



Lipid Profile Evaluation in Second and Third Trimester of Pregnancy and Fetomaternal Outcome

Nirmala Sharma¹, Jaswant Raj², Neha Seehra*³

¹ MBBS, MS, Department of Obstetrics and Gynecology, Senior Professor, Head of Department and Unit Head. Government Medical College, Kota, Rajasthan, India.

² MBBS, Department of Obstetrics and Gynecology, Postgraduate Student, Government Medical College, Kota, Rajasthan, India.

³ MBBS, MS, DNB, Department of Obstetrics and Gynecology, Assistant Professor, Government Medical College, Kota, Rajasthan, India.

*Corresponding author's E-mail: dr.nehasehra@gmail.com

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ABSTRACT

Increase in maternal cholesterol levels are thought to be an adaptive change necessary for proper fetal development and growth. However maternal dyslipidemia has been shown to be associated with complications during pregnancy. Objective of this study is evaluation of changes in lipid profile during pregnancy and their association with fetomaternal outcome. It was a prospective descriptive study conducted over 200 pregnant women from December 2018 to August 2020 at jay kalyon hospital, kota, Rajasthan. 3 ml serum samples of enrolled pregnant women and 100 non pregnant women were obtained for the estimation of serum lipid profile by ERBA manheim EM360 auto analyzer. 56% women belonged to the age group of 21-25 years, 70% patients were from urban population, 63.5% women had vegetarian diet, 49.5% were primigravida. Statistically significant rise found in the lipid profile values ($p < 0.001$) during pregnancy when compared to non-pregnant women. 25% pregnant women developed gestational hypertension, 5% patients developed preeclampsia, 69.5% women delivered vaginally while 30.5% by cesarean section. 27 fetus failed to achieve birth weight of >2.5 kilogram. Pregnancy furnishes a unique opportunity for detection of subclinical dyslipidemia, significant increase has been found in the lipid profile when compared to non-pregnant women. However higher lipid levels have shown to be associated with gestational hypertension, preeclampsia and their complications along with low birth weight. Hence, we recommend lipid profile evaluation should be a part of routine antenatal investigations for early detection and management of these complications.

Keywords: Dyslipidemia, gestational hypertension, lipid profile.

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INTRODUCTION

Maternal dyslipidemia recognized as a physiological phenomenon essential to provide fuel and nutrition to the growing fetus. Women body undergoes various types of physiological, biochemical and hormonal changes during pregnancy to meet the increased demand of fetus, to maintain metabolism and regulation of the complementary maternal system. As pregnancy advances, there is increased demand of energy for growing fetus; pregnant women require an additional energy of 300 Kcal/day over routine energy intake¹. Physiologically lipid metabolism greatly changes during pregnancy^{2,3} but the way in which these changes affect lipid deposition in the adipose tissue of the fetus and its subsequent growth is not completely understood. The availability of substrate for the fetus depends on their concentration in the maternal circulation and to the extent they are transported across the placenta. Thus, maternal hyperlipidemia during pregnancy facilitates the availability of lipids to fetus and could also contribute

to its accumulation in fat depots. Maternal accumulation of fat depots and hyperlipidemia are the two principle changes in the lipid metabolism that occurred during pregnancy^{4,5}. During first two trimesters, lipid metabolism is 'primarily anabolic', maternal hyperphagia increases the availability of substrates, which together with higher insulin levels and enhanced insulin sensitivity^{6,7} during early pregnancy resulting in enhanced lipogenesis apart from increased activity of adipose tissue lipoprotein lipase⁸.

In early pregnancy, there is an increase intake of the diet and increase synthesis of lipids which leads to accumulation of extra body fat. Various fractions of lipids include Total Cholesterol (TC), Triacylglycerol (formerly known as triglyceride), High density lipoprotein (HDL), low density lipoprotein (LDL-C), Very low-density lipoprotein (VLDL). In later stage of pregnancy, there is accelerated fat breakdown which plays an important role in the fetal development. The energy provided by lipid is used in cellular proliferation of uterus, blood volume expansion of mother, implantation of fetus in uterus, uteroplacental and fetal development. There are physiological hyperplastic changes in pancreatic beta cells that results in an increase in the insulin hormone levels in blood⁹. Hyperinsulinemia leads to an increase in peripheral glucose utilization, a decline in fasting plasma glucose levels, increased tissue storage of glycogen, increased glycogen accumulation in the liver as well as increased



storage of lipids and decreased lipid breakdown, increased storage of fats and decreased lipolysis. Due to insulin resistance in pregnancy, there is more utilization of fats than carbohydrates for energy by mother and carbohydrates are spared for fetus, thus it's a physiological adaptation of the mother to ensure adequate carbohydrate supply for rapidly growing fetus¹⁰. Oxidative stress is present in normal pregnancy^{11,12} and could be the result of maternal hyperlipidemia increments of oxidative stress indices over control values have been associated with altered pregnancy outcome, as has been shown in diabetes^{13,14}, pre-eclampsia^{15, 16} and fetal growth restriction¹⁷. Looking over lipid profile at a single point of time in pregnancy may not be able to determine the elevation from baseline; hence with the lipid profile estimation at two points of time during pregnancy, we tried to study the rate of change of maternal cholesterol, LDL, HDL, VLDL levels and their implications over fetomaternal outcome. In our study we compared and analyze the change in the lipid profile in pregnant women versus non pregnant women, and how this changed profile affects the outcome of pregnancy.

MATERIAL AND METHODS

The present study was a descriptive study, conducted prospectively in the department of obstetrics and gynaecology, jay kay lon Hospital, Government medical college, Kota, Rajasthan, during the period of December 2018 to August 2020. We enrolled 200 pregnant women who came for antenatal check up in our antenatal clinic beyond 13 weeks of gestation in second trimester.

Study design

Prospective descriptive study

Study location

Department of obstetrics and gynaecology, jay kay lon Hospital, Government medical college, Kota, Rajasthan.

Study duration

December 2018 to August 2020

Sample size

200 pregnant women

Subject and selection method

We enrolled 200 pregnant women who came for antenatal checkup in our antenatal clinic beyond 13 weeks of gestation in second trimester.

Inclusion criteria

Women \geq 18 years old, Singleton pregnancy with period of gestation beyond 13 weeks.

Exclusion criteria

Pregnant women with diagnosed medical disorders like chronic hypertension, diabetes mellitus, renal disorder, epilepsy, psychotic or neurological disorders.

Procedure methodology

All eligible participants were enrolled for the study after obtaining an informed written consent. After enrolment two serum samples were drawn at two points of times during pregnancy, first serum specimen was collected at the time of enrollment during 13-27 week of gestation; the second sample was collected at 28-40 week of gestation during follow up visits. Serum sample of 100 Non pregnant, healthy women of same age group were taken as control to compare the lipid profile values. Under aseptic precautions, 3 ml intravenous sample taken from antecubital vein and samples were sent to the central laboratory of the medical college, Kota, Rajasthan. Serum separated by centrifugation of samples and processed for the estimation of serum lipid profile. Chemical analysis was done by ERBA manheim EM 360 auto analyzer.(Figure 1)



Figure 1: ERBA manheim EM 360 auto analyzer.

Statistical analysis

Reported data were collected and entered in MS excel sheet, Linear variables were summarized as mean and standard deviation and analyzed by using paired and unpaired student's t test. Nominal or categorical variables were presented as proportions. P value <0.05 was taken as significant. Statistical analysis performed using Medcalc 16.4 version software.

This work was approved by the ethical committee of government medical college, Kota, Rajasthan.

RESULTS AND DISCUSSION

We observed 200 eligible pregnant women to document the changes in lipid profile during second and third trimesters. Following were the main results. 56% of our studied women belonged to the age group Of 21-25 years .70% of women were residing in urban area whereas 30% belonged to rural area. Majority of our studied women i.e 63.5% were vegetarian and 36.5% were non vegetarian. (Table no. 1)

Table 1: Demographical variables

Age (years)	Frequency	Percentage
≤ 20	22	11.0
21-25	112	56.0
26-30	48	24.0
>30	18	9.0
RESIDENTIAL DISTRIBUTION-		
Rural	60	30
Urban	140	70
DIET -		
non-vegetarian diet	73	36.5
vegetarian diet	127	63.5

In our study population 49.5% of women were primigravida, 27% were Gravida 2 while rest were gravida 3 and more (table no.2).

Table 2: Obstetrical parameter

Gravid	Number	Percentage
G1	99	49.5
G2	54	27.0
G3	38	19.0
≥G4	09	4.5
Total	200	100

When we compared the lipid profile values in non pregnant versus pregnant women, all the five parameters increased during pregnancy. The percentage increase between non pregnant women and second trimester of pregnant women were as follows- TC-41.4%, TG- 45.3%, HDL- 16.2%, LDL- 57.4%, VLDL-45.3%. The percentage increase between non pregnant women and third trimester of pregnancy was even higher as follows- TC- 65.7%, TG- 92.8%, HDL-25.9%, LDL- 86.8%, VLDL- 92.8%. The percentage increase between second and third trimester in pregnancy also found to be raised with a statistically significant difference ($p < 0.001$). (Table no. 3)

Table 3: Lipid profile values in non pregnant women

Lipid profile	N	Mean	SD	Median	Minimum	Maximum
S. cholesterol	100	151.88	25.84	149	116	202
HDL	100	55.63	5.20	54.5	44	67
TG	100	117.89	29.03	124	80	200
LDL	100	72.64	23.23	76.5	43	120
VLDL	100	23.61	5.89	25	16	40

Lipid profile values in 2nd and 3rd trimester of pregnancy-

Lipid profile	trimester	N	Mean	SD	Median	Min	Max	'p' value
S. cholesterol	II	200	214.37	38.34	212	143	352	<0.001
	III	200	250.91	43.76	249	159	399	
HDL	II	200	64.62	12.12	63.5	40	90	<0.001
	III	200	70.01	11.55	70	45	94	
TG	II	200	171.43	62.89	155	64	349	<0.001
	III	200	227.51	74.28	202	72	399	
LDL	II	200	114.40	35.84	111	43.2	237.4	<0.001
	III	200	135.81	39.93	132.8	42.6	280	
VLDL	II	200	34.29	12.58	31	12.8	69.8	<0.001
	III	200	45.50	14.86	40.4	14.4	79.8	

67.5% patients delivered without any maternal complications. Among 200 studied patients, 31% patients were diagnosed with hypertensive disorders of pregnancy, 25% patients had gestational hypertension and 5% patients had severe pre-eclampsia. When we compared

the mean of each lipid profile parameters between normotensive and hypertensive groups, statistically significant differences noted in total cholesterol, triacylglycerol, low density lipoprotein, very low density lipoprotein levels. (Table no. 4)

Table 4: Comparison of percentage increase in the lipid profile parameters with respect to gestational hypertension.

	Population (N=200)		Trimesters	Mean		Median		SD		P value
	Normotensive	hypertensive		Normotensive	hypertensive	Normotensive	hypertensive	Normotensive	hypertensive	
TC	138	62	II	200.5	245.2	197.5	250	30.3	36.6	<0.0001
			III	236	284	234	284	31.8	48.6	
TG	138	62	II	157.9	201.6	150	206.5	60.3	58.2	<0.0006
			III	215.6	254	195	255	72.4	72.1	
HDL	138	62	II	64.6	64.6	65	60	12.2	12	0.12
			III	69.2	71.9	69	72	11.3	12	
LDL	138	62	II	102.8	140.2	101.6	139.2	29.3	43.2	<0.0001
			III	124.4	161.3	124.9	157.6	33.5	41.4	
VLDL	138	62	II	31.6	40.3	30	41.3	12.1	11.6	<0.0006
			III	43.1	50.8	39	51	14.5	14.4	

When we compared the observed fetal weight and change in the lipid profile, there was no significant association found in the percentage increase in lipid profile with the fetal birth weight in study population. However, when we compared the mean of each lipid parameters in 3rd

trimester among patients delivered with Normal birth weight versus low birth weight neonates, statistically significant difference was found in TC, VLDL (p value <0.005) levels and low birth weight.(Table no. 5)

Table 5: Changes in the lipid profile with respect to the observed fetal birth weight.

Lipid profile	Birth weight	N	Mean	SD	Median	Min.	Max.	'p' value
S. cholesterol	LBW	27	266	47.4	261	189	396	0.054
	NBW	173	248.6	42.8	245	159	399	
HDL	LBW	27	70.5	12.1	68	50	90	0.82
	NBW	173	69	11.5	70	45	94	
TG	LBW	27	266.1	87.5	252	122	399	0.003
	NBW	173	221	70.4	199	72	397	
LDL	LBW	27	143.0	39.7	145	65.2	235.8	0.31
	NBW	173	134.7	40	131.8	42.6	280	
VLDL	LBW	27	53.2	17.5	50.4	24.4	79.8	0.003
	NBW	173	44.3	14.1	39.8	14.4	79.4	

Although increase in maternal cholesterol levels are thought to be an adaptive change necessary for proper fetal development and growth, adverse health outcomes for the mother and fetus have been associated with elevated maternal cholesterol during pregnancy. The most dramatic change observed among the lipid profile was serum hyper triglyceridemia, which may be as high as two to three folds in the third trimester over the levels in non pregnant women.

In our study we observed the same change, total cholesterol, triglyceride, HDL, LDL of the pregnant women in the second and third trimester were found to be higher than those of non pregnant women. This resembles the study done by Wald and Guckle¹⁸ concluding that increase in the maternal lipid profile is in response to the maternal switch from carbohydrate to fat metabolism which is an alternative pathway for energy generation due to high

energy demand. We observed a significant increase in the total cholesterol, triglyceride, HDL, LDL and VLDL levels during third trimester as compared to the second trimester. When we gathered the data on the basis of maternal age, area of residence, and diet, our study didn't find any significant association with the changed lipid profile and above parameters. In our studied pregnant women, women with BMI ≥ 25 , total cholesterol increased by 23.07% from second to third trimester, while an increase of 16.61% was observed in the women with BMI ≤ 25 . For LDL, a 42.06% increase was observed in BMI ≥ 25 against an increase of 19.51% in normal weight group, however no statistical difference was found between BMI and HDL, TG and VLDL values.

In our study we found strong statistical association between dyslipidemia and development of hypertensive disorders of pregnancy. Mean of four analytes i.e TC, TG,

LDL, VLDL found highly statistically significant in hypertensive group over normotensive group ($p < 0.001$) except the changes observed in HDL levels were insignificant. Those pregnant women with increased levels of triglycerides in second and third trimester (>250 mg/dl), the probabilities of developing pre-eclampsia were found to be significant. Our findings were also supported by the results of study done by Singh et al¹¹, they found that the mean serum level of total cholesterol (TC), triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) was significantly higher in women with pre eclampsia as compared to normotensive pregnant women, concluding that the measurement of serum lipid profile in early pregnancy may serve as early predictor of preeclampsia. Women with severe dyslipidemia developed fetal complications of severe fetal growth restriction and intrauterine fetal deaths in their late second and early third trimester. In our study 18 fetus failed to achieve birth weight of >2.5 kilogram, there was no association found in the percentage increase of

lipid profile and fetal birth weight. However when we compared the mean values of lipid profile between low birth weight and normal birth weight group, we found an association between TG and VLDL levels with a p value of <0.05 . Amit D sonagra et al²⁰ in 2017 conducted a study titled study of serum lipid profile in normal pregnancy and found that the mean level of serum triglycerides and total cholesterol were significantly higher and mean level of serum HDL were significantly lower in second and third trimester of pregnancy when compared with healthy non pregnant controls. The mean level of serum LDL was significantly higher in third trimester of pregnancy when compared with controls. They found that as pregnancy advances so does the dyslipidemia, however such changes are more marked in third trimester than second and first trimester.

CONCLUSION

Pregnancy furnishes a unique opportunity for the detection of subclinical dyslipidemia. Normal gestation is characterized by increase in the lipid production to nurture the healthy fetus. Significant increase has been found in the lipid profile during pregnancy when we compared it against non pregnant state. Elevated physiological lipid profile is essential for maintaining the pregnancy and optimal fetal development but we also found that higher lipid levels may result in adverse fetomaternal outcomes in terms of hypertensive disorders like gestational hypertension, preeclampsia and their complications as well as low birth weight at birth. Thus evaluating dyslipidemia in 2nd and 3rd trimester may help in early prediction and management of these complications. Hence, we recommend that evaluation of lipid profile should be a part of routine antenatal investigations during pregnancy.

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