

STUDY OF LIPID PROFILE, LIPID PEROXIDATION AND VITAMIN E IN PREGNANCY INDUCED HYPERTENSION

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Abstract : Pregnancy-induced hypertension (PIH) is a common medical complication of pregnancy with a high incidence. The study comprised of 30 normal and 30 PIH cases in their third trimester of pregnancy and the following estimations were done: Serum Malondialdehyde level (MDA), Vitamin E, triglycerides (TG), total cholesterol (TC), HDL-cholesterol (HDL-C) and LDL-C. The PIH cases had significant rise in both systolic and diastolic blood pressure (BP) ($P < 0.0001$). There was a significant rise in the fasting triglycerides, total cholesterol and LDL-C levels in PIH ($P < 0.0001$). MDA was twice in the cases and Vitamin E was half the levels that of controls ($P < 0.0001$). The level of rise of serum lipids did not significantly correlate with the rise or fall in MDA. In PIH cases there was a negative correlation of diastolic BP with MDA ($P < 0.05$). Early detection of these parameters is going to aid in better management of PIH cases.

Key words : lipid profile vitamin E malondialdehyde (MDA)
oxidative stress pregnancy-induced hypertension (PIH)

INTRODUCTION

Hypertensive disorders are common medical complications of pregnancy with a reported incidence of about 10% of first pregnancies and 20–25% of women with chronic hypertension (1). The association of alteration in serum lipid profile in essential hypertension is well documented. Hormonal imbalance leading to altered lipid profile in serum is attributed to be the prime factor in etiopathogenesis of pregnancy-induced

hypertension (PIH). PIH includes a group of hypertensive disorders developed due the gravid state. It includes gestational hypertension which is without oedema and proteinuria, pre-eclampsia and eclampsia with oedema and proteinuria. Altered lipid synthesis leading to decrease in PGI_2 : TXA_2 ratio causes the vasospastic phenomenon in kidney, uterus, placenta and brain as seen in PIH (2). Lipid peroxidation occurs at low levels in all cells and tissues. In health, oxidation by free radicals and neutralization

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by antioxidants remain in balance. When the reactive oxygen species (ROS) are in abundance, oxidative stress occurs which is thought to be the causative factor in PIH (3).

For the aforesaid reasons, the present study was conducted to study the lipid profile, lipid peroxidation product, malondialdehyde (MDA) and lipophilic antioxidant, vitamin E in cases of pre-eclampsia and healthy controls.

MATERIALS AND METHODS

The departments of Biochemistry and Obstetrics and Gynecology, Pondicherry Institute of Medical Sciences, Pondicherry, jointly carried out the present study. Informed consent was taken from all individual subjects inducted into the study. The study comprised of 30 normal healthy pregnant women and 30 pre-eclampsia cases attending antenatal OPD or labor room in their third trimester of pregnancy.

The diagnosis of pre-eclampsia was based on the definition of American College of Obstetrics and Gynecologists (4).

- 1) Systolic blood pressure greater than 140 mm Hg or a rise of at least 30 mm Hg or
- 2) Diastolic blood pressure greater than 90 mm Hg or a rise of at least 15 mm Hg (manifested on two occasions at least 6 hours apart) and
- 3) Proteinuria of 300 mg or greater in 24 hours urine collection or protein concentration of 1 gm/L (on two occasions of at least 6 hours apart)

Inclusion criteria for cases: Primigravida with diagnosed pre-eclampsia according to the definition of American College of Obstetrics and Gynecologists with an age ranging from 18–35 years. Inclusion criteria for controls: Primigravida with normal BP, no proteinuria and without any other systemic or endocrine disorder. They were age matched with the cases. All subjects included were in their third trimester (gestational age of ≥ 24 weeks). Exclusion criteria included diabetes mellitus with or without treatment, obesity, severe anemia (Hb < 6 gm%) or subjects suffering from any other systemic or endocrine disorder. Patients with eclampsia were also excluded as they will be given only IV glucose and will not be on normal diet.

Fasting blood sample (8ml) was collected by venepuncture and the following parameters were estimated in both cases and controls

- 1) Serum MDA level (5)
- 2) Serum Vitamin E level (6)
- 3) Serum lipid profile included triglycerides (TG), Total cholesterol (TC), HDL-cholesterol (HDL-C) by enzymatic colorimetric methods (7) in the autoanalyser (Dimension AR, Dade Behring Limited, UK).

Serum LDL-cholesterol and VLDL were calculated using Friedewald's formula which is $LDL-C = TC - (TG/5 + HDL-C)$ and $VLDL = TG/5$.

Data were statistically analyzed by students T test and Pearson's correlation and expressed in terms of 'P' value.

RESULTS

The pre-eclampsia cases had significant rise in both systolic and diastolic blood pressure (BP) as compared to healthy pregnant subjects ($P < 0.0001$). There was a significant rise in the fasting triglycerides, total cholesterol and LDL-C levels in PIH ($P < 0.0001$). The lipid peroxidation product, MDA was almost twice in the cases as compared to the controls ($P < 0.0001$). The antioxidant, Vitamin E was half the levels of that of healthy controls ($P < 0.0001$) (Table I).

In our study the maternal age was significantly high ($P = 0.005$) in the cases as compared to controls so we tried to correlate the maternal age with systolic and diastolic BP. There was no consistent significant

TABLE I: General characters of cases and controls.

| | Controls (n=30) | Cases (n=30) | P |
|---------------------------|--------------------|-----------------|--------|
| Maternal age (years) | 22.7±3.3 | 25.8±4.8 | 0.005 |
| Gestational age (weeks) | 34.9±3.1 | 36.3±2.9 | 0.07 |
| Systolic BP (mm Hg) | 107.3±8.3 | 136±4.9 | <0.001 |
| Diastolic BP (mm Hg) | 74.7±5.0 | 89.8±10.57 | <0.001 |
| Total cholesterol (mg/dl) | 172.1±9.3 | 293.3±15.7 | <0.001 |
| Triglycerides (mg/dl) | 86.7±10.8 | 233.57±34.6 | <0.001 |
| LDL-C (mg/dl) | 89.2±11.6 | 196.7±15.3 | <0.001 |
| HDL-C (mg/dl) | 65.6±5.1 | 50±2.7 | <0.001 |
| VLDL (mg/dl) | 17.3±2.2 | 46.7±6.9 | <0.001 |
| Malondialdehyde (nmol/ml) | 3.19±0.3 | 6.04±0.5 | <0.001 |
| Vitamin E (µmol/l) | 7.26±0.9 | 3.76±0.4 | <0.001 |

correlation. However there was negative correlation of systolic and positive correlation of diastolic BP with gestational age in both cases and controls but neither was statistically significant (Table II). The level of rises of serum lipids did not significantly correlate with the rise or fall in MDA in both the cases and controls. There was a rise in MDA levels with the rise in systolic BP (P value not significant). In the pre-eclampsia cases with the rise in diastolic BP there was a negative correlation with MDA ($P < 0.05$).

TABLE II: Correlation of various parameters in cases and controls.

| | Controls | P | Controls | P |
|----------------------------------|----------|----|----------|-------|
| Maternal age and Systolic BP | 0.225 | NS | -0.101 | NS |
| Maternal age and Diastolic BP | 0.077 | NS | 0.170 | NS |
| Gestational age and Systolic BP | -0.089 | NS | -0.073 | NS |
| Gestational age and Diastolic BP | 0.042 | NS | 0.049 | NS |
| Vitamin E and MDA | 0.115 | NS | -0.245 | NS |
| TC and MDA | -0.315 | NS | -0.264 | NS |
| TG and MDA | -0.173 | NS | -0.159 | NS |
| LDL-C and MDA | -0.154 | NS | -0.176 | NS |
| HDL-C and MDA | -0.148 | NS | -0.139 | NS |
| MDA and Systolic BP | 0.229 | NS | 0.072 | NS |
| MDA and Diastolic BP | 0.096 | NS | -0.401 | <0.05 |

DISCUSSION

There is a marked rise in serum TG in normal pregnancy as compared to non-pregnant women, which may be as high as two to three folds in the third trimester (8). The principle modulator of this hypertriglyceridemia is hyperoestrogenemia in pregnancy that induces hepatic

biosynthesis of TGs (9). Serum TG levels rose much more in pre-eclampsia as reported by other studies (10, 11) and as seen in our study also. Increased TG levels results in endothelial cell dysfunction and in pre-eclampsia gets deposited in predisposed vessels (12), causes generation of small dense LDL (13) and hypercoagulability (14).

There was a significant rise in TC levels in pre-eclampsia as compared to normal pregnancy in our study, which was similar to other reports (15, 16) however other studies reported no alteration in TC levels (8, 13).

In our study there was significant fall in HDL-C in pre-eclampsia cases. Estrogen is responsible for induction of TG and HDL-C but in PIH there is a fall in estrogen levels as compared to normal pregnancy. Hence the low HDL-C in pre-eclampsia is due to hypoestrogenemia and insulin resistance (17). A significant rise in the LDL-C levels was seen in pre-eclampsia as compared to controls in our study and also by other workers (18, 19). It is observed that the autoantibodies to MDA-LDL and oxidized LDL liters increase in pre-eclampsia. This enhanced lipid peroxidation is involved in the foam cell formation of decidua in pathogenesis of preeclampsia (19, 20). Increased levels of small dense LDL and soluble vascular cell adhesion molecule-1 (VCAM-1) are supposed to be important contribution of endothelial dysfunction in pre-eclampsia (13, 16, 21).

Dyslipidemia mediated activation of the endothelial cells to the placentally derived endothelial disturbing factors like lipid peroxides and trophoblastic components or combination of these with altered lipids could be a possible cause in the pathogenesis of PIH (22). Thus the assessment of blood lipids maybe helpful in the prevention of complications of pre-eclampsia.

Lipid peroxidation increases during normal pregnancy (23). We observed that MDA levels increased in PIH cases as compared to normal pregnancy. There was a concomitant decrease in antioxidant levels that is Vitamin E as a response to oppose the oxidative stress. Vascular endothelial damage has been implicated in the pathophysiology of preeclampsia. However, some reports have shown no increase in lipid peroxidation in PIH (24). Decrease in Vitamin E in PIH is due to its increased consumption in exerting its action and also due to decreased absorption from gut as a result of vasoconstriction in preclampsia (25).

The present study clearly indicates that significant rise in MDA with decreased vitamin E levels and altered serum lipid levels are possible causative factors for the pathogenesis of PIH. Hence early detection of these parameters is going to aid in better management of pre-eclampsia cases which is important to improve the maternal and fetal outcome in pre-eclampsia.

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