

# Study of Serum Lipid Profile in Pregnancy and its Association with Pre-Eclampsia

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**Abstract:** ***Objective:** To study serum lipid profile in third trimester (28 – 36 weeks) and its relation with pre-eclamptic and normotensive. **Material and Methods:** We carried out a case control study in the department of Obstetrics and Gynaecology at Umaid Hospital, Dr SN Medical College, Jodhpur from March 2022 to December 2022. Total 230 patients were enrolled in study fulfilling inclusion and exclusion criteria between 28-36 weeks of gestation. Serum lipid profile was done in all patients and they were followed till delivery for presence and absence of preeclampsia. **Result:** In our study 20.87% of subjects developed pre eclampsia and 79.13% remained normotensive till delivery. Mean total cholesterol value was higher (302.83 mg/dl) in pre eclampsia group than normotensive group (214.6mg/dl). In pre eclampsia group values of Mean Triglycerides(263.97 mg/dl), LDL(194.56 mg/dl) and VLDL(44.56 mg/dl) were raised than Mean Triglycerides(195.26mg/dl), LDL(122.17 mg/dl) and VLDL(31.82 mg/dl) values of normotensive group. Mean HDL level in both pre eclamptic group (60.6 mg/dl) and normotensive group (59.24mg/dl) was almost similar. **Conclusion:** Pre eclampsia is multisystem, heterogeneous disorder with variable phenotype and enigmatic pathogenesis. Gradual unveiling of pathogenesis by gamut of theories have lead to pulchritude of biomarkers but still unrealistic for developing countries. So, avaricious search for single, feasible, cost effective biomarker is still on. Lipid analysis in early pregnancy may help in prediction of pre eclampsia before it goes berserk. It may serve as simple, cost effective method for prediction of pre eclampsia in developing countries. Lipid profile has evolved as a new kid on the block.*

**Keywords:** Pre-eclampsia, HDOP, lipid profile, pregnant women, cholesterol, triglyceride, primigravida.

## 1. Introduction

Preeclampsia is a multisystem heterogeneous disorder and a leading cause of maternal mortality and morbidity. According to WHO hypertensive disorders complicate 5 to 10% of all pregnancies<sup>1</sup> and preeclampsia is directly responsible for 10% of direct maternal mortality in Asia and also leads to significant neonatal morbidity and mortality. In India, the incidence of preeclampsia is reported to be 8-10% among the pregnant women<sup>2</sup>, 18.35% of maternal morbidity and 0.96% of maternal mortality are attributed to HDOP.

Pre-eclampsia is a pregnancy-specific condition with a multifactorial aetiology characterized by hypertension (systolic blood pressure  $\geq 140$ mmHg or diastolic blood pressure  $\geq 90$ mmHg on 2 occasions at least 4 hrs. apart after 20 weeks gestation in women with a previously normal blood pressure or  $\geq 160$ mmHg systolic or  $\geq 110$ mmHg diastolic) and proteinuria  $\geq 300$ mg/ 24hrs or a Protein/creatinine ratio  $\geq 0.3$ mg/dl or a dipstick reading of  $\geq 1+$ .<sup>3</sup>

The pathogenesis of pre eclampsia has always remained enigmatic, although various theories have been proposed like theory of abnormal trophoblastic invasion and placental ischemia, angiogenic and antiangiogenic proteins, maternal maladaptations to vascular and inflammatory changes, uncontrolled inflammatory changes appear to be the major cause during normal pregnancy.<sup>4</sup>

A two-step model has been described for pathophysiology of pre eclampsia.<sup>5</sup> The first pertaining to abnormal placentation leading to placental ischemia causing secretion of soluble factors that induce endothelial dysfunctioning and maternal pre eclampsia<sup>6</sup> in pregnant women. The second one is related to increase in free radicals and reactive oxygen species causing cell damage<sup>7</sup> and increase vascular tonicity causing pre eclampsia<sup>8</sup>. It implies that abnormal lipid profile has direct effect on endothelial dysfunction leading to decrease in PGI-TxA2 Ratio and subsequent fibrinoid necrosis at uteroplacental implantation site.<sup>9</sup>

Natural rising of plasma lipids is being seen in normal pregnancy, but this event is not atherogenic and it is believed that this process is under hormonal control i.e. elevated levels of estrogen and progesterone. But in complicated pregnancy, (previous history of pre-eclampsia, primiparity, multifetal pregnancy, H.mole, triploidy), there is a possible defect in mechanism of adjusting physiologic hyperlipidemia<sup>24</sup>. There are evidences that abnormal lipid profile in pregnancy could be one of the factors for subsequent development of pre eclampsia, hence serum lipid parameters can be used as a useful predictive tool for it and would be helpful in lowering the mortalities and morbidities associated, by early detection of pre eclampsia, prompt measures can be taken for better management and ultimately lowering down the burden of associated morbidities and mortalities, perinatal outcomes around the world. Therefore, our study was conducted to study the relation between

abnormal lipid profile and pre-eclampsia in order to aid in early prediction of the spectrum and timely management.

## 2. Material and Methods

Case control study was conducted in department of Obstetrics and Gynaecology, Umaid Hospital, Dr SN Medical College, Jodhpur from March 2022 to December 2022. Patients were explained about nature and purpose of study. After obtaining their written informed consent they were enrolled in the present study. The participants women were all primigravida, singleton pregnancy with age between 20-35 years and gestational age between 28-36 weeks. All epidemiological data including name, age, address, occupation, socioeconomic status, were recorded on predesigned proforma and women were subjected to detailed history which includes menstrual history and duration of pregnancy based on last menstrual period (LMP) to know the exact period of gestation (gestational age), dietary history, drug history, past history, history of hypertension, diabetes, asthma, thyroid disorder, cardiac disease, autoimmune disorder.

They were subjected to routine blood investigations including lipid profile and urine investigations (CBC, RFT, LFT, RBS, HIV, HBsAg, VDRL).USG for pregnancy details. General physical Examination, per abdominal examination and all clinical findings were recorded on predesigned proforma. All women were followed up as ANC protocols till delivery. Those who subsequently developed pre eclampsia were considered as case and others who remained normotensive considered as control.

A total of 230 patients were included in the study after sample size calculation at 95% confidence level.12 hours Fasting 5ml venous blood samples (at 8 am) was taken from antecubital vein under strict aseptic condition and stored at 4degree Celsius until serum lipid profile estimation started. In all the subjects, concentrations of serum triglycerides, total cholesterol and HDL were estimated using enzymatic methods using full auto analyser machine- (transasia XL 1000 fully automated analyzer).The low density lipoprotein was calculated using Friederickson- Friedwald's formula: LDL cholesterol (mmol/L) = TC - (TG/2.2 +HDL). Reference values for Serum levels of TG, TC, LDL, HDL, and VLDL were taken according to recommendation of NCEP.

### Lipid Profile

	Desirable	Borderline	High Risk
Cholesterol	<200 mg/dl	200- 239 mg/dl	240 mg/dl
Triglycerides	<150 mg/dl	150- 199 mg/dl	200-499 mg/dl
HDL Cholesterol	60 mg/dl	35- 45 mg/dl	<35 mg/dl
LDL Cholesterol	60-130 mg/dl	130-159 mg/dl	160-189 mg/dl
Cholesterol/ HDL ratio	4.0	5.0	6.0

## 3. Results and Discussion

The present study was conducted to evaluate serum lipid profile between 28-36 weeks of gestation and to look for its

correlation with preeclampsia. Total 230 patients were recruited in our study, out of which 48 subjects became preeclamptic, categorized as case and 182 subjects remained normotensive categorized as control. In our study 20.87% of subjects developed pre eclampsia and 79.13% remained normotensive till delivery, designated as case and control group respectively. (Table 1)

**Table 1:** Categorization of Patients

Category	Case	Control	Total
No. of patients	48	182	230
Percentage	20.87	79.13	100

The prevalence of pre eclampsia in our study was 20.87% which was higher than the global prevalence of 8-10%. The variation in prevalence might be because it is a tertiary level health facility, there are more number of referred patients received, there's early detection and better data reporting of pre-eclampsia.

**Table 2a:** Comparison according to Mode of Delivery

Mode of Delivery	Case		Control		Total	
	N	%	N	%	N	%
ND	23	47.92	138	75.82	161	70.00
LSCS	25	52.08	44	24.18	69	30.00
Total	48	100.00	182	100.00	230	100.00

Chi square 14.08, P value <0.0001 (S)

**Table 2b:** Comparison according to Maturity at the Time of Delivery

Maturity	Case		Control		Total	
	N	%	N	%	N	%
Preterm	22	45.83	14	7.69	36	15.65
Term	26	54.17	168	92.31	194	84.35
Total	48	100.00	182	100.00	230	100.00

Chi square 41.85, P value <0.0001 (S)

**Table 2c:** Comparison according to Maternal Complication

Maternal Complication	Case		Control		Total	
	N	%	N	%	N	%
Eclampsia	4	8.33	0	0.00	4	1.74
APH(Abruption)	5	10.42	3	1.65	8	3.48
No complications	39	81.25	179	98.35	218	94.78
Total	48	100.00	182	100.00	230	100.00

Chi square 24.73, P value <0.0001 (S)

**Table 2d:** Comparison according to Baby Status

Baby Status	Case		Control		Total	
	N	%	N	%	N	%
BW	35	72.92	176	96.70	211	91.74
NICU	13	27.08	6	3.30	19	8.26
Total	48	100.00	182	100.00	230	100.00

Chi square 28.35, P value <0.0001 (S)

Among cases 52.08% underwent LSCS and 47.92% were delivered vaginally.(Table no.2a) Among cases 45.83% were preterm deliveries and 54.17% were full term deliveries.(table no.2b) 94.78% patients were had no complications, 3.48% had AP (abruption placentae) and 1.74% had eclampsia. Among cases 81.25% patients had no complications, 10.42% had AP and eclampsia in 8.33%. (table no.2c) Among cases, 72.92% babies were healthy and shifted to mother side while 27.08% babies had NICU admission for various reasons. (Table no.2d)

The mean total cholesterol value among preeclamptic group was 302.83 mg/dl and among controls mean value was 214.26mg/dl. (table no. 3) This is similar with the findings of Leela et al<sup>13</sup>, Archana S et al<sup>14</sup>, Surbhi et al<sup>15</sup>. Hypercholesterolemia leads to excessive lipid peroxidation resulting in an imbalance between peroxidates and antioxidants, which in turn causes oxidative stress. Oxidative stress may contribute to atherogenicity in pre-eclampsia.

**Table 3:** Comparison according to Total Cholesterol Level

Group	Total cholesterol(mg/dl)			p value
	Mean	SD	SEM	
Case	302.83	63.1	9.108	<0.0001
Control	214.26	47.01	3.485	

The mean total triglyceride value of cases was 263.97 mg/dl and in controls it was 195.26mg/dl. (table no.4) The mean serum triglyceride was almost 1.4 times in those with severe preeclampsia, compared with normal pregnant control. Hypertriglyceridemia may be associated with hypercoagulability and contributes to the endothelial dysfunction. This is also in keeping with findings from previous studies as done by Rajesh A et al<sup>16</sup>, Padma Leela et al<sup>13</sup>, Singh U et al<sup>17</sup>, Hubel et al, Saha et al<sup>18</sup>.

**Table 4:** Comparison according to Triglyceride Level

Group	Triglyceride			p value
	Mean	SD	SEM	
Case	263.97	109.2	15.76	<0.0001
Control	195.26	75.89	5.626	

The mean total HDL value of case group was 60.6 mg/dl and control group had mean value of 59.24mg/dl. (Table no.5) - HDL level was not statistically significant in patients with pre-eclampsia as compared to normal healthy pregnant women. This observation is similar with studies done by Sattar N et al<sup>19</sup>, Tesfa E et al<sup>20</sup> and Rajesh A et al<sup>21</sup>, Belo et al<sup>22</sup>. While Kaloti AS et al<sup>23</sup>, and Latha DP and Ganesan D suggested significant association between HDL and pre-eclampsia. HDL cholesterol facilitates reverse cholesterol transport by carrying excess, potentially harmful cholesterol from peripheral tissue to liver. The Low level of HDL in

preeclampsia because of hypo-oestrogenemia & insulin resistance causes excess harmful cholesterol involve in pathogenesis of preeclampsia.

**Table 5:** Comparison according to HDL Level

Group	HDL			p value
	Mean	SD	SEM	
Case	60.6	9.48	1.369	0.440
Control	59.24	11.19	0.829	

The mean total LDL value of case group was 194.56 mg/dl and control group had mean value of 122.17mg/dl. (Table no.6) -High LDL-C levels were observed in women with pre-eclampsia. This observation was similar with findings from previous studies such as Tesfa E et al<sup>20</sup>, Rajesh A et al<sup>21</sup>, Hubel CA et al. Serum LDL level was increased in hypertensive pregnant women and this may be because of significant increase in the levels of beta-lipoproteins in hypertensive women in the third trimester of pregnancy. The mean total VLDL value of case group was 44.56 mg/dl and control group had mean value of 31.82mg/dl. (Table no.7) ,the serum VLDL-C was significantly higher in the pre-eclamptic group which is in keeping with the study of Surbhi et al<sup>15</sup> and Kaloti at al<sup>23</sup>. The elevated level of VLDL-C is perhaps due to hypertriglyceridemia leading to enhanced entry of VLDL-C that carries endogenous triglyceride into circulation and due to increased VLDL, synthesis causes VLDL accumulation in vascular endothelium damaging uterine and renal vessels.

**Table 6:** Comparison according to serum LDL levels

Group	LDL			p value
	Mean	SD	SEM	
Case	194.56	55.53	8.016	<0.0001
Control	122.17	34.75	2.576	

**Table 7:** Comparison according to Serum VLDL Levels

Group	VLDL			p value
	Mean	SD	SEM	
Case	44.56	13.79	1.991	<0.0001
Control	31.82	8.98	0.665	

**Table 8:** Association of Lipid Profile with Case and Control

Lipid Profile	Case		Control		Odds Ratio	Confidence Interval (95%)	p value	
	N	%	N	%				
TC	Deranged	46	95.83	104	57.14	17.25	4.062-73.25	<0.0001
	Normal	2	4.16	78	42.86			
TG	Deranged	43	89.58	123	67.58	4.125	1.553-10.95	0.002
	Normal	5	10.42	59	32.42			
HDL	Deranged	30	62.50	105	57.69	1.222	0.635 -2.351	0.273
	Normal	18	37.50	77	42.31			
LDL	Deranged	44	91.67	61	33.52	21.82	7.491-63.55	<0.0001
	Normal	4	8.33	121	66.48			
VLDL	Deranged	41	85.42	90	49.45	5.987	2.552-14.04	<0.0001
	Normal	7	14.58	92	50.55			

**Table no. 8-** shows the positive association of deranged lipid parameters with pre eclampsia. TC was elevated in 95.83% among cases and in 57.14% among controls (OR= 17.25), TG was raised in 89.58% among cases and in 67.58% among control (OR= 4.125), HDL was lower in 62.50% among case and in 57.69% among control (OR=

1.22), LDL was deranged in 91.67% among cases while in only 33.52% among control (OR=21.82), VLDL was higher in 85.42% among cases and in 49.45% among control (OR= 5.987). Similar to the study done by Nidhi et al<sup>3</sup>, odds ratio in our study was also more than 1, which signifies the positive statistical relation. Results of our is similar to

studies done by Islam N et al<sup>25</sup>, UshaAdiga et al<sup>26</sup>, Tesfa et al<sup>20</sup>, Spracklen CN et al<sup>27</sup>, that total cholesterol, triglyceride, non-HDL-C, and HDL-C levels measured during pregnancy were significantly related to the risk of preeclampsia.

**Surbhi et al<sup>15</sup>** in prospective observational study aimed to determine association of abnormal lipid profile in 260 subjects in early second trimester (14 to 20 weeks) with development of pre-eclampsia. The overall incidence of preeclampsia in the study was 11.15% (N=29). Lipid profile was found to be normal (group X) in 50 patients (23.8%) and abnormal (group Y) in 210 patients (80.7%). The incidence of preeclampsia in study group 13.33% (28/210) and control group was 2% (1/50). They found that the mean serum total cholesterol was significantly higher in pre-eclampsia group (199.74 mg/dl vs. 171.7 mg/dl;  $p < 0.05$ ). The difference in mean triglyceride, HDL, VLDL and LDL levels between two groups was not significant. Total cholesterol has 44.83% sensitivity, 84.85% specificity, 27.08% PPV, 92.45% NPV with diagnostic accuracy of 80.38% in predicting pre-eclampsia (with 0.65% AUC with 95% confidence interval). While VLDL has maximum sensitivity of 68.97% while HDL has maximum specificity of 86.15% in predicting pre-eclampsia.

**Tesfa E et al<sup>20</sup>** conducted a systematic review and meta-analysis study to generate summarized evidence between maternal serum lipid profiles and risks of pre-eclampsia in African pregnant women. A total of 15 observational studies were included. The mean values of triglyceride (TG), total cholesterol (TC), low density lipoprotein-cholesterol (LDL-c) and very low density lipoprotein-cholesterol (VLDL-c) were significantly higher in pre-eclamptic women as compared with normotensive pregnant women. The serum high density lipoprotein cholesterol (HDL-c) level was lower, but it is not statistically significant (HDL-c =  $51.02 \pm 16.01$  and  $61.80 \pm 25.63$ ) in pre-eclamptic women as compared with controls. The pooled standardized mean difference (SMD) of TG, TC, LDL-C and VLDL-C were significantly increased in preeclamptic women as compared with normotensive pregnant women. They concluded that the maternal serum levels of TG, TC, LDL-c and VLDL-c were significantly associated with the risk of preeclampsia. However, HDL-cholesterol was not significantly associated but it was lower in pre-eclamptic women. Further, it was recommended that lipid profiles should be included as a routine diagnostic test for pre-eclamptic women.

**Rajesh A et al<sup>21</sup>** aimed to study the relationship between serum lipid and risk of PIH. They found that out of these total 90 numbers, 12 subjects developed PIH (study group), while 69 subjects remained normotensive (control group). The mean serum total cholesterol (TC) level was 233.25 mg/dL with  $p$  value  $< 0.001$ , triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) was significantly higher in PIH women. PIH women showed no significant change in high-density lipoprotein cholesterol (HDL-C) level and very low-density lipoprotein cholesterol (VLDL-C) to normal pregnant women.

**Nidhi et al<sup>3</sup>** conducted a longitudinal, Descriptive type of observational study to analysis the study serum lipid profile between 13-20 week of pregnancy in 125 subjects and to

find out correlation, if any, between serum lipids profile and fetomaternal outcome. They found that the mean level of TC in participants developed preeclampsia was  $224.36 \pm 43.68$  mg/dl. This was significantly higher as compared to normotensive group  $180.77 \pm 36.58$  mg/dl. They concluded that early prediction of preeclampsia can be used as a tool for primary prevention before the development

**Yadav S et al<sup>29</sup>** conducted a prospective case-control comparative study to analyse the lipid profile in normotensive pregnant patients and in pregnancy induced hypertension patients, and to investigate the alteration in lipid profile in both groups. The study takes into account 100 normotensive pregnant women (control group) and 100 pre-eclamptic women (study group) in their third trimester of pregnancy. They found that there was a significant rise in serum TC, TGs, LDL-C, VLDL-C, and a significant decrease in HDL-C in the study group as compared to controls.

**Ghodke B et al<sup>30</sup>** conducted a prospective observational study. They aimed to analysis the association of serum lipid levels during the second and third trimesters with the development of pregnancy-associated diseases, such as preeclampsia, GDM, and preterm delivery in 200 subjects. Out of the total 200 patients, 168 had no complications, while 20 (10%) had preeclampsia, six (3%) had gestational diabetes mellitus, and the other six {3%} had preterm deliveries. In preeclamptic patients, the mean serum triglyceride levels were 204.00 mg/dl and 243.20 mg/dl in the second and third trimester, respectively. In GDM patients, the mean serum triglyceride was 214.33 mg/dl and 230.50 mg/dl in the second and third trimester, respectively. In patients with preterm, the mean triglycerides levels were 212.83 mg/dl and 240.16 mg/dl in the second and third trimesters, respectively. They observed a significant association between maternal early pregnancy triglyceridemia and the subsequent risk of preeclampsia, gestational diabetes, and preterm deliveries but no such association was observed with serum cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very-low-density lipoprotein cholesterol (VLDL-C).

**Limitation of our study** was that it was a hospital based study which may not truly represent the population at large. In our study all subjects included were between 28-36 weeks of gestational age, had this study been done in early second trimester of pregnancy, it would have proved to be more impactful, as changes in lipid levels are evident as early as 16-18 weeks gestation.

**Declarations**

**Conflict of interest:** none declared

**Funding:** no funding sources

**Ethical approval:** study is approved by institutional ethics committee



#### 4. Recommendations

Lipid analysis in early pregnancy may help in prediction of pre eclampsia before it goes berserk. It may serve as simple, cost effective method for prediction of pre eclampsia in developing countries. Lipid profile has evolved as a new kid on the block.

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