancy induced hypertension, is likely to be deposited in predisposed vessels, such as the uterine spiral arteries and contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense LDL (9). Moreover, this hypertriglyceridemia may be associated with hypercoagulability (10). In our study, in contrast to normal pregnant women, the rise in serum TG was statistically significant ($P<0.05$) in preeclamptic patients, but not so significant in eclamptic patients ($P>0.05$). In eclamptic subjects, the mean value was a bit lower and the standard deviation was a bit higher than those in preeclamptic subjects, though the mean value in eclamptic subjects was much more than that in normal pregnant women. This finding can be explained in two ways. Firstly, the eclamptic women were only on intravenous glucose drip for more than 12 hours as they were unable to take anything by mouth. Secondly, the eclamptic process is very frequently associated with aggravated hepatic damage which inhibits the enhanced de novo synthesis of triglyceride in liver. Moreover, VLDL which carries the endogenous triglyceride, is also synthesised in the liver and the increase in triglyceride in gestosis is estimated mainly in the VLDL (11).

In present study no significant alteration in TC level could be observed in third trimester of normal pregnancy in any of the groups. These findings are similar to Sattar et al (9). However others have found significant increase in serum TC in toxaemia of pregnancy (5,12).

Though in our own study, the mean value of HDL-C was about 30% higher in the third trimester of normal pregnancy over the nonpregnant women, but statistically the alteration was not significant ($P>0.05$). A tendency to lesser quantities of serum alpha lipoprotein fraction in women with toxaemia, particularly in the third trimester, was reported by many workers (6,7,9). In our study a significant decrease in HDL-C were observed in pre-eclamptic and eclamptic pregnant women. Oestrogen is responsible for induction of TG and HDL and suppression of serum LDL and oestrogen level falls in preeclampsia (1,13). The Low level of HDL in pre-eclampsia is however not only because of hypooestrogenaemia but also due to insulin resistance (14).

In present study, serum VLDL-C level rose significantly ($P<0.001$) in the third trimester of pregnancy in comparison to non-pregnant women, which is perhaps due to hypertriglyceridemia leading to enhanced entry of VLDL that carries endogenous triglyceride into circulation. The VLDL-C level, as reported by some researchers, might rise upto 2.5 folds at term over the pre-pregnancy level (15,16). VLDL level further increase in PIH as evidenced in the present study in corroboration with those of other workers (9, 10, 15), perhaps due to increased VLDL lipoproteins which accumulate over the maternal vascular endothelium, particularly those of uterine and renal vessels (17). Further VLDL may cause injury to the endothelium, while a specific toxicity- preventing-activity-protein (the pI 5.6 form of plasma albumin) protects against the VLDL-induced injury in the

pathogenic process of toxaemia (18). A significant fall in LDL-C level in third trimester of normal pregnancy as observed in present study may be attributed to hyperestrogenaemia, while LDL-C level increases significantly in PIH. A significantly higher level of beta-lipoprotein was also reported by many workers in third trimester of gestational proteinuric hypertension (12,19,20). Some scientists observed significantly higher mean titre of autoantibodies to MDA-LDL, the IgG antibodies to an epitope of oxidized LDL, in pre-eclamptic patients, as enhanced lipid peroxidation is involved in the foam cell formation of decidua in the pathogenesis of toxaemia of pregnancy (20,21). Hypooestro genaemia, predominance of smaller and denser serum LDL particles and significant concentration of soluble vascular cell adhesion molecule-1 (VCAM-1) are supposed to be important contributors for endothelial dysfunction in PIH (1,9,12).

We have also calculated the ratios between different lipids like LDL-C : HDL-C; TC : HDL-C; TG : HDL-C and HDL-C : VLDL-C. In present study there was a significant fall in LDL-C : HDL-C in normal pregnant women as compared to non-pregnant women. LDL-C : HDL-C however increased significantly in eclamptic women as compared to normal pregnant women (6,10). On the contrary, HDL-C : VLDL-C continued to fall in both preeclampsia and eclampsia. On the other hand TG : HDL-C increased significantly in PIH. Trend was slightly different in TC : HDL-C which decreased during pregnancy but increased significantly in both preeclampsia and eclampsia (10). Though the relevance of these rations in pregnancy and PIH is yet to be established, the significance of altered TC : HDL-C, TG : HDL-C and HDL-C : VLDL-C ratios cannot be overlooked as they indicate additional risks in PIH. Dyslipidemia mediated activation of the endothelial cells to the placentally derived endothelial disturbing factors like lipid peroxides and trophoblastic components or combination of placentally derived factors with the lipoproteins could be regarded as possible contributors for pathogenesis of PIH (22). Thus the assessment of blood lipids may be helpful in prevention of complications in PIH.

REFERENCES

1. Dutta, D.C. (2001) Hypertensive disorders in pregnancy, In: Textbook of Obstetrics, Ed. Konar, H.L., 5th edition, New Central Book Agency, Kolkata, p 234-55.

TABLE - BLOOD LIPIDS IN NORMAL PREGNANCY AND PIH

Parameters	Group A (n =50)	Group B (n=50)	Group C (n=50)	Group D (n =50)	Statistical relation with Group B
Triglyceride (mg/dl)	120.7 ± 11.82 (105-140)	215.6 ± 27.22 (176-249)	275.6 ± 38.93 (216-320)	253.2 ± 59.30 (184-352)	P < 0.05 in Group C, P > 0.05 in Group D
Total cholesterol (mg/dl)	211.7 ± 11.38 (192-234)	219.0 ± 16.63 (186-240)	236.3 ± 35.63 (204-309)	230.5 ± 25.72 (191-267)	P > 0.05 in Group C, P > 0.05 in Group D
HDL-Cholesterol (mg/dl)	47.0 ± 10.14 (30-61)	60.7 ± 8.11 (48-80)	45.9 ± 8.00 (37-65)	45.4 ± 11.29 (29-66)	P < 0.01 in Group C, P < 0.05 in Group D
VLDL-Cholesterol (mg/dl)	24.1 ± 2.37 (21-28)	43.1 ± 5.42 (35-50)	55.0 ± 7.83 (43-64)	50.6 ± 11.78 (37-70)	P < 0.05 in Group C, P > 0.05 in Group D
LDL-Cholesterol (mg/dl)	140.6 ± 15.24 (120-170)	114.2 ± 11.32 (101-134)	135.4 ± 23.36 (110-180)	134.5 ± 11.65 (116-153)	P > 0.05 in Group C, P < 0.05 in Group D
LDL-C : HDL-C ratio	3.20 ± 1.03 (2.1-5.3)	1.72 ± 0.62 (!.3-2.2)	2.89 ± 0.50 (2.4-3.5)	3.08 ± 0.68 (2.1-4.2)	P > 0.05 in Group C, P < 0.05 in Group D
TC : HDL-C ratio	4.71 ± 1.21 (3.5-7.2)	3.64 ± 0.35 (2.9-3.9)	5.19 ± 0.56 (4.4-6.2)	5.29 ± 0.92 (4.0-6.6)	P < 0.001 in Group C, P < 0.025 in Group D
TG : HDL-C ratio	3.01 ± 1.13 (1.8-5.0)	3.60 ± 0.51 (2.8-4.2)	6.09 ± 1.01 (5.0-8.4)	5.37 ± 2.19 (3.7-8.0)	P < 0.005 in Group C, P < 0.025 in Group D
HDL-C : VLDL-C ratio	2.00 ± 0.52 (1.1-2.8)	1.42 ± 0.22 (1.2-1.8)	0.84 ± 0.12 (0.6-1.0)	0.93 ± 0.27 (0.6-1.4)	P < 0.01 in Group C, P < 0.05 in Group D

All the parameters in this table are expressed in Mean ± SD and Range within paranthesis

2. Robson, S.C. (1999) Hypertension and renal disease in pregnancy, In: Dewhurst's Textbook of Obstetrics and Gynaecology for postgraduates, Ed. Edmonds, D.K., 6th edition, Blackwell Science Ltd., New York, p 167- 9.

3. Chiang, A.N., Yang, M.L., Hung, J.H., Chon, P., Shyn, S.K. and Ng, H.T. (1995) Alterations of serum lipid levels and their biological relevances during and after pregnancy. Life Sci. 56(26), 2367-75.

4. Glueck, C.J., Fallet, R.W. and Scheel, D. (1975) Effects of oestrogenic compounds on triglyceride kinetics. Metabolism 24, 537-45

5. Adegoke, O.A., Iyare, E.E. and Gbenebitse, S.O. (2003) Fasting plasma glucose and cholesterol levels in pregnant Nigerian women. Niger. Postgrad. Med. J.10(1), 32-6.

6. Enquobahrie, D.A., Williams, M.A., Butler, C.L., Frederick, I.O., Miller, R.S. and Luthy, D.A. (2004) Maternal plasma lipid concentrations in early pregnancy and risk of preeclampsia, Am. J. Hypertens.17(7), 574-81.

7. Cekmen, M.B., Erbagci, A.B., Balat, A., Duman, C., Maral, H., Ergen, K., Osden, M., Balat, O. and Kuskay, S. (2003) Plasma lipid and lipoprotein concentrations in pregnancy induced hypertension, Clin. Biochem. 36(7), 575-8.

8. Mikhail, M.S., Basu, J., Palan, P.R., Furgiusle, J., Romney, S.L. and Anyaegbunam, A. (1995) Lipid profile in women with preeclampsia: relationship between plasma triglyceride levels and severity of preeclampsia, J. Assoc. Acad. Minor Phys. 6(1), 43-5.

9. Sattar, N., Bendomir, A., Berry, C., Shepherd, J., Greer, I.A. and Packard, C.J. (1997) Lipoprotein subfraction concentrations in preeclampsia: pathogenic parallels to atherosclerosis, Obstet. Gynecol. 89(3), 403-8.

10. Kokia, E., Barkai, G., Reichman, B., Segal, P., Goldman, B. and Mashiach, S. (1990) Maternal serum lipid profile in pregnancies complicated by hypertensive disorders, J. Perinat. Med. (Germany) 18(6), 473-8.

11. Yamaguchi, K. (1988) Triglycerides and apoproteins in toxaemia of pregnancy, Nippon Sanka Fujika Gakkai Zasshi (Japan) 40(2), 1875-82.

12. Hubel, C.A., Lyall F., Weissfeld, L., Gandley, R.E. and Roberts, J.M. (1998) Small low-density lipoproteins and vascular cell adhesion molecule-1 are increased in association with hyperlipidemia in preeclampsia, Metabolism 47(10), 1281-8.

13. Bradley, R. and Crook, D. (1995) Pregnancy, oral contraception and hormone replacement therapy, In : Textbook of Clinical Biochemistry : Metabolic and Clinical aspects, Eds. Marshall, W.J. and Bangert, S.K., 1st edition, Churchill Livingstone, London, p 413-22

14. Kaaja, R., Tirkkanen, M.J., Viinnkka, L. and Ylikorkala, O. (1995) Serum lipoproteins, insulin and urinary prostanoid metabolites in normal and hypertensive pregnant women, Obstet. Gynecol. 85(3), 353-6.

15. Teichmann, A.T., Wieland, H., Cremer, P., Knlow, G. and Mehle, U. (1988) Serum lipid and lipoprotein concentrations in pregnancy and at onset of labour in normal and complicated pregnancies caused by hypertensive gestosis and fetal growth retardation. Geburtshilfe Frauenheilkd (Germany, West) 48(3), 134-9.

16. Knopp, R.H., Warth, M.R., Charles, D., Childs, M., Li, J.R., Mabuchi, H. and Von, M.I.A. (1986) Lipoprotein metabolism in pregnancy, fat transport to the fetus and the effects of diabetes, Biol. Neonate (Switzerland) 50(6), 297-317.

17. Potter, J.M. and Netel, P.J. (1979) The hyperlipidaemia of pregnancy in normal and complicated pregnancies. Am. J. Obstet. Gynaecol.(United States) 133(2), 165-70.

18. Arbogast, B.W., Leeper, S.C., Merrick, R.D., Olive, K.E. and Taylor, R.N. (1994) Which plasma factors bring about disturbance of endothelial function in preeclampsia? Lancet 343(8893), 340-1.

19. Gratacos, E., Casals, E., Gomez, O., Llurba, E., Mercader, I., Cararach, V. and Cabero, L. (2003) Increased susceptibility to low density lipoprotein oxidation in women with a history of preeclampsia, British Journal of Obst. & Gynae. 110(4), 400-4.

20. Wakatsuki, A., Ikenoue, N., Okatani, Y., Shinohara, K. and Fukaya, T. (2000) Lipoprotein particles in preeclampsia: susceptibility to oxidative modification, Obstet. Gynecol 96(1), 55-9.

21. Barden, A., Ritchie, J., Walters, B., Michael, C., Rivera, J., Mori, T., Croft, K. and Beilin, L. (2001) Study of plasma factors associated with neutrophil activation and lipid peroxidation in preeclampsia, Hypertension, 38(4), 803-8.

22. Lorentsen, B. and Henriksen, T. (1998) Plasma lipids and vascular dysfunction in pre-eclampsia. Semin Reprod. Endocrinol. 16(1), 33-39.