STUDY OF LIPID PROFILE TRENDS IN WOMEN OF PREGNANCY INDUCED HYPERTENSION CASES IN A RURAL SETUP.

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ABSTRACT: OBJECTIVE: Elevated plasma lipid levels are believed to be probable cause of endothelial cell dysfunction. We planned to measure the changes in the lipid levels in patients of PIH (pregnancy induced hypertension) and compare it with that of normotensive pregnant females. **MATERIALS & METHODS:** We studied 804 pregnant women. 624 patients studied were of PIH and 180 patients were healthy pregnant women. Lipid levels were estimated in these pregnant women. **RESULTS:** We found a significant rise in the serum lipid levels in the PIH patients group as compared to normotensive pregnant females, which were highly significant ($P < 0.001$) except changes in LDL ($P > 0.05$) and total cholesterol. Amongst the different lipoprotein ratios, TC: HDL, LDL: HDL, TG: HDL, and HDL: VLDL ratios were found highly significant ($p < 0.001$) in PIH patients group. **CONCLUSION:** It is essential that blood lipid concentrations be estimated in pregnant women during antenatal care since it could be useful in early diagnosis and prevention of obstetric complications such as PIH.

INTRODUCTION: Pregnancy induced hypertension is recognized since ancient times. It has been described in reviews of Thiagarajha and Chesley¹.

Hypertension after 20 weeks of pregnancy in a woman with edema and proteinuria without previous history of hypertension is called pregnancy induced hypertension (PIH). When associated with proteinuria, the disorder is termed pre – eclamptic eclampsia/ toxemia and when present without protein in the urine, it is called transient hypertension or gestational hypertension². Raised blood pressure is present in 5% of entire pregnancies, in 10% of primiparous women and 20 – 25% of women with previous history of chronic hypertension. It is the major cause of fetomaternal morbidity and mortality³.

When blood pressure rises in pregnancy with significant protein in the urine, it is called pre- eclampsia. It may occur from 20 weeks of pregnancy. It can also occur upto 6 weeks post partum. Delivery of the placenta is the ultimate treatment. It may affect both fetal and mother survival⁴.

Eclampsia is a dangerous complication of pregnancy with a sudden onset and has the features of developing tonic – colonic seizures in a patient who has pre – eclampsia. With increasing age, the risk of developing PIH increases⁵.

Lipoprotein levels increase during pregnancy, but in PIH they increase two to three times more ⁽⁶⁻⁸⁾. Changes in lipoproteins in essential hypertension are documented⁹. Abnormal lipoprotein levels are responsible for damage to the endothelium which leads to high blood pressure and proteinuria; which are important signs of PIH¹⁰.

Change in lipoproteins cause atherosclerosis, damage to endothelium and other heart diseases. The major sign of PIH is hypertension, suggesting that it is due to vasospastic events in placenta, uterus and brain ⁽¹¹⁾.

Abnormal lipid metabolism has a basic role in the pathogenesis of the disease ⁽¹²⁾. Endothelial dysfunction can explain the protein in the urine ⁽¹³⁾. Abnormal lipid metabolism is responsible for the endothelial dysfunction ⁽¹⁵⁾, and it was proposed that small, dense LDL may add to endothelial dysfunction in pre – eclampsia ⁽¹⁶⁻¹⁷⁾. Triglyceride rich lipoproteins may also activate endothelial dysfunction ⁽¹⁸⁾ and atherothrombosis⁽¹⁹⁾. In toxemia of pregnancy, serum triglyceride concentration increases much more notably. In pregnancy, the increased level of estrogen causes increased hepatic biosynthesis of endogenous triglycerides through VLDL ⁽¹³⁾. This process is modulated by hyperinsulinism that starts in pregnancy ⁽¹⁴⁾. All the above mentioned interactions along with increased endothelial triglyceride accumulation may result in endothelial cell damage in pregnancy ⁽¹⁷⁾. In PIH, the triglycerides are likely to be accumulated in vessels like uterine spiral arteries and contribute to endothelial damage by generating small, dense LDL particles. Women with PIH are more likely to develop overweight, dyslipidemia ⁽¹⁶⁻²⁰⁾, insulin resistance ⁽²¹⁻²²⁾ and endothelial dysfunction ⁽²³⁾, which are independent risk factors for cardiovascular disease ⁽²⁴⁻²⁵⁾.

Lipoproteins are classified into: - HDL, LDL, VLDL and chylomicrons.

MATERIALS AND METHODS: This cross sectional /analytical study was conducted in the tertiary referral health care facility of Budhera, Gurgaon, viz, SGT Medical College and Research centre, Budhera, Gurgaon, India. The analytical work was done in SGT Medical College and Research centre, Budhera, Gurgaon.

Study population included pregnant women with PIH as cases and normotensive pregnant women at gestational age of 20 weeks or more as controls.

The study was undertaken on 804 pregnant women. Among which, 624 were pregnant women with PIH admitted to Gynaecology and Obstetrics department or undergoing prenatal care at tertiary referral health care facility, who were randomly selected and screened for PIH at their prenatal visits, on labor and delivery. From the same health facility, 180 healthy pregnant women without history of hypertension, diabetes mellitus, renal or cardiovascular disease were randomly selected as age, weight, BMI gestational period and socio – economic matched control group for comparison.

After explaining aim and objectives, informed consent was taken from each subject for participation in this study.

Ethical approval for the study was obtained from Institutional Ethical Research Board at SGT Medical College and Research Institute, Budhera, Gurgaon.

Biochemical analysis of lipoprotein included total cholesterol, HDL, LDL, VLDL, triglycerides.

Serum lipids were analysed enzymatically by using Semi Auto Chemistry Analyser Microlab 200.

Serum total cholesterol and triglycerides were measured by using enzymatic method of Elitech digi kits of France. Serum HDL was measured by using kits of Merk Diagnostics.

Serum LDL was calculated by Frederickson – Friedawld's formula, according to which $LDL = TC - HDL - VLDL$.

VLDL was calculated as 1/5 of triglycerides. Students t test was used to evaluate mean differences in maternal serum lipids concentration between patient and control subjects. Significance among the mean of groups was expressed in terms of “p” value. 95 % confidence interval $p < 0.05$ was considered significant.

RESULTS: Table 1 compares the mean ($\pm$ SEM) lipoprotein concentration among the study groups. Statistically highly significant ($p < 0.001$) differences were noted in most of maternal serum lipid and lipoprotein concentrations in the patient group of PIH, except changes in LDL ($P > 0.05$), and total cholesterol. Amongst the different lipoprotein ratio, TC: HDL, LDL : HDL, TG :HDL and HDL :VLDL ratios were found highly significant ($P < 0.001$) in the PIH patient group.

Table 1:- blood lipids in Normal Pregnancy and patients for pregnancy induced hypertension.

Lipoprotein (mg/dl)	PIH Mean $\pm$ SEM	Control Mean $\pm$ SEM	% Change	P Value
Total Cholesterol	213.25 $\pm$ 3.14	188.23 $\pm$ 4.6	5.5	NS
HDL – Cholesterol (mg/dl)	43.45 $\pm$ 0.58	52.20 $\pm$ 1.14	16.8	0.001
LDL- Cholesterol (mg/dl)	111.15 $\pm$ 2.91	93.42 $\pm$ 4.07	3.5	NS
VLDL-Cholesterol (mg/dl)	58.74 $\pm$ 1.44	42.22 $\pm$ 1.46	39.1	0.001
Triglyceride (mg/dl)	294.25 $\pm$ 7.24	212.30 $\pm$ 7.28	38.36	0.001

Differences in the mean and standard error of mean in blood lipids of patient and control subjects is represented in table 1.

Women who developed hypertension after 20 wks of gestation had 5.45%, 3.5% 39% , and 38.6% higher concentration of total cholesterol, LDL, VLDL and triglycerides respectively than control subjects.

A significant decrease of 16.76% was noted in HDL in patient group. Comparison of lipoprotein ratio among patient and control groups is given in table 2.

Table 2:- Comparison of lipoprotein ratio in normal and pregnancy induced hypertension.

Parameters	PIH Mean $\pm$ SEM	Control Mean $\pm$ SEM	% change	P Value
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TC : HDL ratio	5.12 ± 0.09	3.74 ± 0.11	32.29	0.001
LDL : HDL ratio	2.66 ± 0.07	1.86 ± 0.09	29.76	0.001
TG : HDL ratio	7.24 ± 0.22	4.35 ± 0.19	66.44	0.001
HDL : VLDL ratio	0.87 ± 0.02	1.36 ± 0.06	38.23	0.001

Total Cholesterol: HDL ratio, LDL : HDL ratio and TG:HDL ratios were higher in PIH group and were found highly significant (P<0.001)

DISCUSSION: Elevated plasma lipid levels are believed to be the probable cause of endothelial cell dysfunction. In the endothelial cell, oxidative stress is stimulated by linoleic acid. During pregnancy serum lipoprotein levels increase considerably and is two times higher in PIH. Alterations that take place during pregnancy include insulin resistance, hyper – lipidaemia and up – regulation of inflammatory markers ⁽²⁹⁻³¹⁾. The increase of serum lipids through pregnancy in general and during PIH in particular are described in a number of studies. Worldwide, diverse studies ^(29, 36-38) have reported elevated lipid levels in PIH patients. Our study also showed that rise in serum triglycerides was statistically significant (p<0.001) in PIH patients when compared to women with normal pregnancy. The major modulator of this hypertriglyceridemia is estrogen as pregnancy is linked with hyperestrogenemia. Hypertriglyceridemia may be linked to hypercoagulability⁽⁴⁰⁾. In the present study cholesterol concentration increased in patients of PIH but no significant changes in total cholesterol were observed. These are consistent with findings reported in other studies ^(29,35). Some other studies have found considerable rise in serum cholesterol in PIH. The finding in our study of 16.8% lower value of HDL –C in PIH patients over patients of normal pregnancy is consistent with the study on Finnish and Peruvian population ⁽⁴³⁻⁴⁴⁾. Statistically the variation was highly significant, (p<0.001).

Estrogen is responsible for induction of triglycerides and HDL and inhibition of serum LDL and estrogen level falls in PIH ⁽⁴⁵⁾. Low levels of HDL in PIH is not only because of hypoestrogenemia but also due to insulin resistance ⁽⁴³⁾.

In our study, serum VLDL levels rose significantly (p<0.001) in the patient PIH group which may be due to hypertriglyceridemia leading to increased entry of VLDL that carries the endogenous triglycerides into the circulation. Some researchers ⁽⁴⁶⁾ have shown serum VLDL levels may rise upto 2.5 folds at term over pre-pregnancy levels. VLDL levels further elevates in PIH as found in the present study in validation with those of other researchers ^(29, 38). due to increased VLDL which accumulates over maternal vascular endothelium, mainly those of uterine and renal vessels. VLDL may cause injury to the endothelium ⁽⁴⁷⁾. Similar results are shown by another study ⁽⁴⁶⁾ and one study from China ⁽⁴⁹⁾.

We have also calculated the ratios between lipids like LDL: HDL, TC: HDL, TG : HDL, HDL: VLDL for patients and control groups. There was great increase in LDL: HDL, TC: HDL, TG: HDL and HDL: VLDL ratios in PIH. This is consistent with other studies ⁽⁴⁸⁾. Dyslipidemia mediates activation of endothelial cells to placental derived factors which can be considered as probable contributors for the pathogenesis of PIH ⁽⁵⁰⁾.

Our results are in comparison with findings from few exiting prospective studies, case control studies ^(29,41), and many prospective cohort studies ⁽⁵¹⁻⁵²⁾ of maternal fasting / non

fasting serum lipid and lipoprotein concentrations in PIH and normotensive pregnancies. In these PIH patients, decrease in HDL regardless of elevation in other lipid components is a probable threat for atherosclerosis⁽⁵³⁾. A similar study has been done by Gratacos E et al.

CONCLUSION: Women who developed hypertension after 20wks of gestation had 5.45%, 3.5%, 39%, to 38.6% higher concentration of total cholesterol, LDL, VLDL and triglyceride levels respectively, than control subjects. A significant decrease of 16.76% was noted in HDL levels of PIH group.

Total cholesterol: HDL, LDL: HDL and TG: HDL ratios were higher (32.3%, 29.8% and 66.4% respectively) among women with PIH and were found to be statistically significant ($P < 0.001$) as compared to normotensive women.

In conclusion, the results of our study show abnormal lipid metabolism, predominantly low HDL and high triglyceride concentration which may promote vascular dysfunction and oxidative stress seen in PIH. It is therefore essential that serum lipid concentration should be estimated in all pregnant women during antenatal care, since it could be useful in the early diagnosis and prevention of obstetric complications such as PIH.

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