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Original Research Article

A study of serum lipid profile in normal pregnancy and pregnancy induced hypertensive disorders: a case-control study

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ABSTRACT

Background: Pregnancy induced hypertensive disorders are one of the commonest complication of pregnancy which accounts for 12% of the maternal and perinatal mortality and morbidity. Dyslipidemias are associated with endothelial dysfunction that may result in proteinuria and hypertension which is a clinical hallmark of PIH. It affects both maternal health as well as fetal growth. Hence, this study was done to assess the role of altered lipid profile in the development of PIH.

Methods: A Case Control study was conducted at the Department of Biochemistry, Kurnool Medical College and Govt General Hospital, Kurnool in collaboration with its Obstetrics Dept during the period of November 2015-2017. A total of 300 pregnant women, primigravida /multigravida with singleton pregnancy, in the age group of 18- 35 years with >20 weeks of gestation were included in the study. Subjects were divided into gestational hypertensives, n=39 (BP ≥140/80) and preeclamptic women, n=111 (≥140/80 and proteinuria) as cases. Age matched normotensive pregnant women, n=150 (BP 120/80) were recruited as Controls. Subjects with history of multiple pregnancies, pregnancy with congenital anomalies, chronic hypertension, diabetes mellitus, cardiac/thyroid/hepatic/renal disease, dyslipidemia were excluded. Total cholesterol, TG, HDL, LDL, VLDL were performed.

Results: A comparison of these values between hypertensive and normotensive women showed a significant rise in TC, TG, LDL and VLDL. HDL-C showed a significant decrease in hypertensive women compared to normal pregnant women. LDL: HDL and TG:HDL ratios were higher in PIH group.

Conclusions: The results of this study suggests an abnormal lipid metabolism, predominantly high TG concentrations and low HDL-C, which may add to the promotion of vascular dysfunction and oxidative stress seen in PIH. This association is significant in understanding the development of hypertension during pregnancy and is useful in early diagnosis and prevention of PIH.

Keywords: Dyslipidemia, Gestational HTN, Lipid Profile, PIH, Pregnancy, Pre-eclampsia

INTRODUCTION

PIH is a syndrome of hypertension in pregnancy, with or without edema and proteinuria, which puts both maternal and fetal health at risk. Hypertensive disorders of pregnancy (HDPs) contribute globally to approximately 30,000 maternal and 50,000 perinatal deaths annually.[1,2] According to National Health Portal, India 2016, the

prevalence of HDPs in India was 7.8%, with preeclampsia in 5.4% of the study population.

HDPs are classified into 4 categories, as recommended by the National High Blood Pressure Education Program: Gestational hypertension is characterized by new onset hypertension after 20 weeks gestation, followed by return of blood pressure to normal within 3 months post-partum. Early presentation (<32 weeks) along with severity of hypertension, increases the chance of gestational hypertension to progress into preeclampsia or an adverse pregnancy outcome in about 25% of cases.[3,4] Preeclampsia is broadly defined by hypertension and proteinuria. High blood pressure contributes to widespread damage to maternal kidneys, liver and especially endothelium. Although 3-10% pregnancies are affected with preeclampsia, it is estimated to be 20% in developing countries.[5] Eclampsia includes preeclampsia with the presence of convulsions not attributable to other neurological diseases. Chronic hypertension is present in up to 5% of pregnant women and is defined as hypertension present before pregnancy or before 20 weeks of gestation.[6] Superimposed preeclampsia develops in 13-40% women with chronic hypertension depending on diagnostic criteria, etiology, duration and severity of hypertension.[7] In a multicentre study conducted by National High Blood Pressure Education Program, approximately 30% of HDPs were due to chronic hypertension while 70% of the cases were diagnosed as gestational hypertension/preeclampsia.

The pathophysiological events resulting in PIH begin early in gestation, and precede the onset of the clinical features.[8] Abnormal lipid metabolism has a basic role in the pathogenesis of PIH where endothelial cell damage is one of the earliest hallmarks.[9,10] Lipoproteins levels increase more in PIH than in normal pregnancy and cause damage to endothelium that may result in high blood pressure and protein uria.[11,12] In pregnancy there is an increase in estrogen levels which is the main factor behind hypertriglyceridemia. Estrogen induces hepatic production of TG's that causes endothelial dysfunction through generation of LDL and VLDL. Dyslipidemia, a maternal factor favours oxidative stress and endothelial dysfunction which may inhibit the synthesis of prostacyclin and increase the production of thromboxane, which are a potent vasoconstrictor and a stimulator of platelet aggregation.[9,11] There are many predictors and markers to identify women at risk of PIH but a simple measurement of lipid profile may be of good predictive value. The present study was conducted to assess lipid profile for screening and early detection of at-risk women so that appropriate treatment can be given even before the setting in of eclampsia and other life threatening complications.

METHODS

A case-control study was conducted at the Department of Biochemistry, Kurnool Medical College and Government General Hospital, Kurnool in collaboration with its Obstetrics department during the period of November 2015-2017. The study was approved by Institutional Ethics Committee (dated 05/11/2015IEC-KMC GGH). Informed consent was obtained from all the participants after comprehensive explanation of the procedure involved. A total of 300 pregnant women, primigravida /multigravida with singleton pregnancy, in the age group 18- 35 years with >20 weeks of gestation were included in the study. Subjects were divided into gestational hypertensives, n=39 (BP ≥140/80) and preeclamptic women, n=111 (≥140/80 and proteinuria) and recruited as Cases. Age matched normotensive pregnant women, n=150 (BP 120/80) were recruited as controls. Women with multiple pregnancies, pregnancy with chronic hypertension, pregnancy with diabetes mellitus, pregnancy diagnosed with congenital anomalies, patients with past history of cardiac, renal, hepatic dysfunction or dyslipidemia were excluded from the study.

A detailed clinical history was taken, blood pressure was recorded using standard mercury sphygmomanometer. 2 measurements were made with an interval of 5 minutes and with the subject in either sitting or reclining position. BMI was calculated after the measurement of height and weight using the formula weight divided by square of height (kg/m^2).

Fasting venous sample was collected in a well labeled, plain, red capped vacutainer tube and left at room temperature for half an hour. Serum was separated by centrifugation and analyzed for Total cholesterol (TC), Triglyceride (TG), HDL-cholesterol (HDL-C), estimated by enzymatic colorimetric methods using ERBA Semi Auto analyzer. Serum LDL-cholesterol was calculated by Frederickson-Friedwalds formula according to which LDL cholesterol=TC-(HDL+VLDL) and VLDL-cholesterol was calculated as (TG/5) along with 24 hour urinary protein estimation.

Statistical Analysis

Descriptive statistics were calculated for all demographic and clinical characteristics of the study subjects. The values obtained were compared between the hypertensive and normotensive groups. Test of significance were Chi Square test and T- test. Mean±SD were calculated. Frequency tables were drawn for distribution of data. All the statistical data analysis was performed using software SPSS (version 21.0).

RESULTS

Total Participants in the present study (2015-2017) were 300 pregnant women attending the Obstetrics OPD. Subjects were divided into gestational hypertensives, n=39and preeclamptic women, n=111and recruited as Cases. Age matched normotensive pregnant women, n=150 were recruited as Controls.

Table 1: Demographic and clinical characteristics in cases and controls.

	Cases	Controls	
	Mean±SD (N=150)	Mean±SD (N=150)	P Value
Age	28.16±4.6	25.9±4.2	0.0001**
BMI	27.72±3.5	24.11±1.6	0.0001**
SBP	160.3±15.39	118.9±8.03	0.0001**
DBP	103.9±17.01	80.6±7.38	0.0001**

Ages of subjects among PIH group were (28±4.6years) while in normotensive group were (25±4.2years).This difference was statistically significant.

BMI of subjects among PIH group were (27.7±3.5) is more than the normotensive group (24.1±1.6). The difference was statistically significant (pvalue0.0001).

SBP in PIH group and normotensive group were (160±15.3) and (118±8) respectively. The mean values of DBP in PIH and normotensive groups were (103±17) and (80±7). The difference is statistically significant with P<0.0001. Anthropometric details are shown in Table 1. 24 hours urinary protein in cases (288.2±216.6) is more when compared to controls (35±23.1). The difference is statistically significant (p value<0.0001).

Table 2: Lipid Profile in cases and controls.

Biochemical Investigations	Cases Mean±SD (N=150)	Controls Mean±SD (N=150)	P Value
Urine protein	288.2±216.6	35.7±23.1	0.0001**
Lipid profile			
(i) TC	222.8±17.67	164.9±14.57	0.0001**
(ii) TG	206.8±34.68	98.5±15.33	0.0001**
(iii) HDL	28.74±3.16	54.05±5.59	0.0001**
(iv) LDL	152.6±18.28	91.17±15.85	0.0001**
(v) VLDL	41.36±6.9	19.71±3.07	0.0001**
Ratios			
(i) TG:HDL	7.27±1.4	1.84±0.35	0.0001**
(ii) LDL:HDL	5.38±0.98	1.71±0.39	0.0001**

Lipid profile in PIH group (TC:228±17.6, TG:206±34.6, LDL:152±18.2, VLDL:41.3±6.9) was more when compared to normotensive group (TC:164±14.5, TG:98±15.3, LDL:91.1±15.8, VLDL:19.7±3.0). Statistically significant (p<0.001) differences were noted.

HDL in cases (28.7±3.16) was decreased when compared to controls (54±5.5). The difference was statistically significant (pvalue0.0001). LDL:HDL ratio and TG:HDL ratios were higher in PIH group and were found highly significant(P<0.0001).

DISCUSSION

Pregnancy-induced hypertension (PIH) 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 present study showed that maximum number of people in the PIH group belonged to 31-35 years and that of controls belonged to 26-30 years showing that the risk of developing PIH was more with increasing maternal age which was in conformity with Sahu et al, Lamminappa et al which reported maternal age to be higher in cases when compared to controls.[14,15] A study conducted by Yadav et al concluded that the threat of PIH was greater in pregnant women with less than 25 years, and a study by Bangal VB et al, also found the incidence of PIH was higher among teenage pregnancy, all of which did not correlate with the present study.[16,17]

In the present study there was a significant rise in the risk of PIH with increasing BMI in hypertensive group as compared to normotensive group which was similar to the studies conducted by Romy G et al, which showed that maternal obesity is strongly associated with increased blood pressure and increased risk of gestational hypertensive disorders.[18] However in a study conducted by Sahu MT et al, concluded that both lean and obese women carry a risk for adverse pregnancy outcome.[19]

The present study observed that the risk of PIH was increased in women with previous history of PIH which was in conformity with the studies conducted by Kumar Gb et al, Mostello et al.[20,21] Study conducted by Sibai et al, reported that 65% of all studied women with a history of preeclampsia at the second trimester showed a recurrent preeclampsia at their subsequent pregnancy, suggesting that past history is also one of the important predictive factors for developing PIH.[22]

The results of the present study showed that mean BP was significantly increased in hypertensive pregnant women as compared to that in normotensive pregnant women which is consistent with Bhutani K et al, Anjum

et al, who also showed that mean systolic and diastolic BP were statistically significantly higher in preeclamptic as compared to controls.[23,24] In the present study the levels of urine protein in hypertensives was higher than that of normotensives which was in conformity with Dong et al, and Kim MJ et al.[25,26] Patients with gestational hypertension showed only <300 mg, those with preeclampsia showed >300- 2000 mg of protein in their 24-hour urine samples.[27]

Altered lipid synthesis leading to decrease in prostacyclin:thromboxane ratio is also supposed to be an important way of pathogenesis in PIH.[9] Total cholesterol (TC) was shown to be significantly raised in the present study as in the study conducted by Dr.VBreetha et al28, however other studies reported no alteration in TC levels.[29,30] Physiological insulin resistance is exaggerated in pre- eclampsia. Gestational insulin resistance may accentuate the suppression of lipoprotein lipase activity and increase mobilization of free fatty acids from visceral adipocytes. This may explain the hypercholesterolemia in pre- eclampsia.[31]

Along with TC, a rise in serum triglycerides (TG) was noted in hypertensive pregnant women when compared to normotensive pregnant women which was similar to the studies conducted by Breetha et al, Amandeep et al, and which also showed that serum TG was significantly higher in PIH patients when compared to normal pregnant women.[28,32] The major modulator of this hypertriglyceridemia is estrogen as pregnancy is linked with hyperestrogenemia. Increased TG, found in PIH, is likely to be 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 LDL.[28,30] Also our findings of greater increase in mean BMI in pregnant females with PIH could explain the significant increase in triglycerides.

In the present study LDL-C, VLDL-C components of lipid profile were increased in the hypertensive group when compared with normotensive group, and HDL-C was significantly lower. These results were similar to the study conducted by Shivanagappa et al, and their results were also comparable to various other studies.[33,34]

It is important to identify the possible risk factors associated with the development of PIH as this would help in the development of appropriate screening modalities for early detection of PIH and preeclampsia to enhance its management. Preventive measures should be taken such as; women should receive adequate counseling to urge them to adopt healthier habits and lifestyles and to seek periodic checkups, in order to detect diseases in its early stages, before irreparable damage or even death. In a systematic review of the literature by Bellamy et al, reported that women with a history of preeclampsia presented increased risk of cardiovascular disease (Relative Risk, RR=3.7), hypertension (RR= 2.16), ischemic heart attack (RR = 1.81), venous thromboembolism (RR = 1.79) and death (RR = 1.49).[35] These findings confirm the possible association between hypertension during pregnancy and future cardiovascular disease. In order to execute preventive healthcare protocols, it is important to recognize patients who are at risk. Enhanced understanding of lipid metabolism, abnormalities and how these changes relate with the endothelial dysfunction of PIH is fundamental from a public health perspective.

CONCLUSION

The findings reported in this study showed that the women who developed PIH had significantly higher triglycerides when compared to normal pregnant women. It was also noted that TC, LDL and VLDL were statistically higher and HDL-C was significantly lower in the hypertensive group. The ratios between TG:HDL-C and LDL-C:HDL-C were also higher in the hypertensive group. 24hours urine protein was higher in the PIH group when compared with that of the normotensive group. The risk of PIH is increased with increasing maternal age, BMI, and past h/o PIH. In conclusion, the results of our study propose that an abnormal lipid metabolism and predominantly low HDL-C and high TG concentrations, may add to the promotion of vascular dysfunction and oxidative stress seen in pregnancy induced hypertension. It is, therefore, essential that, blood lipid concentrations be estimated in pregnant women during antenatal care since it could be useful in the early diagnosis and prevention of obstetric complications. As stated by the WHO, World Health Report (2005), "Make Every Mother and Child Count."

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