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To Study of LIPID Profile and Serum Alkaline Phosphatase in Preeclampsia Women

Biochemistry

KEYWORDS : HDL – High density cholesterol, LDL – low density cholesterol & VLDL- very low density cholesterol

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ABSTRACT

The study was carried out to estimate lipid profile and serum alkaline phosphatase level in preeclamptic women as compare to normotensive women. The study comprised of 60 cases of preeclamptic women who attended in Obstetrics & Gynecology Department in Govt. Medical College, Nagpur from February 2013 to August 2014 and 60 normotensive healthy womens as controls. The mean Serum triglycerides, total cholesterol, LDL & VLDL in preeclamptic cases (preeclampsia women) were increased significantly (p >0.001). On the other hand serum HDL levels were decreased significantly in preeclamptic women when compared to controls (p >0.001). Serum alkaline phosphatase was increased significantly in preeclamptic women when as compared to controls (p >0.001). Serum alkaline phosphatase is positively correlates with systolic blood pressure. From the results all these parameters play an important role in preeclampsia hence early detection of these parameters in preeclampsia may help to improve maternal and fetal outcome.

Introduction

Pregnancy is a physiological state associated with many alterations in metabolic, biochemical, physiological, hematological and immunological processes. If these changes are exaggerated, they can lead to complications during pregnancy.

Pregnancy induced hypertension presents with new onset hypertension and proteinuria after 20 weeks of gestation. Hypertensive disorders are the most common medical complications occurring during pregnancy. Pregnancy induced hypertension was reported with the incidence of about 10% of first pregnancy and 20% to 25% of previous pregnancy. The incidence of Pregnancy Induced Hypertension (PIH) varies among different hospitals, regions and countries.[1]

According to WHO's World Health Report 1998, Preeclampsia is defined as "the development of hypertension (>140/90 mm of Hg) after 20 weeks of pregnancy in a woman with proteinuria associated with or without edema having no previous history of hypertension"[2]

Recent finding related to pathophysiology of pre-eclampsia suggest that the endothelial cell injury and altered endothelial cell function play a pivotal role.[3] It has been proposed that the poorly perfused placenta is the origin of a humoral factor that affects maternal systemic function, directly or indirectly, by activating endothelial cells, with resultant vascular injury.[4] The characteristic pathologic lesion seen in the uteroplacental bed of patients with pre-eclampsia is a necrotizing arteriopathy consisting of fibrinoid necrosis, accumulation of foam cells or lipid-laden macrophages in the decidua, fibroblast proliferation and a perivascular infiltrate. This lesion has been termed "acute atherosis.[5]

During normal pregnancy, there appear a physiological increase in serum triglycerides but it is not athrogenic as being it under hormonal control. The abnormal triglycerides metabolism has also established its important in pathogenesis of preeclampsia.[6,7,8]

Placental synthesis of alkaline phosphatase (ALP) during pregnancy has a role in division of normal and transformed cells. This enzyme is responsible for active transport of phosphate.[9] Lowering of serum ALP in pregnancy may be an indicator of intra uterine growth retardation (IUGR). ALP was also noticed to be increased in pre-eclampsia.[10]

Material and methods

Hospital based cross sectional study was conducted in Department of Biochemistry with the help of Obstetrics and Gynecology Department during period May 2013 to October 2014. The study was approved by institutional Ethics Committee for research work.

The study comprised of 60 cases of preeclamptic women who attended in Obstetrics & Gynecology Department in tertiary health centre from February 2013 to August 2014 and 60 normotensive healthy womens as controls. These patients were all primigravidae aged between 18 to 30 years and in the third trimester of pregnancy

The diagnosis of Preeclampsia was done by the department of Obstetrics and Gynecology based on the definition given by American college of obstetrics and gynecology. Systolic blood pressure > 140 mm Hg or diastolic blood pressure >90 mm Hg; systolic blood pressure increase of > 30 mm Hg or diastolic blood pressure increase of 15 mm Hg over first trimester of pregnancy values (manifested on two occasion at least 6 hrs apart) and proteinuria ≥300 mg or greater in 24 hr urine collection or dipstick protein ≥ 1+ (on two occasion at least 6 hrs apart) is preeclampsia

The inclusion criteria for pre-eclamptic subjects include Age – 18 to 30 years, primigravidae in the 3rd trimester of pregnancy, BP -- 140/90 mm Hg in third trimester of pregnancy (ACOG criteria), Urine albumin ≥ I + dipstick or 300 mg per 24 hour urine. Normal pregnant women in third trimester of pregnancy were taken as controls.

The exclusion criteria for both the groups were Age < 18 years and > 30 years. (Multigravidae with more than one para, previous history of hypertension, diabetes mellitus, thyroid disorder, dyslipidemia, renal disease & convulsions, Family history of preeclampsia. After explaining all details, informed consent was taken from each subject for participation in this study. History of patient was recorded on preformed questionnaire which included detailed history about present pregnancy, family history of preeclampsia and exclusion criteria. 2 ml of fasting blood sample was collected in plane blub and serum is separated by centrifugation.

Serum triglyceride was measured by using Autozyme new triglyceride enzymatic kit manufactured by Accurex Biomedical Private Limited, Thane, India. Kit.Estimation of Serum

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Cholesterol: Serum total cholesterol was estimated by cholesterol oxidase/ Peroxidase (CHOD/POD) colorimetric endpoint method, using Liquizyme kit. HDL cholesterol is detected by the enzymatic CHOD/ POD method.

LDL was calculated by formula
Serum LDL = Total Cholesterol – (HDL + VLDL)
VLDL was calculated by formula
Serum VLDL =

$$\text{Serum VLDL} = \frac{\text{Serum triglyceride}}{5}$$

Serum Alkaline phosphatase determined by kinetic assay (Pnpp-AMP method)

STATISTICAL ANALYSIS-
Unpaired t-test was performed to compare demographic, clinical and biochemical parameters between preeclampsia and control groups.

Result
Characteristics in preeclampsia cases and normal pregnant controls
The mean age in the preeclampsia cases was **23.57 ± 2.99** years and that in controls was **22.90 ± 2.96** years. The mean gestational age of cases was **33.92 ± 2.42** weeks where as in controls **33.98 ± 2.48** weeks.(Table1) There was no significant difference in age and gestational age between cases and controls [p value > 0.05]. Study groups were well matched for age and gestational age.

Comparison of Lipid profile and Alkaline Phosphatase in Preeclamptic cases and normal pregnant control groups
The mean level of serum triglycerides & total cholesterol in the preeclampsia cases was **235.30 ± 66.73 mg/dL &192.45 ± 9.45 mg/dL** and in normal pregnant women was **179.80** ± 37**.08 mg/dl & 180.1** ± 10.21 mg/dl respectively. There was higher serum triglyceride & total cholesterol level in preeclampsia as compared to normal pregnant women and difference was statistically highly significant. (p=<0.001)

The mean level of serum total LDL & VLDL in the preeclampsia cases was **146.94 ± 12.23 mg/dL & 47.06 ± 13.23 mg/dL** and in normal pregnant women was **95.7 ± 11.43 mg/dL & 35.95 ± 7.41 mg/dL** respectively. There was higher serum LDL & total VLDL level in preeclampsia as compared to normal pregnant women and difference was statistically highly significant. (p=<0.001)

The mean level of serum HDL in preeclampsia cases ware **41.3 ± 12.02 U/L** and in normal pregnant women was **49.1 ± 11.2 U/L.** There was lower serum HDL in preeclampsia as compared to normal pregnant women and difference was statistically highly significant. (p= <0.001)

The mean levels of serum Alkaline Phosphatase in preeclampsia cases ware **245 ± 16.3 U/L** and in normal pregnant womens were **187 ± 11.1 U/L**. There was higher serum Alkaline Phosphatase in preeclampsia as compared to normal pregnant women and difference was statistically highly significant. (p= <0.001)(Table 1) Serum Alkaline Phosphatase correlated with systolic blood pressure and r value was r = 0.8018. (table 2) This was statistically significant positive correlation. (p= <0.001)

Discussion
In our study, we compare serum triglycerides level in preeclampsia cases and normotensive pregnant women. We found that, serum triglycerides level was above the normal level in both normal pregnancy and preeclampsia cases. But in preeclampsia, rise in triglyceride level was more and highly significant as compared to normotensive pregnant women. Studies conducted by De J et al[11,12] Adiga U et al[13]and Sattar N et al[14] for lipid profile in preeclampsia had shown significant rise in the serum triglyceride levels in preeclampsia patients as compared to normal pregnant women. In our study, this observation holds true. There was highly significant difference in the serum triglyceride between preeclampsia and normal pregnant woman (p<0.001). The mechanism behind this increase in triglyceride levels in normal pregnancy and preeclampsia is not exactly known however various explanations have been given for same.

Normal pregnancy is associated with hyperlipidemia and hyperestrogenemia.[15] Estrogen causes increase in HDL-C level and decrease in LDL-C level. Estrogen causes decline in hepatic lipase activity. It results into impaired clearance of lipoproteins from circulation.[16] The principle modulator of this hypertriglyceridemia is estrogen as normal pregnancy is associated with hyperoestrogenaemia. Oestrogen induces hepatic biosynthesis of endogenous triglyceride, by raising the hepatic VLDL-C.[17] This process may be modulated by hyperinsulinism found in pregnancy.[18] Also activities of adipose tissue lipoprotein lipase and hepatic lipase are substantially decreased during normal pregnancy (due to insulin resistance and estrogen, respectively). This results into impaired removal of triglycerides rich lipoproteins from the circulation. Thus increased production and impaired removal of TG is responsible for rise of TG in normal pregnancy.[19]

Preeclampsia is a state of hypoestrogenemia and exaggerated insulin resistance.[11] One of the reasons for increased triglyceride in preeclampsia is hormonal imbalance. Decreased utero-placental blood flow is the main pathophysiological event in preeclampsia. This leads to impairment in the formation of dehydroepiandrosterone sulphate (DHEA) by fetal adrenal glands by interfering with the uptake of lipids by the fetus. Ninety percent of estrogen in maternal circulation is from fetal DHEA.[20] Because of the impairment in the formation of DHEA, estrogen levels decreases.[11] Because of decrease uteroplacental blood flow there is redistribution of steroids formed in synctium back to fetus instead of going into maternal circulation. This also results in a state of hypoestrogenemia.[21]

The state of hypoestrogenemia leads to decreased expression of VLDL-C receptors in the placenta that are essential for the lipid transport to the fetus. Resulting in reduced transport of VLDL-C to fetal compartment, which may be the reason for maternal hypertriglyceridemia in preeclampsia. Further LDL-C taken up by the fetus for the synthesis of DHEA is decreased due to reduced fetoplacental perfusion. This leads to increased LDL-C in maternal circulation. The decreased catabolism of triglycerides rich lipoproteins by reduced placental uptake results in the accumulation of triglycerides rich lipoproteins in the maternal circulation.[7,22] Therefore, the level of TG gets elevated in preeclampsia patients

Increased triglycerides found in preeclampsia patients are thought to be deposited in vessels. This contributes to the endothelial dysfunction, both directly and indirectly through generation of small, dense low density lipoprotein cholesterol.[14] Moreover, this hypertriglyceridemia may be linked with hypercoagulability.[15]

In our study, levels of serum VLDL-C were found to be significantly higher (p<0.001) in preeclampsia cases in com-

parison to normal pregnant women (controls). There was highly significant difference in the VLDL-C level in preeclampsia patients and normal pregnancy. Studies conducted by De J et al[11] , Adiga U et al[6] and Sattar N et al[14] showed similar result in their study. This increase in VLDL-C levels in preeclampsia may be due to hypertriglyceridemia. This leads to increased entry of VLDL-C in circulation that carries endogenous triglyceride into circulation. According to some researchers[23,24] the VLDL-C level might raise up to 2.5 folds at term over the pre-pregnancy level. VLDL-C level further elevates in preeclampsia as found in the present study in accordance with the above researchers. This increased VLDL-C may accumulate over the maternal vascular endothelium; mainly those of uterine and renal vessels.[25] Further VLDL-C may cause injury to the endothelium, which may enhance the pathogenic process of preeclampsia.[26]

Placental synthesis of alkaline phosphatase (ALP) during pregnancy has a role in division of normal and transformed cells. This enzyme is responsible for active transport of phosphate.[9](9)Lowering of serum ALP in pregnancy may be an indicator of intra uterine growth retardation(IUGR) ALP was also noticed to be increased in pre-eclampsia.[10]

Many workers have worked on serum alkaline phosphatase showing rising levels in the 2nd and 3rd trimester of pregnancy, which coincides with the period of calcification of fetal skeletal. PALP facilitates the mobilization of calcium from maternal system for fetal calcification process. Human Placental Alkaline Phosphatase (PALP) is synthesized in placenta during pregnancy. Human Placental Alkaline Phosphatase (PALP) was localized in the outer and inner layers of the syncytiotrophoblast. There is increased phosphatase activity in outer and inner layers of syncytiotrophoblast of preeclamptic placenta.[27] Placenta of preeclampsia women on chronic hypertension has maximum intensity of PALP in the outer layer of syncytiotrophoblast.

Alkaline phosphatase of the placenta appears to be moderately resistant to hypoxia. There is considerable increase in lysosomal activity in hypertensive placenta, presumably a response to placental ischemia which occurs in pre eclampsia and which by altering the tissue pH of trophoblast, stimulate lysosomal activity. This leads to syncytial damage and destruction in pre eclampsia, which releases PALP from vesicles into cytoplasm.[27]

Conclusion

Our results suggest that alteration of lipid profile itself might be a predisposing factor for the development of preeclampsia.

In addition to this serum alkaline phosphatase was increased in preeclamptic women as compared to normal pregnant women. Hence at this juncture it can be suggested that serum alkaline phosphatase could be used as predictor of severity of preeclampsia.

A positive correlation in serum alkaline phosphatase was observed with systolic blood pressure

As study was conducted on small group further study with large group is needed for confirmation of our finding.

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Tables

TABLE 1

COMPARISON OF LIPID PROFILE AND SERUM ALKALINE PHOSPATASE IN PREECLAMPTIC CASES AND NORMAL PREGNANT CONTROL GROUPS

Parameter	Cases (n=60) [mean ± SD]	Controls (n=60) [mean ± SD]	P value
Serum Triglycerides (mg/dL)	235.30 ± 66.17	179.75 ± 37.08	0.0001***
Serum Cholesterol (mg/dl)	192.45 ± 9.45	180±10.21	0.0001***
HDL (mg/dl)	41.3±12.02	49.1± 11.2	0.0004***
LDL (mg/dl)	146.94± 13.23	95.7±11.43	0.0001***
VLDL (mg/dL)	47.06±13.23	35.95±7.41	0.0001***
Alkaline Phosphatase (U/L)	245±16.3	187±11.1	0.0001***

n= number of subjects; * = (p<0.05), **= (p<0.01),***= (p < 0.001)

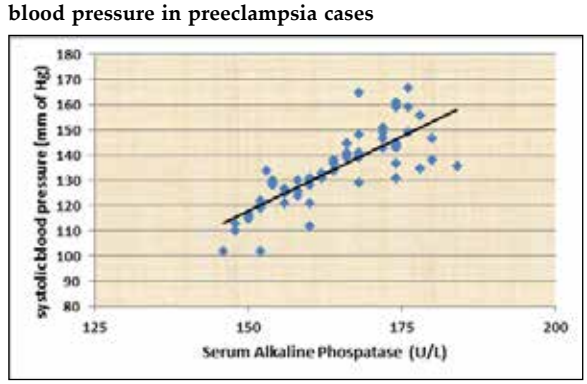
Table 2

Correlations of serum alkaline phosphatase with systolic blood pressure in preeclampsia cases

Parameter	Systolic blood pressure
Serum alkaline phosphatase	r = 0.8018 p = 0.0001***

FIGURE: 1

Correlations of serum alkaline phosphatase with systolic blood pressure in preeclampsia cases



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