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RESEARCH ARTICLE

A STUDY OF SERUM LIPID PROFILE AND OXIDATIVE STRESS MARKER IN HEALTHY PREGNANCY AND IN PREECLAMPSIA

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ABSTRACT

Objective: In India Pre eclampsia contributes to 15.2% maternal mortality. The present study was undertaken to compare the changes in lipid profile and oxidative stress marker (MDA) in normal pregnancy and in preeclampsia.
Methods: A case control study was done on 26 PIH patients and 24 healthy controls. Serum Total Cholesterol, Triglycerides, HDLc, LDLc, VLDLc, Urinary proteins and Malondialdehyde (MDA) were estimated. Maternal Blood pressures were recorded.
Results: Serum total cholesterol, triglycerides, LDLc, VLDLc were elevated. HDLc was decreased.MDA was thrice that of the controls.
Conclusion: This study indicates that, dyslipidemia and oxidative stress leading to endothelial damage can contribute to cardiovascular risk in future in pre eclamptic women.

INTRODUCTION

Preeclampsia is defined by de novo hypertension and proteinuria. It is a pregnancy specific condition that increases maternal and infant mortality and morbidity (Roberts, 1998; Goldenberg and Rouse, 1998). In India, the national incidence of PIH is 15.2% (Vanessa A Rodie *et al.,* 2004). According to current knowledge, dyslipidemia and increased oxidative stress are major contributors in the pathogenesis of preeclampsia. Preeclampsia and cardiovascular disease share common metabolic abnormalities, which may lead to preeclampsia and CVD at different times of a women's life. Alternatively, preeclampsia itself may induce metabolic and vascular changes that may increase the overall future risk for CVD in affected women (Uotila *et al.,* 1993). Serum lipids increase significantly during preeclampsia (Uotila *et al.,* 1993; Maseki *et al.,* 1981; Wickens *et al.,* 1981). Several studies have shown that lipid peroxides like malondialdehyde (MDA) are significantly elevated in mild and severe PIH (Ishihara, 1978; Hubel et al., 1989; Freud and Arvan, 1990).
The present study was undertaken to compare the changes in lipid profile and oxidative stress marker (MDA) in normal pregnancy and in preeclampsia and incite the future risk of atherosclerosis.

MATERIALS AND METHODS

A case control study was done in Vinayaka mission's medical college, Karaikal, consisting of 24 healthy pregnant women and 26 women with preeclampsia, admitted to antenatal ward or labor ward of General hospital, Karaikal. Institutional Ethical committee approval was taken before conducting the study. The diagnosis of PIH was done according to National Blood pressure Education Programme classification (Gifford *et al.,* 2000), by which, preeclampsia is defined as a pregnancy specific syndrome observed after the 20th week of pregnancy, with systolic blood pressure ≥140mm Hg or diastolic blood pressure of ≥ 90mmHg accompanied by significant proteinuria (i.e. urinary excretion of ≥0.3g protein in a 24h specimen) . In women with preeclampsia, blood pressure returns to baseline within days to weeks after delivery. Hypertension before 20th week of gestation was considered as essential hypertension. Blood pressure becoming normal within 10 days of delivery is not considered as pregnancy induced hypertension. The cases and controls having past history of diabetes mellitus, hypertension, renal diseases, and liver disorder were excluded. History and clinical examination findings of both cases and controls were noted. A brief clinical history, Systematic examination was done and informed consent was taken from the study subjects.

Biochemical parameters: Maternal venous samples were collected after overnight fasting for estimation of serum cholesterol, triacylglyceride, HDL and lipid peroxidation product, plasma malondialdehyde (MDA).Serum was separated by centrifugation at 3000 rpm for 10 minutes.

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Estimation of Serum Cholesterol: Serum total cholesterol was estimated by cholesterol oxidase/ Peroxidase (CHOD/POD) colorimetric endpoint method, using Liquizyme kit.

Cholesterol esters are hydrolysed by cholesterol esterase to produce free cholesterol and fatty acid. This free cholesterol gets oxidized in the presence of cholesterol oxidase to liberate cholestenone and hydrogen peroxide. Liberated hydrogen peroxide combines with hydroxyl benzoate and 4 aminoantipyrine in the presence of peroxidase to form red coloured quinonimine complex, the intensity of which is measured at 505nm (490- 530nm).

Table 1. Blood pressure of cases and controls

BP (mm Hg)	Cases=26	Control=24	t-Value	P Value
SBP(mm Hg)	146.4±9.52	111±76	9.91	< 0.0001
DBP(mm Hg)	96.8±10.69	74.12±7.95	4.51	<0.0001

Values are mean ±SD; BP: Blood Pressure, SBP, Systolic blood pressure; DBP, Diastolic blood pressure.

Estimation of Serum HDLC: Serum HDLc was estimated by Direct method using, Liquizyme kit (NCCLS, 1999). The system utilizes a combination of surfactants, phosphoric acid, organic acids, and inorganic acids, specifically binding LDLc, VLDLc and chylomicrons. Only HDL cholesterol is detected by the enzymatic CHOD/ POD method.

Estimation of SerumTriglycerides: Serum triglyceride was estimated by Glycerol phosphate oxidase/ Peroxidase (GPO/POD) colorimetric endpoint method using Liquizyme kit. Triglyceride is hydrolysed by lipoprotein lipase to free fatty acids and glycerol. Glycerol kinase converts glycerol to glycerol phosphate, which gets oxidized to dihydroxy acetone phosphate and hydrogen peroxide by glycerol phosphate oxidase. Hydrogen peroxide so formed reacts with 4 aminoantipyrine in the presence of peroxidase to give a purple coloured complex which is read at 546 nm.

Calculation of LDLc and VLDLc : VLDLc level in serum is derived by dividing serum triglycerides by 5 and LDLc is obtained using Friedwald's formula (Friedwald *et al.,* 1972), namely, LDLc = Total cholesterol – (HDLc + VLDLc).

Assay for Lipid peroxides in Plasma*:* Plasma lipid peroxides was estimated by Esterbauer and Steinberg method (1989) (Nagdeote et al., 2006). Malondialdehyde (MDA) was assayed as a marker of lipid peroxidation using colorimetric reaction, which uses 1-methyl-2-phenylindole as chromogen. Condensation of one molecule of malondialdehyde with two molecules of 1-methyl-2-phenylindole under acidic condition results in the formation of a chromophore with an absorbance of maximum at 586 nm. To determine specifically lipid peroxide in plasma, they are precipitated along with plasma proteins to remove water-soluble MPI reactive substances. The level of lipid peroxide is expressed in term of malondialdehyde. Since the malondialdehyde is unstable, tetramethoxypropane which is converted quantitatively to MDA in the reaction procedure is used as standard.

Estimation of Urinary Protein: Daily urinary protein excretion was estimated by colorimetric Pyrogallol method using Accucare kit in a 24 hour urine specimen.

Measurement of Blood Pressure: Both systolic and diastolic blood pressures were recorded on two occasions separated by an interval of six hours.

Statistical Analysis: Statistical analysis was done using MS Excel. Data are presented as Means±SD. Correlation between measured parameters was assessed using the t- value and p-value. P value less than 0.05 was taken as the level of significance.

Table 2. Serum Lipid Profile, MDA and Urinary Proteins in Preeclampsia and in controls

Biochemical parameters	Cases = 26	Controls = 24	T - Value	P - Value
Total cholesterol (mg%)	232.24± 39.16	188.12± 14.61	7.2	< 0.0001
Triacylglyceride (mg%)	210.36±39.74	145.00±28.88	8.7	< 0.0001
HDLc (mg%)	36.24±3.53	48.06±5.91	5.43	< 0.0001
LDLc (mg%)	153.37±37.517	111.06±16.67	9.03	< 0.0001
VLDLc (mg%)	42.07± 7.947	29.00±5.78	8.7	< 0.0001
MDA (µ Mole/ L)	6.61±3.76	2.21±1.47	4.45	<0.0001
Urinary Protein (g/d)	0.92±1.06	0.24±0.3	0.014	NS

NS - Not significant

RESULTS

The preeclampsia cases have significant rise in both systolic and diastolic blood pressure. The mean value of SBP (Systolic blood pressure) in cases is 146.4± 9.52 and in control, 111.76 ± 8.83, there is significant difference (P<0.0001) between cases and controls. The DBP (Diastolic Blood Pressure) of Mean in cases and control is 96.8±10.69 and 74.12±7.95 respectively, there is significant difference (P<0.001) between cases and controls. Serum cholesterol, triglycerides, LDL and VLDL were found to be significantly elevated in patients of PIH, when compared to the control population (Table 2).

i. There was a significant rise in serum TG, TC, and LDLc and VLDLc (P = < 0.0001) and a fall in HDL-C, in preeclampsia cases.
ii. MDA was nearly thrice in the cases (P= < 0.0001), when compared to that of the controls.
iii. The level of rise of serum lipid did not significantly correlate with the rise or fall in MDA.

The level of urinary protein was relatively higher in PIH cases, when compared to the control

DISCUSSION

Endovascular trophoblastic cells replace the endothelium of spiral arterioles, invade tunica media and destruct medial elastic, muscular and neural tissues. Endothelial lining is reconstituted following the incorporation of trophoblastic cells into the vessel wall (Pijnenborg *et al.,* 1991). The goal of these physiological changes is to increase uteroplacental blood flow

by disruption of maternal vasomotor control and creation of a low-resistance arteriolar system. These physiologic changes do not go beyond maternal decidua in preeclamptic patients, and even no normal vascular transformation may be seen. Lipid-laden macrophage deposition and perivascular mononuclear cell infiltration may also be seen, and this way of acute atherosis may lead to placental infarction. In Pre eclampsia, elevated levels of MDA were found to be associated with elevated serum lipid levels, indicating that PIH is associated with excessive free radical formation. Thus, Preeclampsia shares some similarities with atherosclerosis, namely the involvement of oxidative stress and endothelial dysfunction in their patho physiologies (Ahmet *et al.,* 2003). Abnormal lipid metabolism is not a mere manifestation but is also involved in the pathogenesis of preeclampsia. Lipid mediated oxidative stress is likely to contribute to endothelial hyper stimulation leading to damage and dysfunction, common to that of chronic vascular diseases (DeWolf *et al.,* 1975). Thus, dyslipidemia and oxidative stress can contribute to cardiovascular risk in preeclamptic women in future. To conclude, preeclampsia may prove to be a sentinel of heart diseases.

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