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Original Research Article

ASSOCIATION BETWEEN MATERNAL SERUM LIPID PROFILE AND THE PREGNANCY INDUCED HYPERTENSION IN A TERTIARY CARE HOSPITAL AT MANIPUR

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Abstract

Background: Pregnancy induced hypertension (PIH) are common disorders contributing significantly to maternal and perinatal mortality and morbidity. Increased oxidative stress seen in patients with PIH has been linked with lipid abnormality. This study aims at analyzing the alteration in lipid profile in women who developed pregnancy induced hypertension. **Materials and Methods:** A Case-control study carried out in the Department of Obstetrics and Gynaecology of a Medical College at Imphal from September 2019 to August 2021 on 55 cases of PIH and 55 normotensive controls. After taking written informed consent, venous blood sample (5 mL) was taken from both case and control group after 12 hours of fasting. The samples were subjected to analysis of lipid profile that includes Total cholesterol, HDL cholesterol, LDL cholesterol, Triglycerides. The data analysis was done using SPSS version 21.0 IBM for Windows. Descriptive statistics like mean, standard deviation, percentage and frequency were used. Chi square was used for categorical variables and independent t- test for continuous variables. **Result:** Of the 55 hypertensive and 55 normotensive women who participated in the study, the mean maternal age was 30.38 years and 30.70 years respectively. The mean TC, LDL, HDL, VLDL and TG levels were higher in cases than in controls, with mean difference of 80.5mg/dl, 68.4mg/dl, 6.3mg/dl, 21.5 mg/dl and 106.3mg/dl respectively, and was statistically significant (P=0.001). **Conclusion:** Women with pregnancy induced hypertension have increased serum levels of TC, LDL, HDL, VLDL and TG levels compared to normotensive pregnant women. The dyslipidemia found in the hypertensive women may play a pivotal role in the etiopathogenesis of PIH. Hence, it is imperative to include lipid profile in routine screening of pregnant women for early detection of PIH.

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) affect 2-10% of pregnancies in western world. They are associated with an increased risk of morbidity and mortality for both mother and child.[1] The national incidence is reported to be 8 to 10%.[2] In normal pregnancy, though cardiac output is increased blood pressure is maintained because of the decrease in peripheral vascular resistance. But in pregnancy induced hypertension (PIH) there is increased resistance due to the increased response to vasopressors, altered lipid synthesis leading to decrease in the ratio of Prostaglandin I2 (PGI2)/Thromboxane A2 (TXA2) and antioxidants/lipid peroxides and changes in the local factors like Nitric Oxides, endothelins.[3,4]

Triglycerides levels are significantly elevated in women with HDP/Gestational Diabetes Mellitus (GDM) compared to those without metabolic syndromes and such elevations are consistent in 1st, 2nd and 3rd trimesters of pregnancy.[2] Mean plasma

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triglyceride and free fatty acid (FFA) concentrations increase about 2-fold on average in women with gestational hypertension relative to women with uncomplicated pregnancy.[5] According to several studies, changes in lipid profile seems to be important in the pathogenesis of PIH. Measurement of lipid parameters may be good predictive valve in PIH.[6]

An abnormal lipid profile is known to be strongly associated with atherosclerotic cardiovascular disease and has a direct effect on endothelial cell activation resulting in the generation of reactive oxygen species which have a role in promotion of oxidative stress and vascular dysfunction seen in preeclampsia.[7] Early identification of women at risk for PIH may help in preventing the complications of the disease. This study aims at analyzing the alteration in lipid profile in women who developed pregnancy induced hypertension.

Objective

The objective of the study is to determine the association between maternal serum lipid profile and the pregnancy induced hypertension.

MATERIALS AND METHODS

The study was a Case-control study carried out in the Department of Obstetrics and Gynaecology of a Medical College at Imphal from September 2019 to August 2021. Ethical clearance was taken from the Research Ethics Board of the concerned Medical College vide letter no. A/206/REB-Comm (SP)/RIMS/2015/620/98/2019 dated 24th October 2019.

The study population consist of all pregnant women diagnosed as Pregnancy Induced Hypertension with no other associated complications and normal pregnant women with no other maternal medical complications, admitted for safe confinement on at antenatal ward. The sample size was calculated as 55 each for cases and control using appropriate statistical formula n= (s12+s22)/e2, where e=standard error, s1=Total cholesterol value among pregnancy induced hypertension = 32.46, s2=Total cholesterol value among control group = 30.16 (Josephine LP, Subramanyam G).[8]

Sampling method was convenience sampling; patients were recruited consecutively. All pregnant women who were diagnosed with pregnancy induced hypertension and those who gave consent, participated in the study.

Inclusion criteria:

Any gravida, between 20-45 years, after 28 weeks of pregnancy with systolic blood pressure (SBP) more than or equal to 140 mmHg and diastolic blood pressure (DBP) more than or equal to 90 mmHg were included in case group. While control group included any gravida, between 20-45 years, after 28 weeks of gestation with normal blood pressure (less than or equal to 120/80).

Exclusion Criteria

Chronic hypertension, Pregestational diabetes mellitus, Renal diseases, Cardiac disease, Hepatic disease, Multiple pregnancy, Smoking, Alcohol, Obese, Hyperlipidemia before 28 weeks of pregnancy.

Study variables: Independent variables include age, parity, gravida and socio-economic status while dependent variables include blood pressure, serum lipid profile.

Outcome variables: Total cholesterol (TC), Low density lipoprotein (LDL), Very low-density lipoprotein (VLDL), High density lipoprotein (HDL), Triglycerides (TG).

Working Definitions

- PIH: Development of a SBP ≥140mm Hg and/or a DBP ≥90 mm Hg without proteinuria after 20 weeks of gestation in a previously normotensive woman.
- Preeclampsia: Development of SBP ≥140 mm Hg and/or DBP ≥90 mm Hg with new-onset proteinuria in a random urine sample with no evidence of a urinary tract infection.
- Lipid profile interpretation as per The National Cholesterol Education Program (NCEP) guidelines [9] (units in mg/dl) as follows:
- Total cholesterol- Desirable:<200, borderline high: 200-239, high: ≥240
- Triglycerides- Normal<150, borderline high: 150-199, high: 200-499, very high: ≥500
- HDL- Low<40, normal: 40-60, high: >60
- LDL- Optimal: <100, near optimal: 100-129, borderline high: 130-159, high: 160-189, very high: ≥190

Study tools: Detailed clinical history and basic investigation e.g. Complete blood picture, bleeding time and clotting time, blood grouping and Rh typing, glucose challenge test, liver function test, kidney function test, Serum Electrolytes, R-ab, HbsAg, HCV-Ab, urine routine examination, serum lipid profile.

Instruments: Sphygmomanometer-Diamond BP Apparatus Mercurial-Deluxe. Product code: EHL-DIAMOND-BPMR 120 (made in India), Stethoscope- Littmann Classic III.

Data collection: Voluntary written consent was taken before starting the study. Fasting venous blood sample (5 mL) was taken from study group and control group admitted at the hospital of the Medical College. The samples were subjected to analysis of lipid profile that includes Total cholesterol, HDL cholesterol, LDL cholesterol, Triglycerides. The data was recorded in the pre-determined proforma.

Procedure: All pregnant women who got admitted under Department of Obstetrics and Gynaecology of the Medical College and fulfilling the inclusion and exclusion criteria were enrolled in the study after taking informed written consent. A complete history was taken, examination and investigations according to the proforma was done for the patients.

A 5 mL of venous blood from antecubital vein was withdrawn under strict aseptic conditions after 12 hours fasting period. The lipid profile of the samples was determined using RANDOX RX IMOLA AUTO

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ANALYSER, manufactured in 2007, UK, using RANDOX kits. LDL and VLDL levels were calculated individually using Friedewalds formula.[10]

Patients were classified as case and control groups depending on presence or absence of gestational hypertension, and the two groups were then compared and analyzed depending upon their serum lipid levels following the National Cholesterol Education Program (NCEP) guidelines.

Statistical Analysis: The data analysis was done using SPSS version 21.0 IBM for Windows. Descriptive statistics like mean, standard deviation, percentage and frequency were used.

Chi square test was used for categorical variables and independent t- test for continuous variables. A p-valve <0.05 was taken as statistically significant. Chi square test was used to find out the association between two proportions.

RESULTS

A total of 110 patients were recruited for the study with 55 patients as cases and remaining 55 as controls. The mean systolic blood pressure and diastolic blood pressure among cases were 170.7±15.5 mmHg and 108.8±6.0 mmHg, and that among controls were 108.1±15.2 mmHg and 74.8±10.6 mmHg. Blood pressure was significantly higher among cases in comparison to control (p-value-0.001).

There was no significant difference between the cases and controls in age wise distribution as depicted in [Table 1]. The most common age group was 26 to 30 years. The youngest age was 19 years and oldest one was 39 years. The mean age in the case group was 30.38 years and the mean age among control group was 30.70 years.

There was no significant difference between the cases and controls in parity distribution as shown in [Table 2], the most common group was parity 0 followed by parity 1.

[Figure 1] showed that the majority of cases and controls belonged to lower middle class followed by upper lower class (P=0.462).

As shown in [Table 3], the mean total cholesterol was higher in cases than in controls, with mean difference of 80.5mg/dl and was statistically significant (P=0.001). The mean LDL value was higher in cases than in control group, with mean difference of 68.4mg/dl and was statistically significant (P=0.001). The mean HDL among cases was higher than the control group with a mean difference of 6.3mg/dl which was statistically significant (P=0.001). The mean VLDL among cases was higher than control group and the mean difference was 21.5 mg/dl which was statistically significant (P=0.001). The mean TG among cases was higher when compared to control group; the mean difference was 106.3mg/dl and it was statistically significant (P=0.001).

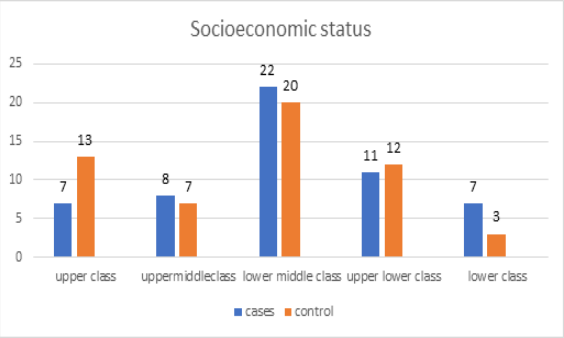

Figure 1: Socioeconomic status distribution among case and control groups.

Table 1: Distribution of patients by age group (N = 110) among case and control groups.

Age (years)	Case n (%)	Control n (%)	p-value
19 – 25	7(58.3)	5(41.7)	0.937
26-30	20(48.8)	21(51.2)	
31-35	20(50)	20(50)	
36-39	8(47.1)	9(52.9)	

Table 2: Parity distribution among case and control groups

Parity	Case n (%)	Control n (%)	p-value
P0	24(49)	25(51)	0.976
P1	18(51.4)	17(48.6)	
P2 or more	13(50)	13(50)	

Table 3: Comparison of mean Total cholesterol, LDL, HDL, VLDL and Triglyceride levels between case and control groups

Variables (mg/dl)	Case Mean ±SD n=55	Control Mean ±SD n=55	Mean difference	95% CI	p-value
Total cholesterol	263.8±47.6	183.3±25.4	80.5	66.1-94.9	0.001
LDL	181.5±48.5	113.0±22.9	68.4	54.1-82.8	0.001
HDL	55.6±12.7	49.2±11.7	6.3	1.7-11.0	0.001
VLDL	50.2 ±12.0	28.6± 6.0	21.5	17.9-25.1	0.001
TG	251.1 ±60.0	144.8±30.0	106.3	88.4-124.3	0.001

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DISCUSSION

The age range of the participants in both case and control groups were between 19 to 39 years with the mean age of 30.38 years and 30.70 years respectively. Kalar MU et al,[11] also found comparable findings and reported that mean age of the women was 29 years. Similarly, Mankunta D et al,[12] demonstrated that the mean age of the pregnant women was 30.4 years. The obstetric characteristics of the cases and controls were similar as the participants were matched for age, parity, and gestational age at the time of recruitment. This eliminated confounders that may have arisen from these variables.

This study showed that there were significantly higher levels of serum total cholesterol, LDL, VLDL, and triglycerides in women with pregnancy induced hypertension compared to normotensive pregnant women [Table 3]. In the present study the mean total cholesterol in study group was 263.8±47.6 mg/dl and in control group 183.3±25.4 mg/dl. The mean LDL in study group was 181.5±48.5mg/dl and control group was 113.0±22.9 mg/dl, mean HDL was 55.6±12.7 mg/dl (study group) and 42.2±11.7 mg/dl (control group), mean VLDL was 50.2±12.0mg/dl (study group) and 28.6±6.0mg/dl (control group), mean TG was 251.1±60.0mg/dl (study group) and 144.8±30.0mg/dl.

Similar results were also found in the study conducted by Gohil JT et al,[13] where the authors observed that lipid profile abnormalities i.e. significantly raised total cholesterol, LDL, VLDL and TG levels were clearly evident in cases having preeclampsia in contrast to non-pregnant, and normotensive pregnant women. Another study conducted by Kalar MU et al,[11] also observed that pre-eclamptic cases had lipid profile abnormalities due to altered lipid metabolism, and increased TG levels along with delayed TG clearance and hypertension are ground for preeclampsia development. Consistently Lima VJ et al,[14] also reported positive correlation between higher VLDL and triglyceride levels and increased proteinuria level in preeclamptic women. The previous published studies demonstrated that plasma lipid concentrations were greater in pre-eclamptic women as compared to normotensive pregnant women.[15]

Ware-Jauregui S et al,[16] found elevated TG level and decreased HDL concentration in preeclamptic women as compared to the control group. Mural JT et al,[17] also reported that maternal TG and fatty acids levels increased significantly in pre-eclamptic patients. A study conducted by Ozdemir O et al,[18] also reported that dyslipidemia could be an important cofactor in preeclampsia. In their results, they found significant positive correlation between proteinuria and total cholesterol, TG, LDL, and VLDL concentrations ($P < 0.05$). Moreover, it was also observed that there were positive correlations between systolic hypertension and the levels of the cholesterol, TG and VLDL, and between diastolic blood pressure and levels of the LDL, TG and VLDL.

Our study, similar to that by Ray JG et al,[19] showed that the mean triglyceride concentration was significantly higher among women with PIH than among the unaffected controls. How does hypertriglyceridemia predispose a woman to preeclampsia, if there truly exists a causal relationship? A likely factor is the higher risk of placental vasculopathy. Persons with the metabolic syndrome of which hypertriglyceridemia is a major feature, display evidence of chronic inflammation, hypercoagulability and endothelial dysfunction.

Our study, similar to Sattar N et al,[20] showed elevated levels of cholesterol and triglycerides in hypertensive group as compared to normotensive group. Kaaja R et al,[7] has found high plasma triglycerides and low HDL concentrations in women with preeclampsia and gestational hypertension. Similar results were also seen in the study conducted by Vani I et al,[21] where positive association of TC, HDL, VLDL, and TG level with PIH cases was observed.

Furthermore, our study group had high levels of TG, which corroborated with the reports of Gratacós E et al,[22] and Evruke IC et al.[23] The study by Barden AE et al,[24] showed that regardless of parity, triglycerides levels were significantly elevated in women with preeclampsia, and the levels of triglycerides after 6 weeks of delivery were found to the decreased. However, in our study the levels of postpartum triglycerides were not measured.

CONCLUSION

Women with pregnancy induced hypertension have increased serum levels of TC, LDL, HDL, VLDL and TG levels compared to normotensive pregnant women. The dyslipidemia found in the hypertensive women may play a pivotal role in the etiopathogenesis of PIH. It is therefore imperative that serum lipid profile shall be continuously monitored throughout the whole pregnancy period as it will be helpful in early detection of PIH and/or developing the strategies to prevent any obstetric-associated complications of PIH during pregnancy and/or at the time of delivery. It is incumbent on health caregivers to ensure that women of childbearing age adopt healthy lifestyles so as to control their weight and lipid levels, especially TGs to reduce their risk of developing pregnancy induced hypertension.

Limitation: The levels of LDL cholesterol and VLDL cholesterol were estimated using Friedewald's formula which was an estimate, not a direct measurement. This method may not be suitable for those with high TG levels (>400 mg/dL), low LDL levels (<70 mg/dL) and certain genetic disorders affecting lipid metabolism. In such cases, more advanced methods like beta quantification or ultracentrifugation may be used for direct estimation of LDL and VLDL cholesterol.

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