

Original Research Article

Study the components of metabolic syndrome in preeclampsia

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ABSTRACT

Background: Long term health implications in women who develop hypertensive disorders of pregnancy (HDP) include an increased risk of developing cardiovascular diseases (CVD) later in life. So based on this the present study was undertaken to investigate parameters of metabolic syndrome in normal pregnant and preeclamptic women.

Methods: Serum HDL cholesterol, serum triglycerides, fasting blood sugar levels and blood pressure (systolic and diastolic) were estimated in 100 normal pregnant women (controls) and 100 pregnant women with preeclampsia (cases) and comparison between cases and age matched controls of age group 18-35 years done using 'z' test. Study was carried out between 2011 to 2015. All statistical analyses were performed using GRAPH PAD PRISM version 5.00 software and Microsoft Office Excel 2007 software.

Results: Serum triglyceride (TG), fasting blood sugar levels and blood pressure (systolic and diastolic) were significantly elevated ($p < 0.0001$) while high density lipoprotein (HDL) was significantly decreased ($p < 0.0001$) in preeclamptic group than in control group.

Conclusions: Serum triglyceride (TG), fasting blood sugar levels and blood pressure (systolic and diastolic) were significantly elevated ($p < 0.0001$) while high density lipoprotein (HDL) was significantly decreased ($p < 0.0001$) in preeclamptic group than in control group.

Keywords: Blood pressure, Fasting blood sugar, HDL, Metabolic syndrome, Preeclampsia, Triglyceride

INTRODUCTION

Hypertensive disorders accounts for 5-10% of all pregnancies, and considering their complications, they are among the major causes of maternal morbidity and mortality.^{1,2} Preeclampsia, the most prevalent hypertensive disorders of pregnancy, is defined as a systolic blood pressure level of 140 mm Hg or higher or a diastolic blood pressure level of 90 mm Hg or higher that occurs after 20 weeks of gestation with proteinuria (≥ 300 mg/24 hours).

Studies have already shown alterations in serum lipid profile in pre-eclampsia. Dyslipidemia has a direct effect

on endothelial dysfunction. The most important feature in preeclampsia is hypertension which is supposed to be due to vasospastic phenomenon in kidney, uterus, placenta and brain. Altered lipid synthesis leading to decrease in PGI₂: TXA₂ ratio. It has also role in pathogenesis of preeclampsia. In this way abnormal lipid metabolism has important role in the pathogenesis of preeclampsia.

The hormonal imbalance is major factor for the etiopathogenesis of preeclampsia and this endocrinal imbalance is well reflected in altered serum lipid profile.³ Early pregnancy dyslipidemia is associated with an increased risk of pre-eclampsia.⁴ Disorders of lipoprotein metabolism are major cause of hypertension and proteinuria in pre-eclampsia.⁵ So that the present study

was undertaken to investigate the lipid profile (Cholesterol, triglycerides, HDL-cholesterol, VLDL-cholesterol and LDL-cholesterol) in normal and pre-eclamptic women. Along with lipid profile we also planned to study blood sugar levels to determine whether it prone to develop metabolic syndrome.

METHODS

The present study has been carried out in Indira Gandhi Government Medical College and Mayo Hospital, Nagpur during the period of November 2011- April 2015. The study protocol was approved by the Institutional Ethical Committee. Informed written consent was obtained from all the study subjects enrolled in the study. Study sample was included total of 200 individuals; 100 diagnosed preeclamptic patients (cases) admitted in ANC ward in this institute and 100 age matched healthy and apparently normal pregnant women (controls) were also selected for study.

The cases and controls were in the age group of 18-35 years were included in the study.

Pre-existing hypertension, IHD, CRF, DM, liver diseases, thyroid disorders, past and family history of hyperlipidemia, treatment with drugs may influence lipid profile were excluded in the study.

Serum lipid profile and blood sugar levels

5 ml of fasting venous blood sample was withdrawn from the anti-cubital vein of each participant after taking all aseptic precautions using sterile needles and syringes without the aid of a tourniquet. Haemolysed samples were excluded from the study.

For estimation of triglycerides and HDL level, 4 ml of the blood sample were then immediately transferred to a clean dry sterile plain bulb and 1ml of blood taken in fluoride bulb for estimation of blood sugar. The blood samples were analyzed immediately. Serum lipid profile and blood sugar were estimated from fasting blood sample.

Blood sugar and triglyceride (TG) estimated by enzymatic method while high density lipoprotein (HDL C) by precipitation method. The estimation was done on

TRANSASIA ERBA CHEM-5 Plus semi-automatic analyzer.

Statistical analysis

Z test was used to assess the significance of the differences in values of the parameters in cases and controls and values were reported as the mean \pm SD. Differences were considered statistically significant at a probability value $p < 0.05$. All statistical analyses were performed using GRAPH PAD PRISM version 5.00 software 6 and Microsoft Office Excel 2007.

RESULTS

In cases the mean age of distribution was 22.86 ± 2.63 years and gestational age was 34.85 ± 1.03 weeks while in controls the mean age of distribution was 22.95 ± 2.27 years and gestational age was 34.85 ± 1.03 (Table 1). On comparing mean age and gestational age of cases and controls, p value was 0.79 and 0.97 respectively which was statistically non-significant. Hence both the groups were comparable.

Body mass index (BMI) in controls and cases were 24.24 ± 1.37 and 27.55 ± 1.17 respectively. Significant difference ($P < 0.0001$) was present in both groups (Table 2).

Table 1: Comparison of mean age and mean gestational age in cases and controls

Parameters	Cases (n = 100) Mean \pm SD	Controls (n = 100) Mean \pm SD	p-value
Mean age \pm SD	22.86 ± 2.625	22.95 ± 2.271	0.79
Mean gestational age \pm SD	34.85 ± 1.030	34.85 ± 1.028	0.97

Table 2: Comparison of body mass index (BMI) in cases and controls.

Parameters	Cases (n = 100) Mean \pm SD	Controls (n = 100) Mean \pm SD	p-value
Body mass index(BMI)	27.55 ± 1.17	24.24 ± 1.37	<0.0001

Table 3: Comparison of systolic and diastolic blood pressure in cases and controls.

Parameter	Cases (n = 100) Mean \pm SD	Controls (n = 100) Mean \pm SD	p-value	Inference S/NS
Systolic blood pressure (mm Hg)	145.5 ± 2.303	105.7 ± 7.536	<0.0001	S
Diastolic blood pressure (mm Hg)	96.32 ± 2.767	72.08 ± 4.421	<0.0001	S

Systolic blood pressure (SBP) of cases i.e. 145.5 ± 2.30 mm of Hg was higher than that of controls i.e. 105.7 ± 7.54 mm of Hg (Table 3). Statistically, the difference between mean SBP of cases and controls was highly significant ($P < 0.0001$). Cases had diastolic blood pressure (DBP) of 96.32 ± 2.77 mm of Hg which is higher as compared to that of controls which was 72.08 ± 4.42 mm of Hg (Table 3). The mean DBP of cases and controls has shown a statistically highly significant difference ($P < 0.001$).

Table 4: Comparison of serum triglycerides and HDL in cases and controls

Parameters	Group A (n =100) Mean \pm SD	Group B (n = 100) Mean \pm SD	p-value
Triglyceride (mg%)	209.0 \pm 6.44	169.0 \pm 7.25	0.0001
HDL (mg%)	34.02 \pm 3.53	73.86 \pm 2.25	

Table 5: Comparison of fasting blood sugar level in cases and controls.

Parameter	Mean glucose \pm SD		p-value
	Group A n = 100	Group B n = 100	
Fasting glucose (mg/dl)	112.9 \pm 8.24	96.44 \pm 8.24	<0.0001

Triglycerides and HDL in cases were 209.0 ± 6.442 and 34.02 ± 3.533 respectively. In controls triglycerides and HDL levels were 169.0 ± 7.247 and 73.86 ± 2.247 respectively (Table 4). Triglycerides were significantly ($P < 0.0001$) increased in cases than controls while HDL was significantly ($P < 0.0001$) decreased in cases than controls.

Fasting blood sugar levels in cases were 112.9 ± 8.24 . In controls fasting blood sugar levels were 96.44 ± 8.24 . (Table 5, Fig 5) Fasting blood sugar was significantly ($P < 0.0001$) increased in cases than controls.

DISCUSSION

Preeclampsia continues to be a main obstetric problem in present-day healthcare practice. It affects not only maternal health but also puts fetal development at risk. The high blood pressure problems of pregnancy are very frequent. During pregnancy and the puerperium it is accountable for 12% of maternal mortality worldwide.⁷

The relation between a disordered lipid profile, endothelium cell and oxidative stress is of major importance to the patho-physiology of pregnancy induced hypertension. Elevated plasma lipids are believed to be probable cause of endothelial cell activation. In normal pregnancy adaptive alteration occur in women's physiology to setup needs for the rapidly developing

fetus.⁸ This normal alteration exaggerated in preeclampsia includes insulin resistance, hyperlipidemia and up-regulation of inflammatory markers.^{7,9} Studies have revealed that patients having preeclampsia are more exposed to cardiovascular diseases, signifying that preeclampsia and cardiovascular disorders may share similar mechanisms.⁹⁻¹²

Most of the studies showed that total cholesterol level was not much altered in preeclampsia.^{3,5,9,13-15} Some earlier studies reported that the striking change in the lipid profile in preeclampsia was serum hypertriglyceridemia. In our study also this observation holds true and the rise in serum triglycerides was statistically significant ($P < 0.0001$) in pregnancy induced hypertensive patients when compared to women with normal pregnancy.^{3,15,18}

Hypertriglyceridemia may be modulated by hyperinsulinism established in pregnancy.¹⁹ Triglycerides, small dense LDL particles and free fatty acids levels increased in normal pregnancy are correlated with insulin resistance.²⁰ In preeclampsia this insulin resistance is exaggerated and causing further increased in triglycerides levels.²¹ During gestation these interactions along with increased endothelial triglyceride accumulation may result in endothelial cell dysfunction.²² In preeclampsia increased triglyceride found, is probably 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 low density lipoprotein cholesterol.⁹ Moreover, this hypertriglyceridemia may be linked with hypercoagulability.²³

In pregnancy hepatic lipase activity increased and lipoprotein lipase activity decreased. Hepatic lipase induces synthesis of the more triglycerides at the hepatic level, and low lipoprotein lipase activity causing decreased catabolism at the adipose tissue level. In late pregnancy estrogen increases VLDL production and decreases lipolysis. Upregulation of placental VLDL receptors causing a coordinated rerouting of TG-rich lipoproteins from the mother toward the fetoplacental unit to meet the nutritional demands of the growing fetus. But in preeclampsia nutrient uptake by fetus is affected resulting in fetal distress and retardation. So that reduced maternal lipolysis and the low uptake of TG-rich lipoproteins by the fetoplacental unit lead to the accumulation of TG-rich lipoproteins in the maternal circulation.^{24,25}

Another hypothesis is that hypertriglyceridemia is as a result of competition between chylomicrons and very low-density lipoprotein cholesterol for the lipoprotein lipase. Chylomicrons removal occurs in two sequential steps

- Hydrolysis of triglyceride by lipoprotein lipase
- Uptake of the remnant by the liver.

Delay in the second step leads to accumulation of remnants in plasma and is generally thought to represent the atherogenic risk of hyper-triglyceridemia.²⁴

Hypertriglyceridemia leading to increased entry of VLDL-C that carries endogenous triglyceride into circulation. VLDL-C level further elevates in preeclampsia was already proven by other researchers.^{3,9,16,26} Increased VLDL-C accumulate over the maternal vascular endothelium, mainly those of uterine and renal vessels.³ Further VLDL-C may cause injury to the endothelium, while a particular toxicity preventing- activity-protein protects against the VLDL-induced damage in the pathogenic process of toxemia.²⁷

In present study HDL cholesterol was significantly decreased ($p < 0.0001$) in preeclamptic group than healthy control group. Decrease in HDL-C level in preeclampsia supported by other studies also.^{4,14,15,17} Oestrogen is responsible for induction of HDL and suppression of serum LDL in pregnancy but oestrogen level falls in preeclampsia.³ Low level of HDL in pre-eclampsia is not only because of hypooestrogenaemia but also due to insulin resistance.²¹ So that low LDL-C level is observed in normal pregnancy may be attributed to hyperoestrogenaemia and significantly higher LDL-C level in pre-eclampsia are due to low oestrogen level in preeclampsia.²⁹ Increased LDL-cholesterol ($p < 0.0001$) in preeclamptic group also proved by various studies.^{4,14,15,28} Low HDL C level in preeclampsia reduces prostacyclin level and antioxidative protection for the other lipoproteins.¹³

We had also accessed blood sugar level in study groups and found that fasting blood sugar was significantly ($p < 0.0001$) high in preeclampsia group than normal pregnant women.. This increased in fasting sugar is may be because of insulin resistance in preeclampsia. Insulin resistance in preeclampsia was proved by various studies.³⁰⁻³² Insulin resistance is one of the components of the metabolic syndrome that is present in preeclamptic women.

Association between preeclampsia and metabolic syndrome proved by various studies.^{33,34} Finding of our study i.e. high blood pressure ($>140/90$ mmHg), high fasting blood sugar level (>110 mg %), high serum triglycerides (>150 mg %), low HDL-C (< 39 mg%) satisfied all three criteria i.e. WHO, ATP III and AACE for diagnosis of metabolic syndrome.³⁵ BMI ≥ 25 kg/m² which satisfying AACE criteria. Available literature suggests that women who develop pregnancy induced hypertension and/or preeclampsia have metabolic abnormalities similar to those present in patients with insulin resistance syndrome.^{9,21}

By appropriately recognizing the metabolically challenged pregnancy, we could have the opportunity to prevent or delay the onset of clinical disease and because of the increased risk of morbidity and mortality

associated with the metabolic syndrome, an understanding of the presentations of this syndrome is vital especially among pregnant women.

CONCLUSION

Findings from this study support an association between the metabolic syndrome and the hypertensive state associated with preeclampsia. Also, the results of this study have shown that women with preeclampsia have components of the metabolic syndrome which is in good agreement with the notion that women prone to preeclampsia are predisposed to developing metabolic syndrome. It is well known fact that metabolic syndrome is predisposed to cardiovascular diseases. So preeclampsia can be risk factor for future cardiovascular diseases.

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