

Valuation of Serum Lipid Profile in HDP Patients Comparative Study

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Abstract

Introduction: Pregnancy is associated with changes in anatomy, physiology, biochemistry¹. As a result of these changes serial alteration in the lipid profile mainly TGs, cholesterol occurs. In current knowledge hyperlipidemia plays a major role in pathogenesis of hypertensive diseases of pregnancy. Therefore, we propose to analyse the lipid profile changes in hypertensive pregnant women visiting Department of Obstetrics and Gynaecology in Rajkiya Mahila Chikitsalaya, JLN Medical College, Ajmer during Jan 2020 to June 2021.

Methods: 100 healthy pregnant women and 100 HDP patients were taken (inclusion and exclusion criteria applied) and Matched in age, BMI, residency, gestational age. They were subjected to detailed history taking, BP, urine albumin, CBC, LFT, RFT, USG. Lipid profile (TC, TGs, LDL, VLDL, HDL) of the samples was analysed using automated analyser. Further data was subjected to appropriate statistical analysis.

Results: Mean age of both cases and controls in 25.13 years and it remained statistically insignificant. It was observed that HDP was more common in unbooked

patients. If HDP diagnosed in present pregnancy the chance of recurrence is high in next pregnancy. Mean T cholesterol in Cases is 217.93mg/dl and in Control is 180.5mg/dl, mean HDL level in Case is 57.36mg/dl and Control is 45.23mg/dl, mean VLDL level in Case is 48.67mg/dl and in Control in 35.86mg/dl, mean TGL level in Case is 249.9 and in Control is 171.67mg/dl, mean LDL level in Case is 127.94mg/dl and in Control is 101.92mg/dl. Statistically there is significant difference in lipid profile between cases and controls (P-value 0.001). TGs, TC, VLDL were significantly increased

Conclusion: Findings of the study are consistent with the previous studies. TGs, TC, VLDL were increased. Lipids play a major role in the pathogenesis of hypertensive diseases of pregnancy. Understanding the pathological process of hypertensive diseases of pregnancy may help in developing strategies for prevention and early diagnosis of pre-eclampsia

Keywords: Lipid Profile, Hypertensive Diseases, Pre-eclampsia.

Introduction

Hypertensive disorders in pregnancy affect approximately 4% to 25% of all pregnancy women worldwide^{1,2}. The incidence of gestational hypertension is on rise. Hypertensive disorders in pregnancy may be a sequela of chronic hypertension (which exists even prior to pregnancy) or develop first time in pregnancy in second trimester. This can affect both mother and fetus.^{3,4} Even in normal pregnancy there is increase in plasma lipid, but in normal pregnancy it is not atherogenic, due to hormonal control^{5,6}. Whenever this mechanism of adjusting physiologic hyperlipidemia is altered that lead to complications in pregnancy⁵⁻⁹. So, in pregnancy if serum lipid profiles are estimated it helps to identify high risk cases prone for preeclampsia. So, there is a need to frame a good and effective screening test which can be used during routine antenatal check up to predict pre-eclampsia at the earliest. In this study, I have compared the lipid profiles of HDP women with normotensive. 2. Objectives To analyse lipid profile changes in hypertensive diseases of pregnancy. To compare the lipid profile of HDP patients with normotensive patients 3. Methodology This hospital-based case control study is carried out at Department of Obstetrics and Gynaecology in Rajkiya Mahila Chikitsalaya, JLN Medical College, Ajmer during Jan 2020 to June 2021. Inclusion Criteria 1. Normal healthy pregnant women who develop hypertension for the first time after 20 weeks of gestation diagnosed as HDP with no other associated complications. Further categorisation was done according to diagnostic criteria Gestational hypertension • New-onset blood pressure $\geq 140/90$ mmHg detected at ≥ 20 weeks gestation without proteinuria. PREECLAMPSIA: Blood pressure $\geq 140/90$ mmHg on two occasions at least 4 hrs apart or $\geq 160/110$ mmHg

within a shorter interval (minutes), at ≥ 20 weeks of gestation, in women with previously normal blood pressure and proteinuria*. In the absence of proteinuria, new-onset hypertension plus new onset of any of the following features: serum creatinine concentrations >97 $\mu\text{mol/l}$ or doubling of serum creatinine concentration in the absence of other renal disease; elevation of liver transaminases to twice normal concentration; pulmonary oedema; and cerebral or visual symptoms • Eclampsia: seizures in women with pre-eclampsia that cannot be attributed to other causes • Atypical form of preeclampsia presents with systemic symptoms, abnormal hematological tests or elevated liver enzymes without proteinuria. 2. Normal women in the third trimester of pregnancy with no other maternal medical complications, admitted for safe confinement.

Exclusion Criteria

1. Chronic hypertension
2. Pregestational Diabetes mellitus
3. Nephrotic Syndrome
4. Cardiac Disease.
5. Hepatic Disease.
6. Twin pregnancy
7. Any medications except for vitamins and minerals. 8. Alcohol abuse
9. Thyrotoxicosis.
10. Molar pregnancy

Matching

Case and control groups were matched in age, gravidity and gestational age, BMI.

Methodology

All pregnant mothers included in the study were subjected to detailed history taking, BMI, blood pressure measurement, urine albumin, CBC, LFT, RFT, USG. Lipid profile (TC, TGs, LDL, VLDL, HDL) of the

samples was analysed using automated analyser. Blood pressure was measured by palpatory method and auscultatory method in supine and sitting position. Systolic BP was taken by Korotkoff sound (phase I) and diastolic BP was taken by Korotkoff sound (phase V). Fasting blood samples were taken from 100 pregnant patients with HDP and 100 normal pregnant women, admitted in RMC, Ajmer.

The samples were subjected to analysis of lipid profile.

Reagents used: The following reagents were used for determination of the lipid values.

Total Cholesterol: Cholesterol Oxidase, Peroxidase

HDL Cholesterol: Phosphotungstate / Magnesium precipitation

LDL Cholesterol: Catalase / cholesterol esterase / cholesterol oxidase Triglycerides: Glycerol Phosphate oxidase/ Peroxidase

Results

Among 100 cases and 100 controls, maximum 97 patients each in both the groups were in age group of 19-34 years. Equally, in cases and controls, the mean age was 25.13 ± 3.478 years. Preliminarily, BMI in both the groups were documents and found that, cases had slightly higher BMI 22.83 ± 1.96 than control BMI 21.57 ± 1.87 , moreover, the BMI did not confer any statistically significant p -value=0.78. Residing factor was also checked whether it is contributing the disease susceptibility. Among 100 cases 49% patients were from rural area and 51% were from urban area. Similarly in controls 44% patients from rural and 56% patients from urban areas. Statistically there is no significant difference in residential area between cases and controls (P -value 0.47). Among 100 controls and cases, maximum 57 and 44 patients had period of gestation as 32-37 weeks. Whereas, the mean gestational age of cases was

34.86 ± 3.80 weeks and that of control were 37.1 ± 2.15 weeks. Difference in mean gestational age between cases and controls showed statistical significance P -value=0.001. Among 100 cases, 56% patients were primi gravida, 16% patients were multipara (parity of ≥ 2 deliveries after 28 weeks of gestation). Among 100 controls, 48% patients were primi gravida, 13% patients were multipara (parity of ≥ 2 deliveries after 28 weeks of gestation). It conferred statistical significance p -value=0.001. In majority of cases no abnormality was detected (60%), IUGR was second most common findings (19%) followed by severe oligohydramnios in 15%, mild oligohydramnios in 4% and 2% patients had RPH. Similarly in controls majority of cases no abnormality was detected (94%), severe oligohydramnios was 5% and 1% moderate oligohydramnios. Statistically there is significant difference in USG findings between cases and controls (P -value 0.001) significant USG finding in more common in cases. In cases 17% had pregnancy induced hypertension in previous pregnancy and in controls only 3% had pregnancy induced hypertension in previous pregnancy. Statistically there is significant difference in history of PIH in previous Pregnancy between cases and controls (P value 0.001). Among 100 cases, 46 patients had SBP in the range of ≥ 160 , 32 patients had SBP in the range of 140-149 and 22 patients had SBP in the range of 150-159. Among cases mean systolic blood pressure was 154.8 ± 12.81 were is controls mean systolic blood pressure was 120.57 ± 9.64 . Among 100 cases, 38 patients had DBP in the range of 90- 99, 33 patients had DBP in the range of 100-109 and 109 patients had DBP in the range of ≥ 110 . Among cases mean diastolic blood pressure was 101.32 ± 8.88 were is controls mean diastolic blood pressure was 73.67 ± 7.51 .

Mean T cholesterol in Cases is 217.93mg/dl and in Control is 180.5mg/dl, mean HDL level in Case is 57.36mg/dl and Control is 45.23mg/dl, mean VLDL level in Case is 48.67mg/dl and in Control in 35.86mg/dl, mean TGL level in Case is 249.9 and in Control is 171.67mg/dl, mean LDL level in Case is 127.94mg/dl and in Control is 101.92mg/dl. Statistically there is significant difference in lipid profile between cases and controls (P-value 0.001). TGs, TC, VLDL were significantly increased.

Table 1: Demographic variables of patients

Demographic Variables		100 Cases	100 Controls (n%)	p-value
Age in years	19-34 years	97	97	
Mean Age in years		25.13±3.478	25.13±3.664	0.98
Mean BMI in kg/m2		22.83±1.96	21.57±1.87	0.78
Residential area	Rural	49	44	0.47
	Urban	51	56	
Booking Status	Booked	30	70	0.001
	Unbooked	81	19	

Table 2: Clinical variables of patients

Clinical Variables		100 Cases	100 Controls (n%)	p-value
Period of gestation distribution	32-37 weeks	44	57	
Mean gestational age in years		34.86±3.80	37.1±2.15	0.001
Obstetric history	Primi	56	48	0.001
	G2P1	24	33	
Significant USG Findings	IUGR	19	0	0.001
	Severe Oligohydramnios	15	5	
PIH in previous Pregnancy	No	83	97	0.001
	Yes	17	3	
Systolic Blood Pressure	≥160	46	0	0.001
Mean systolic blood pressure		154.80±12.811	120.57±9.649	0.001
Diastolic Blood Pressure	90-99	38	0	
Mean diastolic Blood Pressure		101.32±8.882	73.67±7.517	0.001

Table 3: Lipid Profile Distribution in Cases and Controls

		Mean	Std. Deviation	P value
T cholesterol	Case	217.9	43.66	0.001 (s)
	Control	180.5	27.24	
HDL level	Case	57.36	15.55	0.001 (s)
	Control	45.23	8.89	
VLDL level	Case	48.67	16.47	0.001 (s)
	Control	35.86	6.39	
TGL level	Case	249.9	86.09	0.001 (s)
	Control	171.7	36.23	
LDL level	Case	127.9	43.74	0.001 (s)
	Control	101.9	16.52	

Discussion

In recent times there is a great interest about the role of lipid metabolism in the development of preeclampsia (PE). Previous studies have reported that plasma lipid levels were higher in preeclampsia women than the healthy pregnant women. It is thought that the lipid changes might have a role at endothelial cell damage which is characteristic of Preeclampsia. Lipid peroxidation occurs at low levels in all cells and tissues. In health, oxidation by free radicals and neutralization by antioxidants remains in balance. In preeclampsia antioxidant nutrients are excessively utilized to counteract the cellular changes mediated by free radicals like lipid peroxides. Abnormal lipid metabolism is not a mere manifestation of PE; but it is involved in the pathogenesis of preeclampsia. Lipid mediated oxidative stress is likely to contribute to endothelial hyper stimulation leading to dysfunction and damage. Interaction between reactive oxygen species with polyunsaturated fatty acids lead to production of lipid peroxides with a much longer half-life than in normal pregnancy leading to oxidation stress thought to be the causative factor in pregnancy induced hypertension¹⁰. The mean age of cases is 25.13 years and that of control is 25.13 years. Statistically there is no significant difference in mean age between cases and controls. Bishnoi et al (2019)¹¹ found mean age of cases is 21.86 years and that of control is 22.86 years, statistically no

significant difference in mean found. Nazir et al (2019)¹⁰ found The Mean \pm SD of age distribution among the two groups (Cases and Controls) was 27.20 \pm 4.13 and 27.07 \pm 4.23 respectively. Blessy et al (2019)¹² found that Ages of subjects among PIH group were (28 \pm 4.6years) while in normotensive group were (25 \pm 4.2years). This difference was statistically significant. Lamminappa et al (2012)¹³ reported maternal age to be higher in cases when compared to controls. A study conducted by Yadav et al (1997)¹⁴ concluded that the threat of PIH was greater in pregnant women with less than 25 years, and a study by Bangal VB et al (2011)¹⁵ also found the incidence of PIH was higher among teenage pregnancy, all of which did not correlate with the present study. In cases 49% belong to rural and 51% belong to urban. Similarly in controls 44% cases from rural and 56% cases from urban areas. Statistically there is no significant difference in residential area between cases and controls (P-value 0.47). Nazir et al (2019)¹⁰ found that majority of the subjects in both the study (71%) and control groups (74%) were from rural areas. In cases majority has complaint of convulsion (26%) followed by headache (4%) and other complaint likes bleeding, blurred vision, epigastric pain and IL constitute 2% each and edema is present in 1% cases. In controls there are no complaints. The mean gestational age of cases is 34.86 weeks and that of control is 37.1 weeks. Statistically there is significant difference in mean gestational age between cases and controls (P-value 0.001). Bishnoi et al (2019)¹³ found mean gestational age of cases is 35.04 weeks and that of control is 34.44 weeks. Statistically there is no significant difference in mean gestational age between cases and controls (P-value 0.2050). Nazir et al (2019)¹⁰ found Mean \pm SD gestational age of the study groups at the time of study was 35.21 \pm 3.04 weeks. The

minimum and maximum gestational age ranges from 24-38 weeks. Blessy et al (2019)¹² 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 (2010)¹⁶, Mostello et al (2008)¹⁷ Study conducted by Sibai et al (2002)¹⁸ 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. In cases mean SBP and DBP is 154.80 mm of hg and 101.32 mm of hg respectively. Similarly in controls mean SBP and DBP is 120.57 mm of hg and 73.67 mm of hg respectively. Statistically there is significant difference in SBP and DBP between cases and controls (P-value 0.001). Bishnoi et al (2019)¹¹ found mean SBP and DBP is 144.52 mm of Hg and 95.28 mm of Hg respectively. Similarly in controls mean SBP and DBP is 117.36 mm of Hg and 78.44 mm of Hg respectively. Statistically there is significant difference in SBP and DBP between cases and controls (P-value 0.001).

Bishnoi et al (2019)¹¹ found mean SBP and DBP is 144.52 mm of Hg and 95.28 mm of Hg respectively. Similarly in controls mean SBP and DBP is 117.36 mm of Hg and 78.44 mm of Hg respectively. Statistically there is significant difference in SBP and DBP between cases and controls (P-value <0.0001).

. Nazir et al (2019)¹⁰ found the Mean systolic [153.28 mm Hg] and the Mean diastolic [100.903 mm Hg] blood pressure among the cases was significantly higher than the Mean systolic [125.38 mm Hg] and the Mean diastolic [74.94 mm Hg] among the controls. The difference was statistically significant. Islam et al (2010)¹⁹ reported that mean Systolic, Diastolic, and

Mean arterial pressure were (110.75 ± 8.88 , 159 ± 18.47), (68 ± 10.42 , 100.75 ± 10.92), (82.25 ± 9.46 , 120.16 ± 12.04) mm Hg in Group I (Controls) & Group II (cases) respectively. There was significant difference of all blood pressure parameter between cases & controls ($p < 0.001$).

Blessy et al (2019)¹² found 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 $P < 0.0001$.

Bhutani K et al (2015)²⁰, Anjum et al, (2013)²¹ who also showed that mean systolic and diastolic BP were statistically significantly higher in preeclampsia. Here, mean T cholesterol in Cases is 217.93 and in Control is 180.5, mean HDL level in Case is 57.36 and Control is 45.23, mean VLDL level in Case is 48.67 and in Control is 35.86, mean TGL level in Case is 249.9 and in Control is 171.67, mean LDL level in Case is 127.94 and in Control is 101.92. Statistically there is significant difference in lipid profile between cases and controls (P value 0.001). Statistically there is significant difference in total cholesterol and LDL within group (P-value 0.001), with maximum in eclampsia followed by preeclampsia, Gestational hypertension and normotensive. Similarly, statistically there is significant difference in mean TGL and VLDL within group (P-value 0.001) with maximum in preeclampsia followed by eclampsia, Gestational hypertension and normotensive. Lastly, statistically there is significant difference in mean HDL within group (P value 0.001), with maximum in Gestational hypertension followed by eclampsia, preeclampsia and normotensive. TC, TGs, VLDL significantly increased in cases compared controls. HDL

is within normal level in cases with significant mean difference among groups.

LDL within normal level in cases and controls but statistical significance is seen between cases and controls.

Bishnoi et al (2019)¹¹ found triglycerides and VLDL C were significantly increased ($p < 0.0001$) and HDL-C was significantly decreased in preeclampsia group compared to control group. Total cholesterol and LDL-C were increased in preeclampsia group as compared to normal pregnant group but the results were not statistically significant.

Latha et al (2013)²² suggest that Abnormal lipid metabolism in preeclampsia may not be a manifestation but may also be involved in the pathogenesis of disease. Hyperlipidemia during preeclampsia is transient, therefore its pathological role in these women have been ignored. Hypoestrogenism, seen in preeclampsia, leads to decreased expression of VLDL/apoE receptors resulting in reduced transport of VLDL to fetal compartment and so there is maternal hypertriglyceridemia.

Gohil et al (2011)²³ suggest that Elevated triglycerides may compromise vascular functions in several ways. For example, triglyceride rich lipoprotein has a prothrombotic effect. Gohil et al (2011)²³ demonstrated significant fall in HDL-C in preeclampsia than in non-pregnant and normal pregnant women. Increased triglycerides play a role in increased atherogenic small dense LDL and reduced HDL. A low level of HDL C hinders reverse cholesterol transport, which may be a reason for the atherosclerosis like features in preeclampsia mentioned in some studies. Nazir et al (2019)¹⁰ found that Mean \pm SD of triglycerides, total cholesterol, VLDL cholesterol and LDL cholesterol among the women in the study group was higher than the

Mean \pm SD of triglycerides, total cholesterol, VLDL-cholesterol and LDL cholesterol among women in the control group. Further, mean \pm SD of HDL-cholesterol among the study group was higher than the Mean \pm SD of HDL Cholesterol among the control group. Statistically, there is a significant difference in case of triglycerides, HDL cholesterol and VLDL-cholesterol and in significant difference in case of total cholesterol and LDL cholesterol between the two groups.

Islam et al (2010)¹⁹ reported that Serum lipid profile was compared between cases & controls & between subgroups of cases. Mean Triglycerides (225.6 ± 28.93 vs 165.6 ± 17.22) levels are significantly higher in group of women who had preeclampsia as compare to normal controls ($p < 0.05$). While mean High density lipoproteins cholesterol (42.4 ± 9.29 vs 55.7 ± 7.11) levels were significantly lower in women with preeclampsia than in normal control subjects ($p < 0.05$) as shown in Table-II. In Case of eclampsia mean LDL cholesterol (133.4 ± 11.75 vs 115.2 ± 10.72) are significantly higher and mean High density lipoproteins' cholesterol (41.8 ± 8.79 vs 55.7 ± 7.11) levels were significantly lower than in normal control subjects ($p < 0.05$). Mean cholesterol levels were not statistically different between pre-eclamptic, eclamptic and normal subjects. Blessy et al (2019)¹² found 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 (p value 0.0001). LDL:HDL ratio and TG:HDL ratios were higher in PIH group and were found highly significant ($P < 0.0001$). in our study LDL to HDL & TGs

to HDL ratio were found higher in HDP study groups as compared to controls.

Conclusion

In summary, the findings reported in this study suggest that the women who develop pre-eclampsia and eclampsia had disturbed lipid profile due to abnormal lipid metabolism, increased triglyceride levels, delayed triglyceride clearance and high blood pressure. The findings showed that TGs, LDL and VLDL were statistically higher and HDL-Cholesterol was significantly lower but within normal limit in the hypertensive group. 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 HDP.

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