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EVALUATION OF MATERNAL LIPID PROFILE IN PREGNANCY AND ITS FETO-MATERNAL OUTCOME

Divyanee Gulati[1], Manjit Kaur Mohi[2], Jasvir Singh[3], Navneet Kaur[4], Beant Singh[5]

1. Senior Resident, Department of Obstetrics and Gynaecology, GMC, Patiala, Punjab, India.
2. Professor and Head, Department of Obstetrics and Gynaecology, Gian Sagar Medical College, Banur, Punjab, India
3. Associate Professor, Department of Biochemistry, GMC, Patiala, Punjab, India
4. Assistant Professor, Department of Obstetrics and Gynaecology, GMC, Patiala, Punjab, India
5. Professor, Department of Obstetrics and Gynaecology, GMC, Patiala, Punjab, India

Corresponding Author:
Dr. Navneet Kaur
Address: #267 SST Nagar, near Guru Harkrishan Public School, PATIALA, PUNJAB, INDIA 147001
Email: nav_neetu8@yahoo.in Contact No.: +919780424342

ABSTRACT

INTRODUCTION: Lipid profile derangement in pregnancy that is, increase in levels of total cholesterol, triglycerides, low density lipoprotein cholesterol, very low-density lipoprotein and decrease in levels of high-density lipoprotein cholesterol results in increased risk of adverse maternal and fetal outcomes.

OBJECTIVES: To find out proportion of dyslipidemia during pregnancy in population visiting, Department of Obstetrics and Gynaecology, Rajindra hospital Patiala and to study outcome of dyslipidemia in both mother and fetus.

MATERIAL AND METHODS: This prospective observational cross-sectional study was conducted in this institution in 1000 women attending antenatal clinic and labor room. Their lipid profile was done and proportion of dyslipidemia during pregnancy was recorded and final data was extracted to see effect of dyslipidemia in pregnancy.

RESULTS: The mean age was 26.36±4.84 years. Majority of patients were from urban area, and most of the patients were consuming mustard oil (63.7%). Mean calorie intake in our study population was 2305.9 Kcal and calorie intake increased from 1st to 2nd and 3rd trimester. There were 36.20% primigravida and 63.80% were multiparous females respectively. Overall proportion of dyslipidemia seen in 47.8% population among total 1000 patients. Dyslipidemia was found in 14.6% GDM patients, 14.02% patients of Pre-Eclampsia and 35.36% patients with preterm labor pains. Among perinatal outcomes Dyslipidemia was found in 18.41% Patients with SGA baby, 4.18% patients with LGA baby and 50% patients with preterm birth.

CONCLUSION: Maternal dyslipidemia is observed in conditions like maternal obesity, preterm deliveries, fetal growth restriction, gestational diabetes mellitus and pre-eclampsia. Women with dyslipidemia experience increased maternal mortality and morbidity as a result of pregnancy.

KEYWORDS: Dyslipidemia, cholesterol, lipid profile, triglycerides.

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INTRODUCTION

Lipid profile derangement in pregnancy that is increase in levels of TC, TG, LDL-C, VLDL and decrease in levels of HDL-C results in increased risk of adverse pregnancy outcomes both maternal as well as fetal. In pregnancy many metabolic and endocrinological changes occurs which may result in increased levels of carbohydrate, protein, amino acids and maternal triglyceride levels further causing hypercholestrolemia and it is of concern because of its association with complex collection of metabolic disorders including hypertension, elevated insulin resistance and further increase in risk of cardiovascular disorders. [1] [2]

During early pregnancy, maternal metabolic environment is modified by rise in serum levels of oestrogen and progesterone, which causes pancreatic beta cell hyperplasia and increase in secretion of insulin [3] Hyperinsulinemia leads to increase in peripheral glucose utilization, a decline in fasting plasma glucose levels, increase tissue storage of glycogen, increase storage of fats and decrease lipolysis hence increases serum lipid levels in early pregnancy. [3] [4]

Maternal fuel adjustments during late pregnancy includes sparing of glucose for the foetus and increase concentration of fatty acids in plasma hence increase levels of lipids in late pregnancy. Maternal hyperlipidemia is one of the most consistent and striking changes of lipid metabolism during late pregnancy. During third trimester, the average level of total serum cholesterol is 267± 30 mg/dl, of LDL is 136±33 mg/dl of HDL-C is 81±17 mg/dl and of TG is 245±73 mg/dl [5]

Normal foetal development needs the availability of both essential fatty acids and long chain poly unsaturated fatty acids, and the nutritional status of the mother during gestation has been related to foetal growth, however excessive intake of certain long chain fatty acids may cause both decline in arachidonic acid and enhance lipid peroxidation, reducing anti-oxidant capacity.[6]

Maternal dietary factors also play an important role in alteration of lipid profile, Saturated fatty acids having single bond between carbon atoms found primarily in dairy products derived from animal sources tends to raise the level of LDL in blood while the vegetable oils including soybean, sunflower, safflower, mustard and olive oil are low in saturated fats trans type of unsaturated fatty acids baked/fried products (industrial food) and vanaspati also have unfavourable effect of lipid profile. [7]

Increased level of TG and TC are taken up by placenta which is then metabolized and transported to foetus in various forms[8] [9]. This shows that both lipids are essential for development of foetus. However, high level of maternal TC and TG are associated with preterm birth [10], Pregnancy induced hypertension [11], preeclampsia [12] and LGA [13] these conditions will also have serious manifestation in later life, for instance preterm delivery and being born small for gestation age (SGA) or large for gestation age (LGA) are associated with increased risk for type 2 diabetes, cardiovascular diseases and hypertension at adult age. Although obstetric care has improved, pregnancy complications and perinatal morbidity are still present. Therefore, it is of clinical and economic importance to prevent adverse pregnancy outcome factors by exploring casual factors for these outcomes.[14]

MATERIALS AND METHODS

Source of data:

1000 randomly selected pregnant females visiting in our Obstetrics and Gynaecology Department in year 2019-2020

Method of collection of data:

This prospective observational cross-sectional study was conducted in this institution in 1000 women attending antenatal clinic and labor room. Their lipid profile was done and proportion

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of dyslipidemia during pregnancy was recorded. Due to operational constraints only the first lipidogram after enrollment irrespective of trimesters was considered for analytical purpose and the fetal and maternal outcomes were recorded and analyzed.

Inclusion criteria:

1. Pregnant women with singleton pregnancy.
2. Pregnancy confirmed with last menstrual period or ultrasound.
3. Females were taken between age group 18-45 years.

Exclusion criteria:

1. Family and personal history of dyslipidemia.
2. Pregnant women with gestational diabetes mellitus, hypertension, smoking, alcoholism, and women with other diseases that may affect the lipid levels in body.
3. Adolescents and women over 45 years of age because these may lead to high-risk pregnancy.
4. Those using lipid altering medication (e.g., antiepileptic drugs, steroids, insulin, antidepressants, or sleep medication)

Sample Randomization and Selection:

1. To randomize the study sample, first 5 cases who fulfilled the inclusion and exclusion criteria and reported in outdoor and first 2 cases in labor room daily were enrolled till the sample size of 1000 were achieved.
2. Informed consent was obtained from all the participants and inclusion and exclusion criteria was confirmed and assessment of the patient was done.
3. All cases were followed till immediate post-partum period

Sample size- Following formula was used for the calculation of the sample size (n):

$n = N*X / (X+N-1)$

Where $X = Z\alpha/22x\ p\ x\ (1-p)/d2$,

And Za/2 is the critical value of the normal distribution at a/2 (e.g. for a confidence level of 95%, a is 0.05 and the critical value is 1.96), d is the margin of error, p is sample proportion and N is population size. Note that a finite population correction has been applied to the sample size formula.

From the previous records of the number of patients who presented to Obstetrics OPD at Rajindra hospital Patiala was around 20,000 patients in a year. So, N = 20,000 considered.

From different studies the hypothesized presence of dyslipidemia among the general population is 15-30%.i So we take the upper limit of 30% as hypothesized outcome factor.

We have kept confidence limit as percentage of 100. Margin of error was taken to be 2% for this study. Using this formula sample size was at 95% confidence limit = 979.

By rounding off the above estimated sample size, for the study sample size was taken as 1000. Samples from all subjects were collected under aseptic precautions, 5 ml of non-fasting venous blood was collected in plain vacutainer from antecubital vein. After the clot retracts the sample was centrifuged at 4000 rpm for 5 min the serum separated and stored at 4°C pending assay for lipid profile. Serum TGs, TC, and HDL cholesterol was analyzed by enzymatic methods with the help of Glaxo kits on ERBA Chem-5 plus semi-auto analyzer in the department of biochemistry in our institution. Serum LDL cholesterol were calculated by Frederickson-Friedwald‘s formula according to which:

LDL cholesterol = TC − (HDL cholesterol + Very low density [VLDL] cholesterol) VLDL cholesterol was calculated as 1/5 of TGs.

Statistical analysis:

The data was collected and analyzed using Microsoft excel software version 2019 and epi info CDC (Atlanta) version 7.2.4.0 Most of the figures were in numbers and percentage where Chi-

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square test, Mann Whitney test and Kruskal Wallis test were used for assessment of level of significance. P value of less than 0.05 was taken as significant in two tailed test.

RESULTS

Demographical details

Out of 1000 patients, 5.6% patients were from <20 years age groups and 88.20% patients were from 20-35years age group while 6.20% patients were 35 years and above, Mean age was **26.36±4.84** years. 20.5% patients came from rural area while majority of patients that is 79.5% were from urban area. There were 36.20% primigravida and 63.80% patients were multiparous. Majority of patients were literate that is 83.30% while 16.70% patients were illiterate. 30% patients were non-vegetarian and 70% patients were vegetarian. Among all the patients 63.7% patients have taken mustard oil while remaining patients consumed sunflower and soyabean oil and groundnut oil (Table 1)

The mean calorie intake increased from 2261.1 Kcals to 2302.1 Kcals to 2326.4 Kcals from 1st to 2nd to 3rd trimester respectively. This increase was not statistically significant.

Out of 1000, 6.9% patients were classified in underweight, 59.3% patients were classified in normal, 27.9% patients were classified in overweight and 5.9% patients were classified in obese category. (Fig. 1)

DYSLIPIDEMIA

Overall proportion of dyslipidemia seen in 47.8% among total 1000 patients, out of which dyslipidemia was found in 34.6%. 47.67%, and 53.23% patient in first second and third trimester respectively (Fig. 2)

Dyslipdemia due to TC was found in 23.38% 22.58% and 25.05% patient in first second and third trimester

Dyslipidemia due to TG was found to be 16.19% 16.49% and 20.74% patient in first second and third trimester

Dyslipidemia due to HDL was found in 1.9%, 20.79% and 22.7% patiens in first second and third trimester

Dyslipidemia due to LDL was found in 1.43%, 16.13% and 12.92% patients in first second and third trimester (Table 2)

Mean age was found higher in patients with dyslipidemia (26.85) as compared to patient without dyslipidemia.

Dyslipidemia was found in 46.71%of patients with normal BMI, 37.68% of underweight patients, 49.1% of overweight patients and 64.41% of obese patients, comparison of BMI and dyslipidemia showed statistically significant results. (Fig. 3) Mean pre-pregnancy BMI was higher in patients with dyslipidemia as compared to dyslipidemia free patients.

Association of dyslipidemia with Maternal and fetal complications (Table 3)

Prevalence of GDM in our study population was 8.70% out of all GDM patients' dyslipidemia was present in 14.64% cases which showed statically significant result. (Fig. 4)

Prevalence of pre-eclampsia among study population was 7.80%, and out of all patients of PE, dyslipidemia was found in 14.02% cases which showed statistically significant result. (Fig. 5)

Prevalence of preterm labor pains in our study population was 28.3%, out of all such cases dyslipidemia was found in 35.36% which showed statistically significant results (Fig. 6)

Among perinatal outcomes15.4% patient had SGA babies, out of which 18.41% patients had dyslipidemia ,3% had LGA babies out of which 4.18% patients had dyslipidemia while 40.5% babies were preterm out of which 50% patients had dyslipidemia, all these parameters showed statistically significant results (Table 3)

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Tables & figures

TABLE 1: TYPE OF OIL USED

Oil	Frequency	Percent	Cum. Percent	Wilson 95% LCL	Wilson 95% UCL
Groundnut oil	2	0.20%	0.20%	0.05%	0.73%
Mustard	637	63.70%	63.90%	60.67%	66.62%
Soyabean	56	5.60%	69.50%	4.34%	7.20%
Sunflower	210	21.00%	90.50%	18.59%	23.63%
Vegetable oil	24	2.40%	92.90%	1.62%	3.55%
Other	71	7.10%	100.00%	5.67%	8.86%
TOTAL	**1000**	**100.00%**	**100.00%**		

TABLE 2: Dyslipidemia due to various factors

Dyslipidemia due to	1ST TRIMESTER	2ND TRIMESTER	3RD TRIMESTER
TC	23.8%	22.58%	25.05%
TG	16.19%	16.49%	20.74%
HDL	1.9%	20.79%	22.7%
LDL	1.43%	16.13%	12.92%

TABLE 3: ASSOCIATION OF DYSLIPIDEMIA WITH MATERNAL AND FETAL COMPLICATION

CONDITION	PREVALENCE IN STUDY POPULATION	PREVALENCE OF DYLIPIDEMIA IN CONDITION
GDM	**8.70%**	**14.64%**
Pre-eclampsia	**7.80%**	**14.64%**
Preterm labor	**28.3%**	**35.36%**
SGA babies	**15.4%**	**18.41%**
LGA babies	**40.5%**	**4.18%**
Preterm births	**18.41%**	**50%**

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TABLE 4 Table showing comparison of various studies

Parameter {mg/dl}	Trimester	PRESENT STUDY	R. Pusukuru et al	Giuseppe lippi et al.,	abdelhai at jamil et al.,	idonije O Blessing et al.,	Shital S Phuse et al.,
Serum Cholesterol	Second Trimester	252.36±50.41	214.59 ± 18.16	243.0 ± 53	162.50 ± 24.01	191.4 ± 12.8	255.1
	Third Trimester	294.43±59.65	242.64 ± 20.43	267.0 ± 30	170.10 ± 26.23	231.4 ± 9.1	270
Serum Triglycerides	Second Trimester	252.33±100.14	188.68 ± 20.87	151.0 ± 80	136.80 ± 58.3	217.5 ± 34.5	178.4
	Third Trimester	309.97±134.12	216.78 ± 20.09	245.0 ± 73	175.90 ± 70.93	211.1 ± 26.3	198.8
Serum HDL-Cholesterol	Second Trimester	57.91±7.41	49.12 ± 6.14	83 ± 19	58.84 ± 19.27	44.4 ± 6.4	32.8
	Third Trimester	54.07±10.51	43.06 ± 4.36	81 ± 17	38.09 ± 13.64	47.9 ± 3.8	27.6
Serum LDL-Cholesterol	Second Trimester	144.8±51	92.410±18.938	130 ± 46	67.94 ± 23.35	103.5 ± 16.2	170.9
	Third Trimester	178.4±61.7	137.81 ± 13.45	136 ± 33	76.62 ± 26.95	141.2 ± 8.6	195.7
Serum VLDL-Cholesterol	Second Trimester	48.5±17	28.22 ± 7.66	Not Described	Not Described	Not Described	40.2
	Third Trimester	57.6±20.2	36.27 ± 6.72	Not Described	Not Described	Not Described	45.7
	Table representing few study results in comparison to the present study.						

Fig.1 Figure showing pre-pregnancy BMI in study population

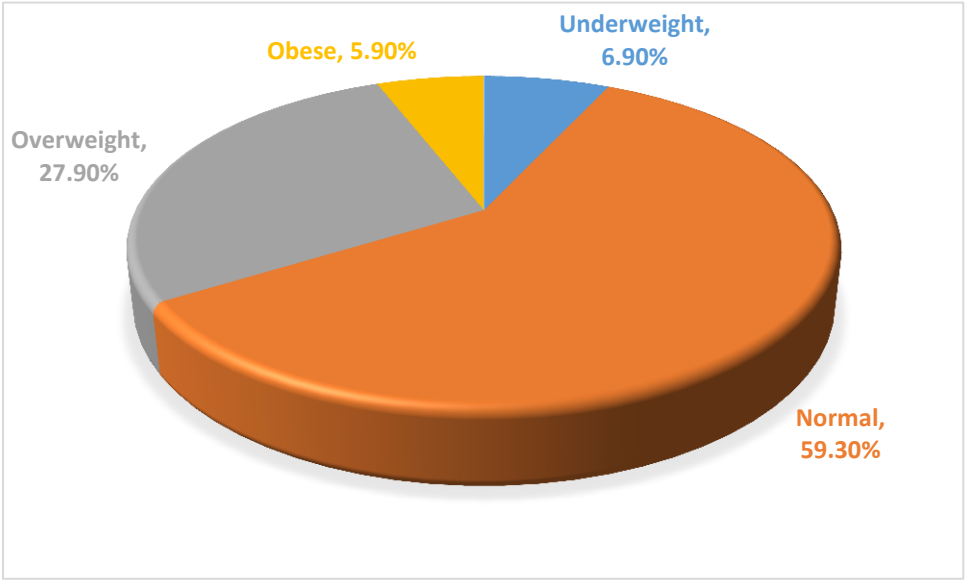

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Figure 2 showing dyslipidemia in all three trimesters

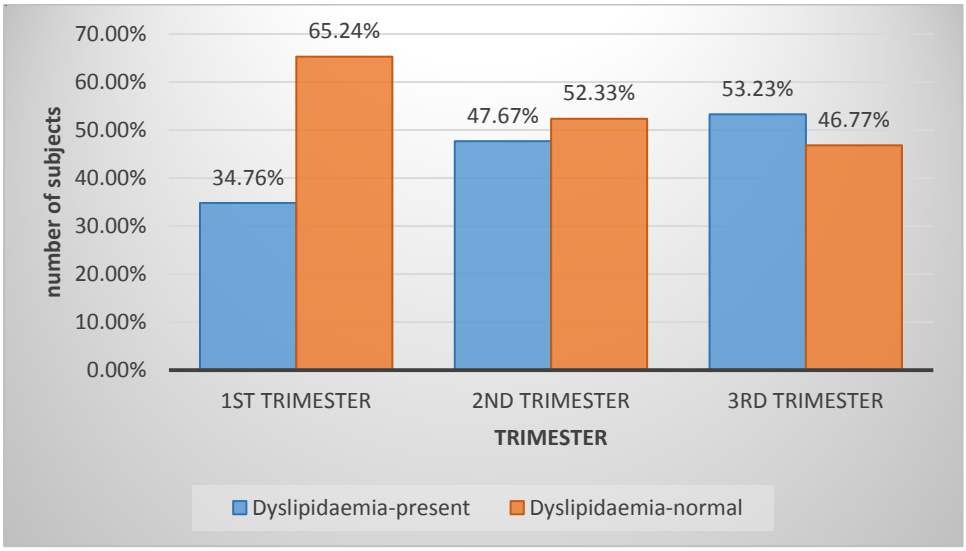

Figure 3 Association of dyslipidemia with BMI

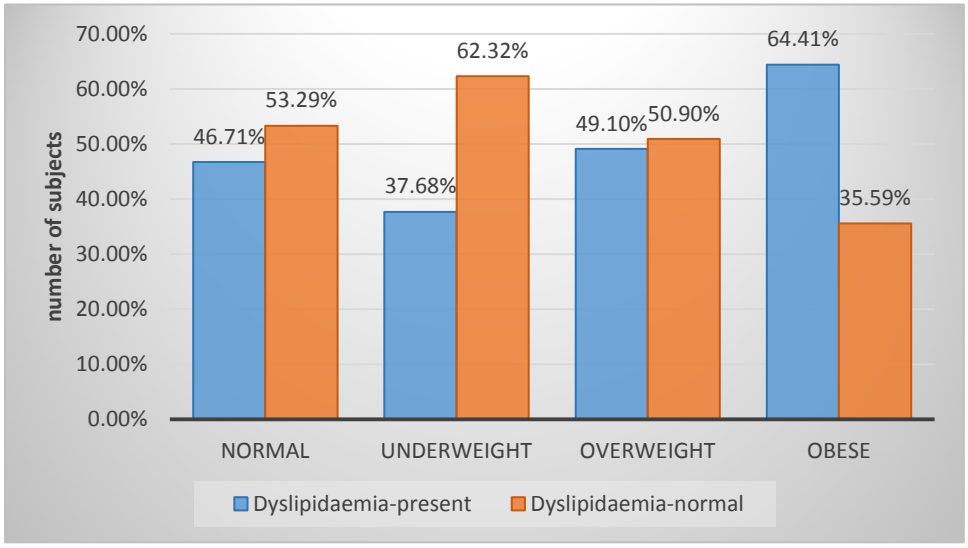

Figure 4 association of dyslipidemia with GDM

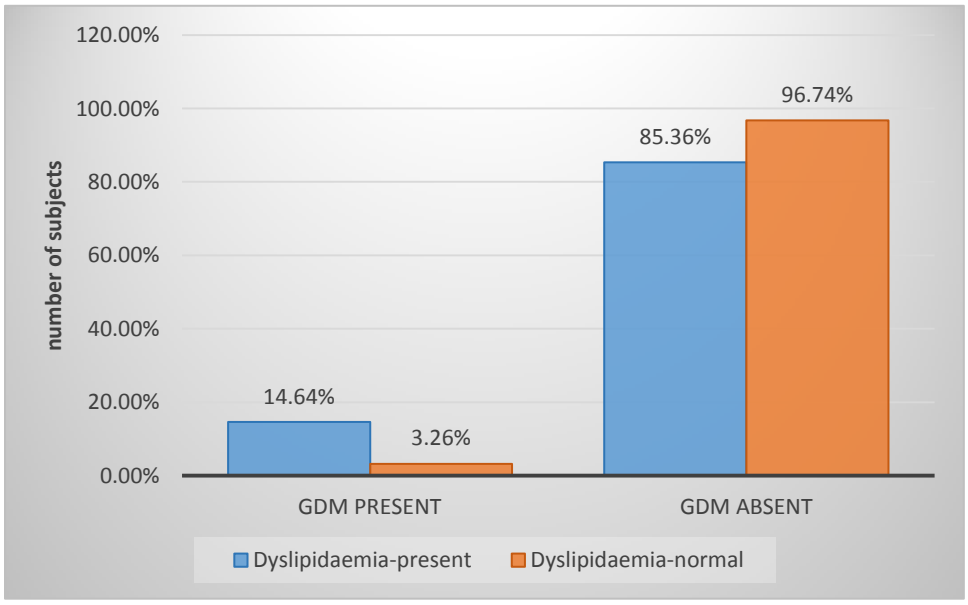

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Figure 5 association of dyslipidemia with Preeclampsia

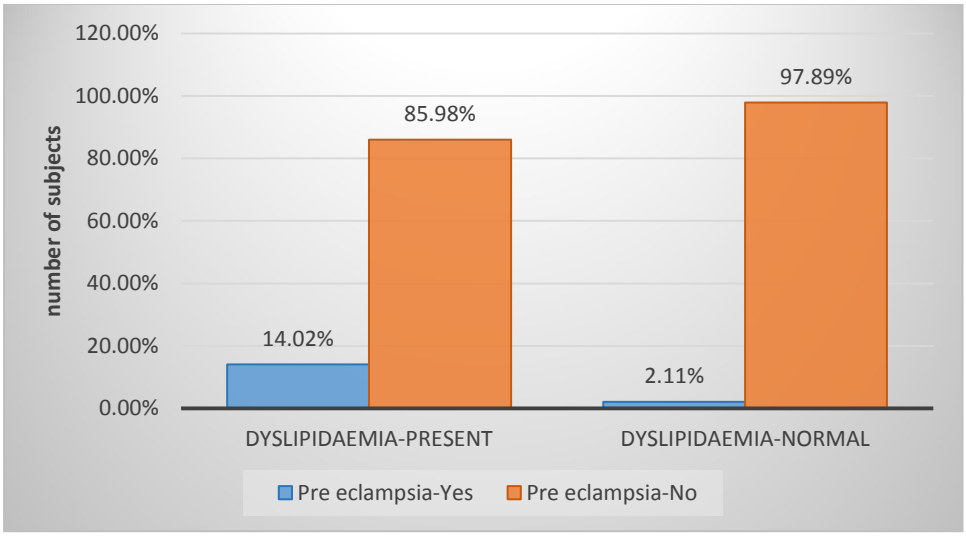
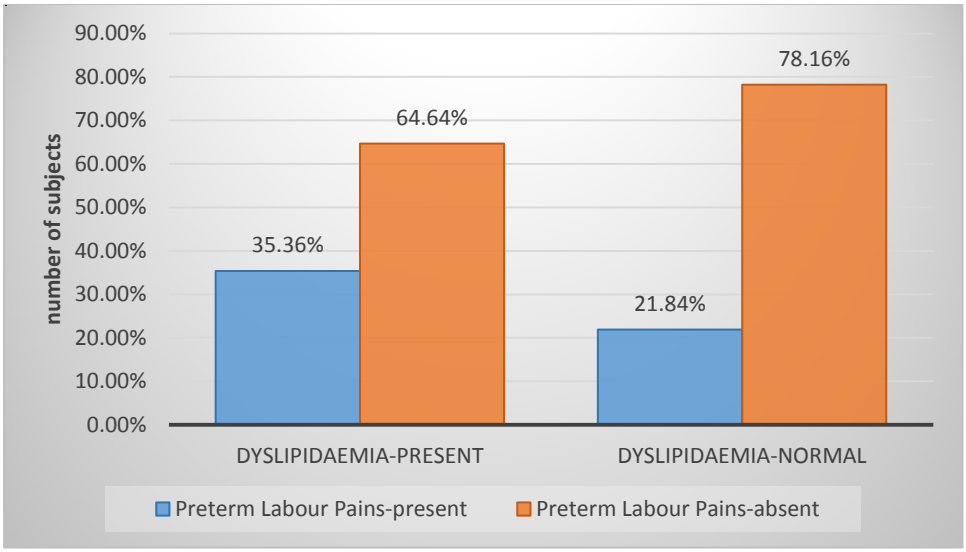


Figure 6 Association of dyslipidemia with preterm labor pains



DISCUSSION

During pregnancy there are profound adjustments in the anatomy and physiology of almost every organ system. These adjustments start to occur during the conception process and proceed through the entirety of pregnancy. The physiology of maternal metabolism is particularly affected by placental hormones during the last trimester of pregnancy.

In our study 1000 pregnant patients were taken out of which dyslipidemia was found in 47.02%, likewise a study done by **Mankuta D et al. in 2010** compared lipid levels in pregnancy with non-pregnant females observed decline in HDL levels in pregnancy with subsequent elevated levels of TC, TG and LDL explaining impact of various physiological changes in pregnancy on lipidogram. [15]

Our study also observed that there was a substantial increase in TC TG, LDL, VLDL and TG/HDL ratio which was supported by previous studies conducted by **Parchwani and Patel (2011) et al and Pusukuru R et al (2016)** [16,17]

In clinical research conducted by **Lippi G et al In 2007,** they found that all lipid parameters were deranged in pregnant patients and values increased in second and third trimester as

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compared to first trimester which is in support of our study.[18] Similar findings were observed by **Okojie FO et al in 2011 and Phuse SS et al in 2012** comparing lipid levels in different trimesters observing similar results. [19,20]

The increase in TG is due to rise in activity of lipase, and increase in levels of apolipoprotein A1 A2 and B in pregnancy, which explains subsequent rise of lipid levels in later half of pregnancy .The results seen in our study showed mean TG levels in first, second and third trimester were 142.2 mg/dl, 252.33 mg/dl and 309.97 mg/dl respectively, which showed significant rise as compared to non-pregnant values, similar changes were seen with TC, while there is rising trend in value of LDL in subsequent trimester, values of HDL rises in 2nd trimester and a decline is seen in 3rd trimester as seen in our study.

In our study we have observed elevated lipid levels is associated with Pre-eclampsia, pre term delivery, GDM and fetal growth restrictions which was similar to observation seen by **Vrijikotte TG et all in 2012 and Wen Yuan WY et al in 2016** [21-22]

A study determining lipid abnormalities in India was conducted in 2013 revealed that lipid abnormalities were highest in Chandigarh (82.9%) Jharkhand (80%) Maharashtra (77%) and Tamil Nadu (76.9%) this support higher prevalence of dyslipidemia in northern population due to dietary factors followed in northern population which is in support of our study [23,24]

CONCLUSION

Human gestation is associated with ―atherogenic lipid profile which could act as a potential risk factor for pre-eclampsia and endothelial cell dysfunction, if further significantly enhanced than the normal limits. Lipid profile i.e., Cholesterol, TG, LDL, VLDL and TG/HDL ratio were showed statistically significant increased with trimester. Cholesterol, TG, LDL, VLDL increased in both second and third trimester. The increase is more in third trimester, when compared to second trimester. HDL levels had significant rise in second trimester followed by a fall in third trimester. Inadequate intakes, defects, or alterations in fatty acid metabolism and transport can have adverse effects on fetoplacental development and maternal health. Maternal dyslipidemia is observed in conditions like maternal obesity, preterm deliveries, fetal grown restriction (FGR), GDM, and pre-eclampsia. It is however not clear whether this dyslipidemia is a cause or consequence of underlying pathology in these conditions and extensive research is needed in this direction. Women with dyslipidemia experience increased maternal mortality and morbidity as a result of pregnancy. It is recommended that dyslipidemic mothers receive recommended nutritional, exercise, and lifestyle adjustments to help avoid complications in the mother and infant. Since hypertriglyceridemia is a risk factor for pre-eclampsia, GDM and preterm, it is strongly recommended that patients have a lipid profile during pregnancy so as to institute prompt management strategies to protect against the deleterious effects of hyperlipidemia associated with pregnancy. All such childbearing-age women on lipid lowering therapy should receive pre-pregnancy counselling as well as contraception advice.

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