www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i4.111

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Comparative Study of Serum Lipid Profile in Preeclampsia and Normal Pregnancy

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Abstract
Background: *Preeclampsia affects 5-15% of pregnancies and is a major cause of maternal, fetal and neonatal morbidity and mortality worldwide. The aim of the study was to demonstrate a positive correlation between dyslipidemia and preeclampsia.*
Method & Materials: *This study was a case control study conducted in the Post Graduate Department of Obstetrics and Gynecology, Government Lal Ded Hospital Srinagar. A total of 200 (two hundred) were selected, out of which 100 (one hundred) normotensive pregnant women served as a control and 100 (one hundred) preeclampsia women constituted the study group. Besides baseline routine investigations, estimation of Serum lipid profile was done by collecting blood samples from antecubital vein of every case and control following a fast of 12-14 hours and collected in plain vials and were analysed at department of Biochemistry, Government Medical College Srinagar.*
Results: *The preeclampsia group had a significant rise in Triglyceride (TG) and VLDL-C levels and decreased HDL-C levels as compared to the control group. Non-significant differences were observed for total cholesterol and LDL-C levels among case and controls.*
Conclusion: *Abnormal lipid profile results during pregnant women plays an important role in development of pre-eclampsia.*
Keywords: *Preeclampsia (PE); Lipid Profile; Triglycerides (TG), High Density Lipoproteins (HDL-C), Very Low Density Lipoproteins (VLDL-C).*

Introduction

Preeclampsia (PE) is one of the most common complications of pregnancy and a measure cause of maternal and neonatal mortality and morbidity worldwide[(1,2)]. It is diagnosed by elevated blood pressure and proteinuria after 20 (twenty) weeks of gestation in a patient known to be previously normotensive.

Mild Preeclampsia: Blood Pressure (BP) ≥140/90 mmHg confirmed on two measures at least 6 (six) hours apart but not more than 7 days apart, and proteinuria ≥300 mg on a 24 hour urine collection or two random urine dipstick results of at least 30 mg/dl (" 1+").

Severe Preeclampsia: Blood Pressure during bed rest of ≥ 160 mmHg Systolic or ≥ 110 mmHg Diastolic, and proteinuria ≥ 5 gm on a 24 hour urine collection even if BP is in the mild range.

In India the incidence of PE in hospital practice varies widely from 5-15%; the incidence in primigravidae is about 10% and in multigravida is about 5%[(3)]. The dreaded complications associated with PE includes eclampsia, HELLP syndrome, pulmonary edema, abruption-placenta, postpartum

circulatory collapse acute renal failure, hepatic rupture, cerebral hemorrhage and visual disturbances. The fetal neonatal morbidity includes preterm delivery intrauterine growth restriction, intrauterine fetal demise or early neonatal death. The only intervention that reverses the syndrome effectively is delivery. The following pathophysiological considerations have been put forth as shown in the Figure 1.

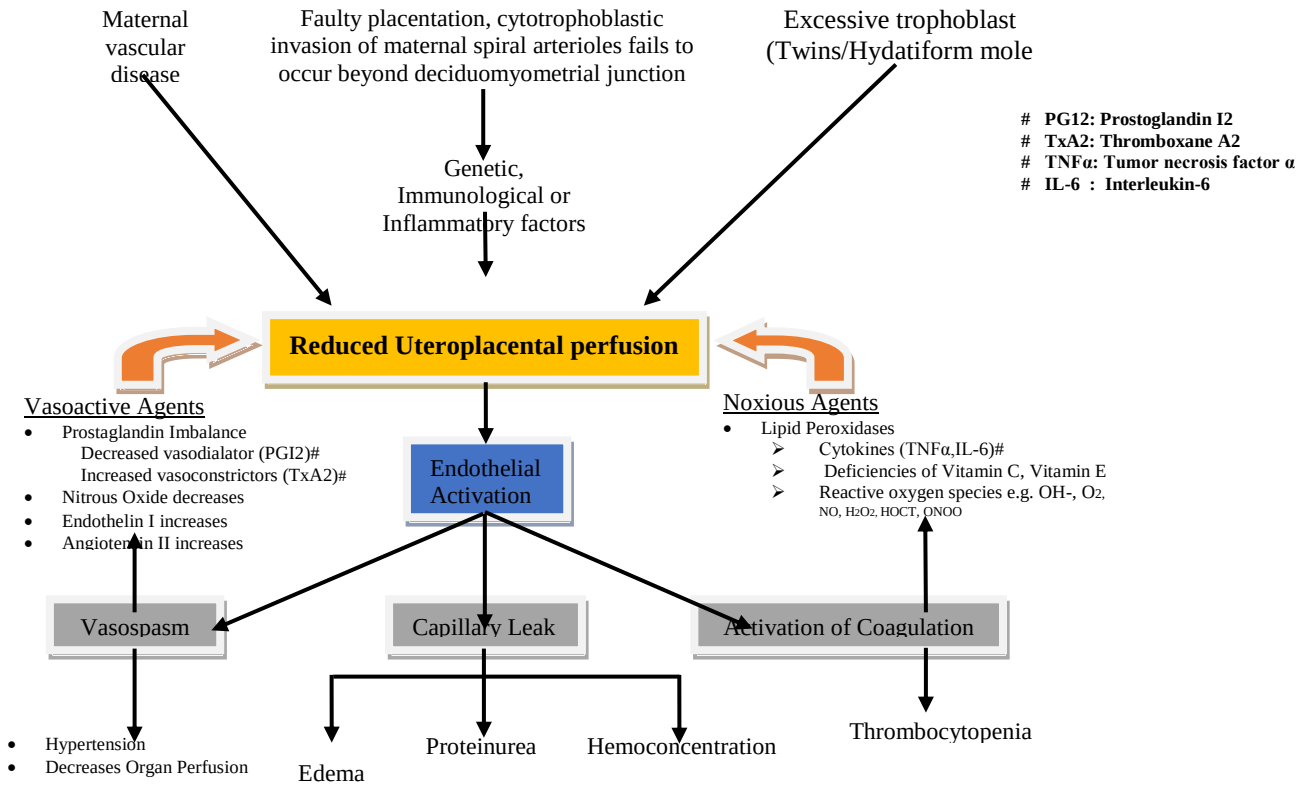

Figure 1: Pathophysiological considerations in the development of Hypertensive disorders due to Pregnancy

The most important feature of PE is hypertension via vasospasm in kidneys, uterus placenta and brain. In normal pregnant women, endothelial prostacyclin reaches 8-10 times more than a non-pregnant women. But in preeclampsia women this rise is only 1-2 times more. Also in preeclampsia women, thromboxane rise more than normal pregnant women[(4)]. Because prostacyclin is a vasodilator and thromboxane is a vasoconstrictor; endothelial cell destruction ensures leading to vasospasm[(5)]. Increase in lipid synthesis causes rise in the thromboxane prostacyclin rate and plays a role in the pathogenesis of pregnancy induced hypertension[(6)]. Endothelial cell injury and impaired endothelial functions are important in the pathogenesis of PE Women with a history of PE have significant differences in lipid parameters and increased susceptibility to lipoprotein per-oxidation when compared with women who have normal pregnancy-the most common factor associated with PE is placental vasculopathy. If PE is multicausal disease then triglyceride related vasculopathy may be one of the possible etiological factor[(7)].

Increases triglycerides found in preeclampsia patients is likely to be deposited in predisposed vessels such as uterine spiral arteries and contribute to the endothelial dysfunction both directly and indirectly through generation of small dense LDL cholesterol; leading to endothelial

dysfunction and hence feto-placental insufficiency and proteinuria respectively. The present study was conducted with the objectives to investigate the alteration in lipid profile among normal and the preeclampsia women.

Material and Methods

Study Design: Case control study.

Study Site: Post Graduate Department of Obstetrics and Gynecology, Government Lal Ded Hospital, Srinagar Kashmir which is a tertiary care maternity hospital in collaboration with Department of Biochemistry; Government Medical College, Srinagar.

Study Duration: *June* 2011-Dec 2012.

Sample Size: The sample size calculated via online sample calculator came out to be 100 in each group. A total of 200 study participants were recruited among which 100 were women with preeclampsia who were taken as cases while 100 women who were normotensive were taken as controls.

Inclusion Criteria: Women with singleton pregnancy, age between 20-37 years, gestational age between 20-42 weeks and who were known cases of pre-eclampsia.

Exclusion Criteria: Women with eclampsia, multiple pregnancies, severe anemia, and history of smoking or any chronic medical illness were excluded.

Consent: An informed written consent was obtained before recruiting any participants for the study and participants were explained about the objectives of the study.

Procedure: A thorough general physical examination was done along with ultrasonography for confirmation of gestation age. Routine laboratory investigation was done viz., CBC, KFT, LFT, HIV, HBSAg, VDRL, Blood pressure, 24 hour urine sample was taken from each patient and evaluated for total volume and protein. Blood pressure was measured by the sphygmomanometer from the right arm while the patient was in semi recumbent position with the arm roughly at the level of heart.

Estimation of serum lipid profile: Peripheral blood sample (5ml) was collected from antecubital vein of every case and control following a fast of 12-14 hours, and collected in vacutainer and sent to the Department of Biochemistry for analysis. The sample were analyzed for serum triglyceride, total cholesterol and HDL-Cholesterol by enzymatic methods with the help of ROCHE diagnostic kit in auto-analyzer-Hitachi 912.Serum LDL-C and VLDL-C were calculated by using friedwauld's formula:

LDL-C = TC – (TG/5+HDL-C) and

VLDL = TG/5

Statistical Analysis: Data was expressed as mean and percentage. Statistical analysis was done using Chi-square, Mann Whitney test, Student T test. Statistical package for social sciences (SPSS-19) and Microsoft Excel software were used for analysis. $P < 0.05$ was considered as significant at 95% CI.

Ethical Issues: The study was conducted as per already established guidelines and protocols and had no ethical issue related to animal or human experimentation.

Results

Table 1: The majority of the subjects in both the study (71%) and control groups (74%) were from rural areas. The Mean±SD of gravidity and parity of the study group was 1.65± 0.968 and 0.69±0.889 respectively and that of control group was 1.62±0.908 and 0.64±0.927 respectively. Among both the group when the percentage of women with different gravidity and parity were compared, non-significant difference between the two was observed. The Mean±SD of BMI among the two groups was 23.30±2.48 and 22.55±2.78 respectively and the association was statistically significant.

Table 2: The Mean±SD of age distribution among the two groups (Cases and Controls) was 27.20±4.13 and 27.07±4.23 respectively. Majority of the women among the both groups were in the age range of 25-29 years.

Table 3: The Mean±SD gestational age of the study groups at the time of study was 35.21±3.04 weeks. The minimum and maximum gestational age ranging from 24-38 weeks.

Table 4: In our study, the Mean±SD systolic [153.28±9.84 mmHg] and the Mean±SD diastolic [100.90±6.73mmHg] blood pressure among the cases was significantly higher than the Mean±SD systolic {125.38±10.25 mmHg] and the Mean±SD diastolic [74.94±6.87 mmHg] among the controls. The difference was statistically significant.

Table 5: The Mean±SD of 24 hours urinary proteins in the study group was 1.94±0.76 g/day while as that in the control group was 0.11±0.07 g/day. The difference between the groups was found to be highly significant.

Table 6: The mean±SD of kidney function test in the study group was significantly higher than the Mean±SD of kidney function test in the control group. The difference was found to be statistically significant.

Table 7: The mean±SD of liver function test in the study group and the Mean±SD of liver function test in the control group didn't differ too much. The difference was found to be statistically insignificant.

Table 8: Itwas found that Mean±SD of triglycerides, total cholesterol, VLDL-cholesterol and LDL cholesterol among the women in the study group was higher than the Mean±SD of triglycerides, total cholesterol, VLDL-cholesterol and LDL cholesterol among women in the control group. Further, Mean±SD of HDL-cholesterol among the study group was higher than the Mean±SD of HDL-Cholesterol among the control group. Statistically, there is a significant difference in case of triglycerides, HDL-cholesterol and VLDL-cholesterol and insignificant difference in case of total cholesterol and LDL cholesterol between the two groups.

Table 9: The Mean±SD of platelet count in the study group was 2.201±0.058 lac/microliter and 2.207±0.056 lac/microliter in case of control group. Further, the Mean±SD of hematocrit in between the group was not much different. The difference in the platelet count and hematocrit in-between the groups was statistically insignificant.

Table 10: Funduscopy examination among the study groups revealed 3% cases of mild edema while in the control group, there was only 1% cases of mild edema. The difference was statistically insignificant.

Table 1: Baseline characteristics of the studied subjects

		Study Group		Control Group		P-Value
		n	%	n	%	
Dwelling	Rural	71	71	74	74	0.635
	Urban	29	29	26	26	
Gravidity	1	61	61	62	62	0.821
	2	20	20	19	19	
	3	14	14	14	14	
	4	3	3	5	5	
	5	2	2	0	0	
	Mean ± SD (min, max)	1.650 ± 0.968 (1, 5)		1.62 ± 0.908 (1, 4)		
Parity	0	61	61	62	62	0.757
	1	20	20	19	19	
	2	14	14	14	14	
	3	3	3	5	5	
	4	2	2	0	0	
	Mean ± SD (min, max)	0.60 ± 0.899 (0, 4)		0.640 ± 0.927 (0, 3)		
Body Mass Index	Normal	56	56	63	63	0.045*
	Obese	19	19	15	15	
	Overweight	25	25	22	22	
	Mean ± SD (min, max)	23.30 ± 2.48 (18.5, 29.5)		22.55 ± 2.78 (18.5, 30.6)		

NB: * denotes significant p-value

Table 2: Age distribution (years) Studied Subjects

Age (Years)	Study Group		Control Group		P-Value
	n	%	n	%	
< 25	31	31	29	29	0.826
25 to 29	40	40	44	44	
> 29	29	29	27	27	
Mean ± SD (min, max)	27.20 ± 4.13 (20, 37)		27.07 ± 4.23 (20, 37)		

Table 3: Gestation Age (weeks) at the time of sampling in Studied Subjects

Gestation Age (Years)	Study Group		Control Group		P-Value
	n	%	n	%	
22 to 27	6	6	5	5	0.717 (NS)
28 to 32	5	5	12	12	
33 to 36	62	62	47	47	
≥ 37	27	27	36	36	
Mean ± SD (min, max)	35.05 ± 3.19 (22, 37)		35.21 ± 3.04 (24, 37)		

Table 4: Systolic and Diastolic Blood Pressure (SBP and DBP) of the Studied Subjects (mm Hg)

Variable	Study Group Mean ± SD (min, max)	Control Group Mean ± SD (min, max)	P-Value
SBP	153.28 ± 9.84 (140, 170)	125.38 ± 10.25 (105, 140)	< 0.001 (Sig)
DBP	100.90 ± 6.73 (90, 110)	35.21 ± 3.04 (24, 37)	< 0.001 (Sig)

NB: SBP=Systolic Blood Pressure, DBP: Diastolic blood pressure

Table 5: 24 Hour Urinary Protein (g/day) in the Studied Subjects {Mean ± SD (min, max)})

24 Hour Urinary Protein Control Group	Study Group	Control Group	P Value
	1.94 ± 0.76	0.11 ± 0.07	< 0.001 (Sig)

Table 6: Kidney Function Test (KFT) of the Studied Subjects

Parameters	Study Group Mean ± SD (min, max)	Control Group Mean ± SD (min, max)	P-Value
Sr. Urea (mg/dl)	23.96 ± 4.77 (15.0, 36.0)	20.50 ± 2.65 (15.0, 28.0)	< 0.001 (HS)
Sr. Creatinine (mg/dl)	0.655 ± 0.136 (0.20, 0.90)	0.613 ± 0.123 (0.30, 0.90)	< 0.023 (S)
Sr. Uric Acid (mg/dl)	6.014 ± 0.063 (4.80, 7.00)	4.014 ± 0.063 (4.80, 7.00)	< 0.001 (HS)

Table 7: Liver Function Test (LFT) of the Studied Subjects

Parameters	Study Group Mean ± SD (min, max)	Control Group Mean ± SD (min, max)	P-Value
Total Protein (g/l)	6.31 ± 0.74 (4.9, 8.0)	6.48 ± 0.62 (5.4, 7.7)	0.081 (NS)
Albumin (g/l)	3.31 ± 0.16 (3.0, 3.6)	3.34 ± 0.20 (3.3, 3.8)	0.155 (NS)
AST (IU/l)	26.04 ± 7.87 (10, 40)	26.78 ± 8.6 (10, 40)	0.528 (NS)
ALT (IU/l)	26.87 ± 8.32 (10, 40)	25.75 ± 8.11 (10, 40)	0.336 (NS)

Table 8: Serum Lipid Levels in Study Group and Control Group

Parameters	Study Group Mean ± SD (min, max)	Control Group Mean ± SD (min, max)	P-Value
Triglyceride (mg/dl)	265.70 ± 35.9 (190, 390)	212.90 ± 25.20 (118, 280)	< 0.01
Total Cholesterol (mg/dl)	219.06 ± 35.05 (184, 303)	214.51 ± 28.81 (174, 294)	> 0.05
HDL- Cholesterol (mg/dl)	42.82 ± 8.70 (27, 70)	60.44 ± 7.85 (41, 80)	< 0.01
VLDL-Cholesterol (mg/dl)	56.65 ± 7.20 (38, 78)	41.17 ± 5.06 (31, 56)	< 0.01
LDL-Cholesterol (mg/dl)	124.40 ± 14.0 (111, 184)	120.8 ± 16.4 (100, 165)	> 0.05

Table 9: Hematological Parameters in the Studied Subjects

Parameters	Study Group Mean ± SD	Control Group Mean ± SD	P-Value
Platelet Count (lac/microliter)	2.201 ± 0.058	2.207 ± 0.056	0.940 (NS)
Hematocrit (%)	35.15 ± 5.85	36.63 ± 5.62	0.071 (NS)

Table 10: Funduscopy of the Studied Subjects

Funduscopy	Study Group		Control Group		P-Value
	n	%	n	%	
Normal Funduscopy	97	97	99	99	0.311
Mild Edema	3	3	1	1	

Discussion

At recent times there is a great interest about the role of lipid metabolism on the development of preeclampsia (PE). Previous studies have reported that plasma lipid levels were higher in preeclampsia women than the health pregnant women[8-9]. It is thought that the lipid changes might have a role at endothelial cell damage which is characteristic of PE. Lipid per-oxidation occur at low levels in all cells and tissues. In health, oxidation by free radicals and neutralization by antioxidants remains in balance [10]. In PE 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 PE[11]. 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 hypertension[10-13].

Based on these observations the present study was conducted to compare serum lipid in preeclampsia and normal pregnancy. It was seen that in the preeclampsia group Mean ± SD serum triglyceride level was 265.70±35.9. Whereas in the control group the Mean ± SD of serum triglyceride level was 212.90±25.20; the difference is statistically significant. Jayante De et al (2006)[14] also observed a significant increase in triglyceride levels in preeclampsia women compared to normotensive women.

Ray JG Diamond (2006) also in their study concluded that there exists a positive association between elevated maternal levels and risk of preeclampsia[7]. Non significant increase in total cholesterol (219.00±35.05 mg/dl) compared to control group (214.5±28.81) was seen. The findings are similar to the results observed by Mustafa Baki Cekman (2003), who found an increased total cholesterol levels in preeclampsia patients but the increase didn't reach the significant levels [15].

In present study a significant decrease in the HDL-C; was observed in the study group Mean ± SD (42.82±8.70) compared to the control group (60.44±7.85) with the observations are consistent with Jayanti D et al (2006)(14) and Ekambara Padmini (2011) (16).We observed a significant increase in the VLDL-C levels in the preeclampsia patients with PL 0.01 when compared to normotensive pregnant women. The mean ± SD levels of VLDL-Cholesterol in the study group was (56.65±7.20) and in the control group was (41.17±5.06) with PL 0.01.The results are comparable with Jayante D et al (2006)[(14)], Lakshmiprabha et al (2011)[(17)] who also observed the similar results in their study .Increases LDL-C levels were also seen in the preeclampsia group when compared with the normotensive pregnant women but the difference is statistically insignificant.

Conclusion

The present study clearly shows that there exists a consistent association between serum lipid profile levels and preeclampsia. Increased triglyceride levels along with decrease in HDL-Cholesterol levels and delayed triglyceride clearance and high blood pressure are associated with the development of preeclampsia.

This association may be significant in understanding the pathologic process of preeclampsia and may help in developing strategies for prevention and early diagnosis of preeclampsia. Dyslipidemia being a modifiable risk factor, pre-pregnancy weight reduction and dietary modification can lead to decrease in the incidence of preeclampsia and its complications.

Conflict of Interest: None Declared

Source of Funding: None

Acknowledgement: Authors would like to acknowledge gratitude to Prof. (Dr.) Sabiha Majid, Head, Department of Biochemistry for her support and guidance. Authors would like to thank Prof. (Dr.) Shehnaz Teing for her support and guidance.

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