



## MID-TRIMESTER SERUM LIPID PROFILE AS A PREDICTOR OF PREECLAMPSIA

**DR. MOHINI PAUL**

M.D Senior Specialist, and Unit Head Obstetrics and Gynaecology Department of Obstetrics and Gynaecology Kasturba Hospital, Delhi, India

**Dr. RANJANA MILIND**

3<sup>rd</sup> Year MS(Obstetrics and Gynaecology) PG Department of Obstetrics and Gynaecology Kasturba Hospital, Delhi, India

### ABSTRACT

**Objective:** To estimate serum lipid profile in early second trimester and evaluate these as a predictor of preeclampsia.

**Material and Methods:** Serum lipid profile was measured by fully automatic biochemistry autoanalyser in 276 antenatal pregnant women between 14-20 weeks of gestation. Of this 63 developed preeclampsia were taken as study group while 213 who remained normotensive control group. Lipid levels in two groups were compared. The data was analysed statistically and dyslipidemia as a predictor of preeclampsia was studied.

**Results:** The mean serum level of total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C) was significantly higher in preeclampsia group as compared to control group while high density lipoprotein (HDL-C) was significant low in study group as compared to control group. There was elevation of the ratios of TC: HDL cholesterol, LDL: HDL cholesterol and TG: HDL cholesterol while diminution of ratio of HDL: VLDL cholesterol in the study group as compared to normotensive group.

**Conclusion:** Measurement of all these parameters in early second trimester can help in predicting preeclampsia.

**KEYWORDS :** Dyslipidemia, Lipid profile, preeclampsia

### Introduction

Preeclampsia occurs in 2-8% of all pregnancies and it is the most common medical complication of pregnancy with multisystem disorder, making one of the deadly triad (with haemorrhage and infection) that contribute greatly to maternal morbidity and mortality accounting for about 50,000 maternal deaths worldwide annually<sup>1,2</sup>. Preeclampsia is diagnosed as hypertension of 140/90 mmHg or greater for the first time after 20 week on at least two occasions at least 6 hours apart **and a)** proteinuria- >300mg/24h, or Prote in: Creatinine ratio >0.3 or Dipstick 1+ persistent. **or b)** platelets <100,000/ $\mu$ L, Creatinine >1.1 mg/dl or doubling of baseline, Serum transaminase level twice normal, headache, visual disturbance, convulsion or pulmonary edema.

Various risk factors known to be associated with the development of preeclampsia include sociodemographic factors (extremes of reproductive age, socio economic status, ethnic group), genetic factors, pregnancy factors (multiple pregnancies, primigravida, previous pre-eclampsia) or medical history (obesity, chronic renal disease, chronic hypertension, diabetic mellitus and thrombophilia<sup>3,4</sup>). Identification of women at risk by suitable predictive tests will enable timely intervention, thereby decreasing maternal and fetal morbidity and mortality. Most current hypotheses regarding pathophysiological mechanism in preeclampsia point to endothelial cell dysfunction<sup>5,6</sup>, faulty placentation, impaired placental perfusion and early placental abnormalities<sup>7,9</sup>. Various biochemical and biophysical screening markers to predict the occurrence of preeclampsia have been tested.

Correlation between serum lipid levels and pre-eclampsia has been suggested by Van den Elzen et al.<sup>10</sup> and Sattar et al.<sup>11</sup>. An abnormal lipid profile is strongly associated with atherosclerotic cardiovascular disease and has a direct effect on endothelial dysfunction<sup>8</sup>. The most important feature of pre-eclampsia is due to a vasospastic phenomenon in kidneys, uterus, placenta, and brain. Altered lipid synthesis leading to a decrease in PGI<sub>2</sub>:TXA<sub>2</sub> ratio is also suggested to be an important pathway of pathogenesis in pre-eclampsia<sup>12</sup>. Elevated plasma lipid and lipoprotein has been seen to be associated with endothelial alterations by increasing oxidative stress<sup>10,11</sup>. Markers of oxidative stress like serum triglyceride, free fatty acid, and malondialdehyde are increased in preeclampsia<sup>13</sup>. Small dense LDL, triglycerides rich lipoproteins might also activate endothelial Dysfunction<sup>14</sup> and atherosclerosis<sup>15</sup>.

If alterations in circulating lipids are of pathognomonic importance in the development of pre-eclampsia, then changes in lipid parameters should be demonstrable much before the clinical onset of disease. The measurement of lipid profile in early pregnancy may offer a reliable predictive test to detect women at risk of developing preeclampsia later in pregnancy.

### Materials and Methods

This is a Prospective case control study. Conducted in the department of Obstetrics and gynaecology, Kasturba Hospital Delhi for a period of 1 year. After the approval of institutional ethics committee randomly 300 antenatal OPD patients at 14-20 weeks ranging in age from 18-35 yrs were randomly selected for the study.

Singleton pregnancy who were sure of dates with known last menstrual period or with first trimester ultra-sonogram were included in study after informed consent and pregnant women with past history of cardiac, renal disease or hepatic dysfunction, chronic hypertension, chronic diabetes mellitus, thyroid disorder, obesity were excluded.

5ml Venous blood was collected after 12hrs fasting at the first antenatal visit (14-20wk) and estimation of serum lipid level i.e. serum triglyceride, total cholesterol, very low-density lipoprotein, low density lipoprotein and high density lipoprotein was done by fully automatic biochemistry autoanalyser. Serum LDL was calculated by Frederickson-friedwalds formula when triglyceride level <5, according to which  $LDL = Total\ cholesterol - (HDL\ cholesterol + VLDL\ cholesterol)$ . VLDL was calculated as 1/5 of triglyceride.

Out of 300 patients taken, 15 had spontaneous abortion and 9 of them had missed abortion before 20 weeks of gestation and hence only 276 could be followed up. A detailed medical, menstrual and obstetrical history was taken followed by general, systemic and obstetrical examination along with routine investigation and followed in ANC O.P.D till delivery. 63 patients developed preeclampsia and were labelled as study group and 213 of them who were normotensive as control group.

### Statistical Evaluation:

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version

21.0. Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD. Quantitative variables were compared using independent t-test between the two groups. Qualitative variables were correlated using Chi-Square test /Fisher's exact test. A p value of <0.05 was considered statistically significant.

**Results and Discussion**

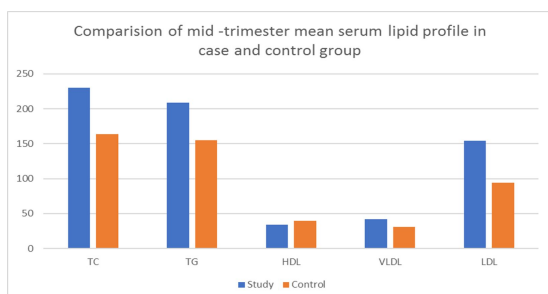
**Baseline demographic characteristics**

Among the study group 69.84% developed mild and 30.15% developed severe preeclampsia. 41.27% of study group and 54.46% women of control group were ≤25 years of age, 57.14% of study group and 40.85% of control group were between 26-30 years of age, 1.59% of study group and 4.69% of control group were >30 years of age. Majority in study group belonged to lower middle class, which included 42.86% of study and 39.91% of control group. 69.84% of study group and 70.89% of control group were Muslim. Whereas 26.98% of study group and 28.17% of control group were Hindu. 76.53% of control group and 80.95% of study group were nonvegetarian. Whereas only 23.47% of control group and 19.05% of study group were vegetarian. These baseline demographic characteristics of the two group were similar.

**Table 1: Mid-Trimester maternal serum lipid profile in study-control group and odds ratio (OR) with 95% confidence intervals (CI) with preeclampsia risk.**

Lipid profile	Study group	Control group	p value	Unadjusted OR (95% CI)	P value
Total cholesterol	230.38 ± 23.79	164 ± 21.65	<0.0001	1.15 (1.10-1.19)	<0.0001
Total Triglyceride	209.08 ± 42.42	154.91 ± 25.66	<0.0001	1.04 (1.03-1.05)	<0.0001
High density lipoprotein	34.19 ± 11.53	39.17 ± 9.29	<0.0001	0.94 (0.91-0.97)	0.0007
Verylowdensity lipoprotein	41.82 ± 8.48	30.98 ± 5.13	<0.0001	1.25 (1.18-1.32)	<0.0001
Low density lipoprotein	154.38 ± 21.29	93.85 ± 23.22	<0.0001	1.15 (1.10-1.20)	<0.0001

Serum lipid levels (TC, TG, VLDL-C, LDL-C) were significantly (p<0.0001) higher in the study group compared to the control group while levels of HDL-C were significantly low in the preeclamptic group compared to normotensive group (p<0.0001). Mean serum levels of TC, TG, VLDL-C, LDL-C was 28.8%, 25.9%, 25.92%, 39.2% at midtrimester respectively higher in patients who later developed hypertensive disorder of pregnancy as compared to normotensive pregnant women. While HDL-C was 12.7% lower in preeclamptic group as compared to normotensive group.



**Table 2 Comparison between mean serum lipid profile in present study to other study at midtrimester**

Mid-trimester mean serum low density lipoprotein mg/dl	Sing U et al (2013) <sup>19</sup>	Mallick MP et al.(2014) <sup>17</sup>	Present study
Control	94.99±25.42	116.55±23.07	93.85±23.22
Case	147.64±20.29	131±30.77	158.38±21.29
P value	<0.001	0.0208	<0.0001

**Table 2b**

Midtrimester mean serum high density lipoprotein mg/dl	Sing U et al (2013) <sup>19</sup>	Dipti A Modi et al. (2015) <sup>18</sup>	Ghodke babita et al.(2017) <sup>21</sup>	Present study
Case	31.33±11.81	47.89±11.46	51.80 ±5.84	34.19±11.53
Control	39.26±21.20	49.33±9.612	-	39.17±9.29
P value	0.007	0.701	0.04	<0.0001

**Table 2c**

Mid-trimester mean serum total cholesterol mg/dl	Madhusen Dey et al. (2013) <sup>16</sup>	Mallick MP et al.(2014) <sup>17</sup>	Dipti A Modi et al. (2015) <sup>18</sup>	Ghodke babita et al.(2017) <sup>21</sup>	Present study
Case	229.63±30.71	223.55±46.75	225.23±41.471	210.75±24.25	230.38±23.79
Control	191.63±35.9	204.10±25.56	183.22±35.912	-	164±21.65
P value	0.0001	0.0154	0.0000	0.38	<0.0001

**Table 2d**

Mid-trimester mean serum very low density lipoprotein mg/dl	Sing U et al (2013) <sup>19</sup>	Yadav Kiran et al. (2014) <sup>20</sup>	Present study
Control	31.78±8.24	27.86±9.14	30.98±5.13
Case	42.50±11.93	34.42±10.03	41.82±8.48
P value	<0.001	0.004	0.0001

**Table 2e**

Mid-trimester mean Serum triglyceride mg/dl	Sing U et al (2013)	Yadav Kiran et al. (2014)	Dipti A Modi et al. (2015)	Ghodke babita et al. (2017) <sup>21</sup>	Present study
Case	207.76 ± 47.31	167.24±50.68	128.04±40.082	204 ±18.90	209.08±42.42
Control	155.22 ± 22.31	139.56±46.89	106.65±29.86	-	154±25.66
P value	<0.001	0.017	0.005	0.00	<0.0001

**TABLE 3: MID-TRIMESTER MEAN SERUM LIPID PROFILE RATIOS IN STUDY AND CONTROL GROUP:**

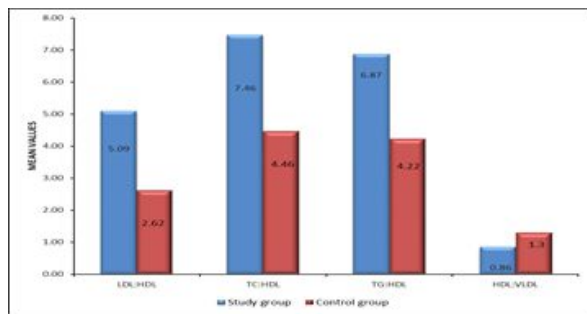
The ratio of LDL: HDL ,TC: HDL ,TG: HDL in the group of patients with hypertensive disorder of pregnancy had raised in mid-trimester mean serum to the level of 48.5%, 40.21% ,38.57% respectively as compared to normotensive group. While mean midtrimester serum HDL: VLDL ratio was 33.8% lower compared to normotensive.

Mid-Trimester mean serum lipid ratios	Study group	Control group	P value
<b>LDL: HDL</b>			<0.0001
Sample size	63	213	
Mean±SD	5.09±2.03	2.62±1.17	
Median	4.59	2.36	
Min-Max	1.41-10.87	0.75-6.93	
Inter quartile Range	3.879 - 6.089	1.850 - 3.238	
<b>TC: HDL</b>			<0.0001
Sample size	63	213	
Mean±SD	7.46±2.61	4.46±1.39	
Median	6.94	4.13	
Min-Max	2.9-15.33	2.31-9.6	
Inter quartile Range	5.931 - 8.516	3.512 - 5.139	
<b>TG: HDL</b>			<0.0001
Sample size	63	213	
Mean±SD	6.87±3.09	4.22±1.39	
Median	6.15	4.05	

Min-Max	2.35-17.33	2-9.72	
Inter quartile Range	5.132 - 7.899	3.173 - 4.951	
<b>HDL: VLDL</b>			<0.0001
Sample size	63	213	
Mean±SD	0.86±0.36	1.3±0.38	
Median	0.81	1.24	
Min-Max	0.29-2.12	0.51-2.5	
Inter quartile Range	0.633 - 0.974	1.010 - 1.576	

**Table 4. Comparison between ratios of serum lipid profile in present study with other study at midtrimester**

Mid Trimster Mean Serum Lipid ratios		Jayanta De et al. (2006)	Amandeep Singh et al. (2013)	Present study
LDL: HDL	Case	2.89±0.50	2.66± 0.07	5.09±2.03
	Control	1.72± 0.62	1.86±0.09	2.62±1.17
	P Value	>0.05	0.001	<0.0001
TC: HDL	Case	5.19±0.56	5.12±0.09	7.46±2.61
	Control	3.64± 0.35.	3.74±0.11	4.46± 139
	P Value	<0.001	0.001	<0.0001
TG: HDL	Case	6.09±1.01	7.24±0.22	6.87± 3.09
	Control	3.60±0.51	4.35±0.19	4.22±1.39
	P Value	<0.005	0.001	<0.0001
HDL: VLDL	Case	0.84±0.12	0.87±0.02	0.86±0.36
	Control	1.42±0.22	1.36± 0.06	1.3±0.38
	P Value	<0.01	0.001	<0.0001



**CONCLUSION**

From the present study, it can be concluded that elevated maternal serum lipid levels (i.e. total cholesterol, triglyceride, low density lipoprotein and very low density lipoprotein) at mid-trimester (14-20 week) is significantly associated with the risk of development of hypertensive disorder later in pregnancy. Also, the degree of elevation of maternal serum lipid level is directly proportional to the severity of the hypertensive disorder and rise in rate of fetomaternal morbidity and mortality. Thus, it may be concluded that the estimation of lipid profile in early second trimester will bring about early recognition of patients at risk of hypertensive disorder of pregnancy before the clinical syndrome and complications appear, thereby enabling timely intervention to reduce the risk of preeclampsia and fetomaternal morbidity and mortality.

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