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TO DETERMINE ASSOCIATION OF LIPID PROFILE, SERUM URIC ACID AND BODY MASS INDEX AS A MARKER FOR PREECLAMPSIA

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ABSTRACT

Objective: To detect association of serum lipid profile, uric acid and body mass index in preeclampsia and to measure their clinical significance.

Methods: A prospective case-control study was conducted at Kamineni Institute of Medical Sciences, Narketpally. One hundered patients with pre-eclampsia were compared with age matched 100 normotensive pregnant woman. Body mass index was calculated. Blood pressure was measured. Their serum levels of triglycerides (TG), Cholesterol, low density lipoprotein (LDL), very low density lipoprotein (VLDL), high density lipoprotein (HDL) & serum uric acid were measured. Data was analysed by students t-test and Chi-square test.

Results: Blood pressure, body mass index ,TG, VLDL, LDL, cholesterol and serum uric acid level were significantly higher in preeclamptic women ($p<0.05$); while serum HDL was significantly low in preeclamptic women ($p<0.05$).

Conclusion: Lipid abnormalities, mostly elevated TG, cholesterol, LDL, VLDL, maternal obesity and uric acid are associated with preeclampsia. Early detection of these parameters may help in their better management.

Key Words: Body mass index, High blood pressure, Lipid profile, Pre-eclampsia, Uric acid

INTRODUCTION

Pregnancy is a physiological stress in which many changes occur in the milieu interior, to meet demands of the rapidly developing fetus including biochemical changes. These changes are exaggerated in complications of pregnancy like pre-eclampsia[(1)]. Pre-eclampsia is a pregnancy specific disorder and is an important cause of fetal and maternal morbidity and mortality. Nearly 7-10% of pregnancies are complicated worldwide[(2)]. While incidence of pre-eclampsia in India ranges between 11-13%. It is a multi-system disorder of unknown etiology and is mediated by placental products that reaches maternal circulation and trigger endothelial dysfunction, thereby evoking cardiovascular diseases, such as vasospasm, increased endothelial permeability and activation of thrombogenic mechanisms and leading to early events of atherosclerosis[(3)]. Susceptibility to preeclampsia is also modulated by maternal factors like obesity, chronic hypertension, diabetes mellitus and hyperlipidemia which exhibits intense vascular reactivity. However, several theories like placental ischemia, genetics, immune maladaptation and oxidative stress have been proposed[(4)]. Out of which oxidative stress theory is most widely accepted and has been linked with lipid abnormalities and vascular dysfunction. Predominantly atherogenic LDL are increased in association with hyperlipidemia in preeclampsia. Also, excessive cellular activity associated placental ischemia leads to overproduction of uric acid which serves as a marker of disease[(5)].So, simple measurement of serum lipid profile, serum uric acid and body mass index may be of good predictive value in preeclampsia. Therefore present study was conducted to find out any association between lipid profile, serum uric acid and body mass index in preeclampsia.

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MATERIAL AND METHOD

Present prospective case-control study was conducted in Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, after taking approval from ethical committee, from June 2014 to March 2015 in 200 pregnant women.

Inclusion Criteria:

- Primigravida between 18- 35 years of age in third trimester
- Singleton live fetus

Exclusion Criteria:

- Refusal for participation in study
- Multiple pregnancies
- Patients with essential hypertension, diabetes mellitus, renal disease, liver disorder, and thyroid disorder
- History of treatment with drug influencing lipid profile

The patients were divided into two groups:

- Control Group - Normotensive pregnant women (n= 100)
- Study Group - Pregnant women with preeclampsia (n= 100)

All patients were explained in detail about aim, objectives of study and written consent was taken. A detailed obstetric history and examination was done. Height was measured, maintaining an accuracy of 0.5cm.Weight was measured, up to nearest 100gm. Prepregnancy body mass index (Quetelet index) was calculated as weight in kilograms/height in square meters. According to WHO, normal BMI ranges from 18.5 to 24.9 kg/m^2. BMI between 25-29.9 kg/m^2 is overweight, while a BMI > 30 kg/m^2 is considered obese. Blood pressure was measured by sphygmomanometer in right arm in left lateral position after 10 minutes of rest. Preeclampsia was diagnosed as blood pressure >140/90 mmHg on 2 separate occasions 4 hours apart in association with proteinuria (>0.3gm in 24 hours or at least 1+ on dipstick examination[6].

With fasting of 8 hours, under all aseptic precautions 8-10 ml of blood was collected and analysed for lipid profile and serum uric acid. Triglycerides were measured by Glycerol phosphate oxidase/ Peroxidase (GPO/POD) colorimetric endpoint method. Cholesterol and HDL were measured by cholesterol oxidase/ Peroxidase (CHOD/ POD) colorimetric endpoint method. LDL measured directly using semi-auto analyzer by enzymatic method. VLDL was calculated as 1/5th of triglycerides.Pregnant women were diagnosed as having dyslipidaemia according to American Association of Clinical Endocrinologists Guidelines[7]. Uric acid was measured by uricase – POD enzymatic method . Abnormal serum uric acid was defined as values >5mg/dl.

Statistical Analysis: The data collected was tabulated in microsoft excel sheet. They were analysed and compared using unpaired students t-test and Chi square test. 'p' value less than 0.05 was considered significant.

RESULTS

Mean body mass index in preeclamptic women was 29.4 ±2.8 Kg/m^2 which was significantly higher then control group ($p < 0.05$) (Table 1).

Blood pressure were high in preeclamptic women (Table 2).

TG, VLDL, LDL, cholesterol, serum uric acid level were significantly higher in preeclamptic women ($p<0.05$), while serum HDL was significantly low in preeclamptic women ($p < 0.05$) (Table 3).

DISCUSSION

In present study, 100 patients with pre-eclampsia were compared with 100 age matched normotensive pregnant woman. Our aim was to detect association of serum lipid profile, uric acid & body mass index in preeclampsia.

Women with preeclampsia had significantly higher BMI compared with controls ($p< 0.05$)(Table-2) which is similar to finding of Sharami et al[8]. Probable, mechanism of increased BMI in preeclampsia is increased insulin resistance and a state of inflammation associated with obesity[9]. Insulin resistance leads to lipolysis, leading to increased flux of fatty acids to liver promoting synthesis of TG[10]. Also maternal obesity is independently associated with development of placental endothelial dysfunction and ultimately preeclampsia[9]

The mean levels of TG, VLDL, LDL and cholesterol were significantly higher in preeclamptic women than in normotensive controls ($p<0.05$). Also there was a significant decrease in HDL in study group as compared to control ($p<0.05$) (Table-3). Hypertriglyceridemia in preeclampsia is also attributed to insulin resistance due to obesity. During early pregnancy, anabolic phase encourages lipogenesis and fat storage in preparation for rapid fetal growth in late pregnancy. Therefore there is physiologic hyperlipidemia with gestational rise in triglyceride and cholesterol as high as two to three times in third trimester[11] Risk of preeclampsia was four times higher in women with elevated TG[12].

Oestrogen induces biosynthesis of endogenous triglyceride by stimulating hepatic lipase[13].

There is decreased activity of lipoprotein lipase which is responsible for decreased catabolism at adipose tissue level, Thus in preeclampsia, there is hypertriglyceridem-

ia whereas placental VLDL receptors are up regulated. This results in re-routing of TG rich lipoproteins to fetoplacental unit. However in preeclampsia the vascularization of fetoplacental unit may be impaired, resulting in yet-undefined compensatory mechanisms that may further increase synthesis of maternal TG levels[14].

As already discussed, obesity and insulin resistance also promotes synthesis of TG.

Another hypothesis is that hypertriglyceridemia is probably a consequence of competition between chylomicrons and VLDL for lipoprotein lipase. Classically, chylomicron clearance occurs in two sequential steps: 1) triglyceride hydrolysis by lipoprotein lipase . 2) uptake of remnant by liver. Delay in second step leads to accumulation of TG in plasma and is thought to represent the atherogenic risk of hyper-triglyceridemia[15].

Abnormal lipid metabolism is not a mere manifestation but is also involved in pathogenesis of disease. Increased serum triglyceride is likely to be deposited in predisposed vessels such as uterine spiral arteries and contributes to endothelial dysfunction, both directly and indirectly through generation of LDL. Hypertriglyceridemia also has prothrombotic activity which may be associated with hyper-coagulability. Altered lipid synthesis leading to decreased in Prostaglandin I2 (PGI2) : Thromboxane A2 (TXA2) ratio is also supposed to be an important way of pathogenesis in pre-eclampsia[13].

VLDL transports TG in peripheral blood therefore hypertriglyceridemia also leads to increased serum levels of VLDL[9]. As already discussed, insulin resistance causes lipolysis, leading to increased flux of fatty acids to liver promoting synthesis of VLDL[10].

Increased LDL levels are due to elevated estrogen and progesterone levels in preeclampsia.

It has been shown that LDL (specially oxidized LDL) increases arterial sensitivity to pressor agents and inhibits endothelium dependant vasodilatation. This endothelial dysfunction, leads to glomerular lesions and subsequently proteinuria, which also gives an indication of its severity[5].

Low HDL in preeclampsia is due to insulin resistance[16]. According to Pirzado et al[17], there is a direct correlation between adipose tissue lipoprotein lipase activity and plasma HDL. This is responsible for low levels of HDL .

HDL carries excess, potentially harmful cholesterol from peripheral tissues to liver, where it can be excreted. In addition, it is involved in activating lipoprotein which releases fatty acids that can be oxidized by β-oxidation pathway to provide energy. Low levels of HDL may compromises these functions.

Hypercholesterolemia promotes formation of free radicals (free radical theory). Thus several studies have linked 'atherogenic' lipid profile as a potential contributor to increased risk of preeclampsia[9].

Thus, dyslipidemia mediated endothelial dysfunction & placentally derived endothelial disturbing factors like lipid peroxides could possibly contribute in pathogenesis of pregnancy induced hypertension.

Thus, estimation of lipid profile may have a predictive role in assessing extent of endothelial damage and may help by preventing or foreseeing complications in preeclampsia [11].

Serum uric acid level were significantly higher in preeclamptic women ($p < 0.05$). This is consistent with previous studies[5,18,19].Excessive cellular activity is associated with placental ischemia also leads to overproduction of uric acid which serves as a marker of the disease. Uric acid levels have been consistently reported to be elevated in preeclampsia. Hyperuricemia may predate proteinuria by several weeks [18,19].

CONCLUSION

Present study concludes that there is 'atherogenic' lipid profile in preeclampsia and may contribute in its pathogenesis. Prime duty of all obstetrician is to decrease perinatal morbidity and mortality by early diagnosis and its management. Therefore serum lipid profiles should be continuously monitored throughout pregnancy and early detection of alteration in these parameters will help Obstetricians to make right decision at right time and intervene early to improve maternal and fetal outcome in pre- eclampsia.

As a primary prevention, women should be given effective counselling to adopt healthier lifestyles to control their weight and lipid levels.

Future Scope: Studies on associations of 'atherogenic' lipid profile and preeclampsia may be helpful in understanding its pathophysiology. Development of preventive and therapeutic strategies in pregnant women at risk will help in better maternal & fetal outcome that subsequently improves health of the community.

Following are the limitations of the present study.

It was performed in a single hospital, therefore sample may not be representative of all Indian women .

The single determination of lipid profile as done in present study instead of serial measurements during pregnancy as done in longitudinal studies may lead to misleading data.

We recommend a cross-sectional multicentric study to confirm results of present study & to define possible relationship between preeclampsia and lipid metabolism.

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ABBREVIATIONS:

TG: Triglycerides

HDL: High Density Lipoprotein

LDL: Low Density Lipoprotein

VLDL: Very Low Density Lipoprotein

WHO : World Health Organization

BMI : Body mass index

BP : Blood pressure

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Table 1: Distribution of Body Mass Index (BMI)

S. No	BMI (Kg/m^2)	Control Group (n=100)	Study Group (n=100)	'p' value
1	18.5 -24.9 (Normal weight) *	70%	18%	< 0.05
2	25-29.9 (Over weight) *	22%	52%	
3	>30 (Obese) *	8%	30%	
Mean ± SD*		27.0 ± 2.1	29.4 ±2.8	< 0.05

* Statistically significant

Table 2: Distribution of Blood Pressure in Control and Study Group

S. No	Parameter (mm Hg)	Control Group (n=100) (mean ± SD)	Study Group (n=100) (mean ± SD)
1	Systolic BP	114.76 ±0.43	152 ±0.47
2	Diastolic BP	68 ±0.82	104 ±0.26
3	Mean Arterial Pressure	82.16 ±1.46	120 ±0.24

Table 3: Distribution of Lipid profiles and Uric acid level in Control and Study groups

S.No	Parameters (mg/dl)	Control Group (n=100) (mean ± SD)	Study Group (n=100) (mean ± SD)	'p' value
1	TG*	136.60 ± 39.67	238.75 ±0.29	< 0.05
2	HDL*	48.34 ±5.46	38.31 ±7.70	< 0.05
3	LDL*	98.17 ±14.75	130.45 ±26.21	< 0.05
4	VLDL *	41.47 ±1.38	113.06 ±2.05	< 0.05
5	Cholesterol*	158.90 ±7.86	232.14 ±7.63	< 0.05
6	Uric acid*	4.01 ±0.23	6.01 ±3.24	< 0.05

* Statistically significant
TG: Triglycerides, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, VLDL: Very Low Density Lipoprotein