

Maternal Lipid Profile and Adverse Pregnancy Outcome: A Cohort Study

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Abstract

Aim: The present cohort study was undertaken to explore the association between dyslipidemia in pregnancy and its adverse pregnancy outcome.

Methods: The present study was undertaken in the Department of Obstetrics & Gynecology, Madhubani Medical College and Hospital for one year. 200 pregnant women were included in the present study. N=200 Study Group: 100 pregnant women who had deranged lipid profile. Control Group: 100 pregnant women who had normal lipid profile.

Results: In our study the mean age of pregnant women in the study group was 24.89 ± 3.12 years whereas in the control group it was 24.72 ± 3.76 years. Both groups were comparable with regards to age distribution. In our study maximum number of pregnant women had pre-pregnancy weight of 51 kg to 55 kg in both study and control group. In the study group 76% of pregnant women delivered by caesarean-section while in the control group 82% of pregnant women delivered by caesarean-section. On comparing the data of body weight and diet, there was statistically significant difference among the two groups ($p < 0.05$).

Conclusion: Evaluation of lipid profile during 2nd and 3rd trimesters can predict pregnancy associated complications. It may help in counseling the pregnant women to have a modified life style with increased physical activities, dietary modifications and timely interventions when required as the treatment of hyperlipidemia is a challenging issue in pregnancy due to the fact that most of the drugs used for the treatment of dyslipidemia.

Keywords: Pregnancy, Cholesterol, Low-density lipoprotein (LDL-c), High-density lipoprotein (HDL-c), Triglycerides, Intrauterine development, Fetal growth

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Introduction

Pregnancy is a physiological state in which there is an alteration in lipid levels. There is accumulation of TG-rich remnants in maternal circulation due to reduced lipolysis of TG-rich lipoproteins, reduced uptake by the placental tissue, and

concomitant decrease in lipoprotein lipolysis. [1] During pregnancy there is an increased levels of both TG and TC, which are essential for the development of fetus; [2–5] however, high levels are associated with adverse outcomes like gestational diabetes mellitus, preterm labor, [6]

pregnancy-induced hypertension (PIH), [7,8] large for gestational age babies. [9–11] Conversely decreased level of total cholesterol is associated with SGA babies. [12,13] These may have a long-term impact on the health of the baby and mother. Previous researches have shown that pregnancy-induced hyperlipidemia contributes to increased occurrence of gestational diabetes mellitus and preeclampsia. Despite this, there are still controversies on the relationship between maternal lipid disturbances and pregnancy complications and perinatal outcomes.

In pregnancy, lipids are crucial for the developing fetus and to maintain placental function. [14] Lipids are fatty substances that are either absorbed from food or synthesized by the liver, and comprise of cholesterol, triglycerides and lipoproteins. Cholesterol is crucial to provide structural integrity to the cell membrane. [15,16] Triglycerides are nonpolar lipid molecules associated with various lipoproteins that primarily store energy in adipocytes and muscle cells. Lipoproteins are structures that possess surface proteins that are cofactors and ligands for lipid-processing enzymes. They are classified by their size and density as either low-density lipoprotein cholesterol (LDL-c) and high-density lipoprotein cholesterol (HDL-c). [17] Low-density lipoproteins transport cholesterol, the main substrate for progesterone synthesis, and thereby support the maintenance of a pregnancy. [18,19]

Conversely decreased level of total cholesterol is associated with small for gestational (SGA) babies. [13,14] Adverse pregnancy outcome like PIH, GDM, Macrosomia, IHCP, IUGR, Preterm birth can affect the long term maternal and fetal health. Previous researches have shown that pregnancy induced hyperlipidemia contributes to increased occurrence of gestational diabetes mellitus and preeclampsia. At all gestational high triglyceride levels are associated with

adverse pregnancy outcome. Maternal TG concentration in pregnancy was positively associated with risk of GDM, preeclampsia and macrosomia. Despite this, there are still controversies on the relationship between maternal lipid disturbances and pregnancy complications and perinatal outcomes. So the present cohort study was undertaken to explore the association between dyslipidemia in pregnancy and its adverse pregnancy outcome.

Methods

The present study was undertaken in the Department of Obstetrics & Gynecology, Madhubani Medical College and Hospital 200 pregnant women were included in the present study. N=200

Study Group: 100 pregnant women who had deranged lipid profile.

Control Group: 100 pregnant women who had normal lipid profile.

After obtaining an informed consent from all participants underwent detailed history, examination and relevant investigation. Complications developed in the mother like pre-eclampsia, gestational diabetes mellitus, intrahepatic cholestasis of pregnancy (IHCP), preterm labor and fetal complications like intrauterine growth restriction (IUGR), small for gestational age (SGA) and fetal macrosomia were noted.

Inclusions Criteria:

- All pregnant females beyond 28 weeks of pregnancy
- Naturally conceived
- Singleton pregnancy

Exclusion Criteria:

- Multiple pregnancies
- Diabetes mellitus
- Inherited metabolic disease thyroid disease before pregnancy
- Coronary artery disease
- Chronic obstructive pulmonary disease

- Chronic hypertension

Methodology:

Pregnant women included in study underwent a detailed history, general and systemic examination. Women were requested to complete questionnaire about maternal age, height, parity, pre pregnancy weight, gestational weight gain, life style. Any variations in blood pressure

proteinuria, lipid profile, and altered blood sugar were recorded. Information on delivery mode whether it was a normal, preterm or caesarean section delivery and fetal complications like preterm birth, birth weight, Apgar score were recorded.

Pregnant women were divided into two groups according to lipid profile

	NORMAL VALUE	ABNORMAL
Total Cholesterol	<200	>200
TG	<150	>150
HDL	30-70	<70
LDL	<100	>100
VLDL	2-30	>30

Glucose Screening Test (GST):

Pregnant women were asked to take 75g oral glucose irrespective of last meal and after 2 hours venous blood sample were taken. Glucose levels were assessed by an enzymatic method known as the glucose oxidase and peroxidase (GOD-POD) method.

Biochemical Analysis of lipids

Venous blood samples were collected after an informed consent. Samples were collected in the morning after overnight fasting under all aseptic precautions. A total of 4ml blood was taken in plain vial and allowed to clot at room temperature, it was then centrifuged at 3000rpm for 5min and the serum is used for lipid profile.

Biochemical Analysis of lipids

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Estimation of Total cholesterol

Total cholesterol is determined using enzymatic kit based on method of Avantor India.

Estimation of triglycerides

Triglycerides were determined using a kit based on modified enzymatic method of Bucolo and David.

Estimation of High Density Lipoprotein (HDL-Cholesterol) Principle

Estimation of HDL was carried out using the cholesterol enzymatic method described above (153). Low Density Lipoprotein (LDL), very low density lipoproteins (VLDL), and chylomicrons were precipitated using buffered polyethylene glycol (PEG 6000). After centrifugation, HDL remains in supernatant. The cholesterol content of supernatant was then estimated by an enzymatic method using cholesterol esterase, cholesterol oxidase, peroxidase, 4-aminoantipyrine and phenol.

Estimation Low Density Lipoprotein (LDL- cholesterol)

LDL- cholesterol was calculated by using friedwald and fredrickson's formula (1972).

Statistical Analysis

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 2.0 statistical Analysis

Software. The values were represented in Number (%) and Mean \pm SD.

Results

Table 1: Demographic details

AGE (years)	Study Group	Control Group	P value
	N%	N%	
≤ 20	10 (10%)	19 (19%)	P > 0.05
21-25	50 (50%)	35 (35%)	
26-30	38 (38%)	43 (43%)	
≥ 30	2 (2%)	3 (3%)	
Mean	24.89 \pm 3.12	24.72 \pm 3.76	
Body Weight (Kg)			
40-45	8 (8%)	2 (2%)	P < 0.05
46-50	12 (12%)	22 (22%)	
51-55	38 (38%)	49 (49%)	
56-60	32 (32%)	23 (23%)	
61-65	10 (10%)	4 (4%)	
BMI			
Underweight ≤ 18.5 kg/m ²	3 (3%)	0	P > 0.05
Normal weight 18.5-24.9kg/m ²	91 (91%)	97 (97%)	
Overweight and obese >25 kg/m ²	6 (6%)	3 (3%)	
Mean	21.89 \pm 1.89	21.52 \pm 1.47	
Demography			
Semi urban	20 (20%)	12 (12%)	P > 0.05
Urban	80 (80%)	88 (88%)	
Literacy status			
Literate	94 (94%)	95 (95%)	
Illiterate	6 (6%)	5 (5%)	
Parity			
Primigravida	81 (81%)	80 (80%)	P > 0.05
Multigravida	19 (19%)	20 (20%)	
Diet			
Mixed	90 (90%)	98 (98%)	p<0.05
Vegetarian	10 (10%)	2 (2%)	
Mode of delivery			
LSCS	76 (76%)	82 (82%)	P > 0.05
NVD	24 (24%)	18 (18%)	

In our study the mean age of pregnant women in the study group was 24.89 \pm 3.12 years whereas in the control group it was 24.72 \pm 3.76 years. Both groups were comparable with regards to age distribution. In our study maximum number of pregnant women had pre-pregnancy weight of 51 kg to 55 kg in both study and control group. Both groups were comparable with regards to pre-pregnancy

weight. In our study, the mean BMI of the pregnant women in study group was 21.89 \pm 1.89 kg/m² whereas in the control group it was 21.52 \pm 1.47 kg/m². Both groups were comparable with regards to pre-pregnancy BMI. In our study 20% pregnant women were from semi urban area and 80% women were from urban area. In control group, 12% women were from semi urban area and 88% were from

urban area. In our study 94% of pregnant women were literate in study group while in control group 95% women were literate. In our study 81% of pregnant women were primigravida and 19% of women were multigravida in study group similarly in control group 80% of pregnant women were primigravida and 20% of pregnant women were multigravida. In the study

group 76% of pregnant women delivered by caesarean-section while in the control group 82% of pregnant women delivered by caesarean-section. The two groups were comparable when compared in terms of mode of delivery. On comparing the data of body weight and diet, there was statistically significant difference among the two groups ($p < 0.05$).

Table 2: Comparison of study and control group in terms of various maternal and fetal complications

GESTATIONAL DM	Study Group	Control Group	P value
Yes	20 (20%)	17 (17%)	P > 0.05
No	80 (80%)	83 (83%)	
GESTATIONAL HYPERTENSION			
Yes	14 (14%)	9 (9%)	P > 0.05
No	86 (86%)	91 (91%)	
PRE-ECLAMPSIA			
Yes	13 (13%)	2 (2%)	P < 0.01
No	87 (87%)	98 (98%)	
Preterm Labor			
Yes	12 (12%)	18 (18%)	P > 0.05
No	88 (88%)	82 (82%)	
Intra hepatic cholestasis of pregnancy			
Yes	29 (29%)	5 (5%)	P < 0.001
No	71 (71%)	95 (95%)	
Macrosomia			
Yes	2 (2%)	8 (8%)	P > 0.05
No	98 (98%)	92 (92%)	
Small for gestational age			
Yes	8 (8%)	10 (10%)	P > 0.05
No	92 (92%)	90 (90%)	
APGAR Score			
< 7	24 (24%)	17 (17%)	P > 0.05
≥ 7	76 (76%)	83 (83%)	
NICU Admission			
Yes	20 (20%)	7 (7%)	P < 0.05
No	80 (80%)	93 (93%)	

In study group 20% pregnant women developed GDM while in control group 17% pregnant women developed GDM. In study group 14% pregnant women developed Gestational Hypertension while in control group 9% pregnant women developed Gestational Hypertension. In the study group, 12 % pregnant women developed preterm labor while in control

group 18% pregnant women developed preterm labor. In the study group, 2% pregnant women had macrosomic baby while in control group 8% pregnant had macrosomia. Study group had higher incidence of macrosomia when compared to control group. In the study group, 8% pregnant women developed SGA while in control group 10% pregnant women

developed SGA. Control group had higher incidence of SGA as compared to study group. In the study group 24 % of newborn had Apgar score of less than 7 while 76% of newborns had Apgar score ≥ 7 . In Control group 17 % of newborns had Apgar score of < 7 while 83 % had Apgar score of ≥ 7 . No statistically significant difference was observed when the two groups were compared ($p > 0.05$). In the study group 13% pregnant women developed pre-eclampsia while in control

group 2% women developed pre-eclampsia. In the study group, 29% pregnant women developed IHCP while in control group 5% pregnant women developed IHCP. In the study group 20% of newborn had NICU admission while 80% were handed over to their families. In Control group, 7% of newborns had NICU admission while 93% were handed over to their families. Statistically significant difference was observed when the two groups were compared ($p < 0.01$).

Table 3: Comparison of lipid profile of women who developed diagnosing complications vs who did not develop diagnosing complications in study group

GDM	Total Cholesterol	Triglyceride	HDL	LDL	VLDL
Yes	313.10 \pm 27.77	245.20 \pm 19.77	39.50 \pm 5.79	128.40 \pm 8.38	59.15 \pm 3.28
No	281.11 \pm 47.49	205.37 \pm 42.63	40.41 \pm 5.91	120.55 \pm 12.33	51.07 \pm 11.40
P value	P < 0.01	P < 0.001	P > 0.05	P < 0.01	P < 0.01
GHTN					
Yes	289.71 \pm 51.08	223.00 \pm 41.98	39.42 \pm 7.00	124.78 \pm 11.51	54.85 \pm 8.78
No	287.15 \pm 45.40	211.76 \pm 42.28	40.36 \pm 5.71	121.68 \pm 12.12	52.33 \pm 11.08
P value	P > 0.05	P > 0.05	P > 0.05	P > 0.05	P > 0.05
Pre-Eclampsia					
Yes	320.15 \pm 33.95	243.23 \pm 32.34	42.30 \pm 5.76	127.76 \pm 7.38	59.15 \pm 5.41
No	282.63 \pm 45.68	208.87 \pm 41.83	39.91 \pm 5.86	121.27 \pm 12.39	51.72 \pm 11.07
P value	P < 0.01	P < 0.01	P > 0.05	P > 0.05	P < 0.05
Preterm Labor					
Yes	324.33 \pm 21.48	251.25 \pm 19.93	40.75 \pm 4.24	131.08 \pm 8.12	61.75 \pm 2.76
No	282.48 \pm 46.19	208.17 \pm 41.85	40.15 \pm 6.08	120.89 \pm 11.99	51.45 \pm 10.89
P value	P < 0.01	P < 0.01	P > 0.05	P < 0.01	P < 0.01
IHCP					
Yes	321.03 \pm 15.11	238.24 \pm 19.87	36.93 \pm 5.24	129.34 \pm 9.57	60.20 \pm 3.12
No	273.81 \pm 47.34	203.16 \pm 44.72	41.57 \pm 5.61	119.16 \pm 11.73	49.61 \pm 11.30
P value	P < 0.001	P < 0.001	P < 0.001	P < 0.001	P < 0.001
SGA					
Yes	317.75 \pm 22.03	229.37 \pm 30.64	43.62 \pm 7.65	130.37 \pm 7.72	60.62 \pm 1.76
No	284.88 \pm 46.63	211.94 \pm 42.91	39.93 \pm 5.65	121.40 \pm 12.10	52.00 \pm 10.97
P value	P < 0.05	P > 0.05	P > 0.05	P < 0.05	P < 0.05

The mean cholesterol, TG, LDL and VLDL among women who developed GDM in study group was 313.10 \pm 27.77, 245.20 \pm 19.77, 128.40 \pm 8.38, 59.15 \pm 3.28 respectively while in women who did not develop GDM was 281.11 \pm 47.49, 205.37 \pm 42.63, 120.55 \pm 12.33, 51.07 \pm 11.40 respectively. The mean HDL in women who developed GDM was 39.50 \pm 5.79 while in women who did not develop

GDM was 40.41 \pm 5.91. The increase in total cholesterol, TG, LDL and VLDL was statistically significant ($p < 0.01$) when the groups were compared while there was no statistically significant difference in HDL levels when the groups were compared ($p > 0.05$). The mean cholesterol, TG, LDL VLDL and HDL among women who developed GHTN in study group was 289.71 \pm 51.08, 223.00 \pm 41.98, 124.78 \pm

11.51, 54.85 ± 8.78 , 39.42 ± 7.00 respectively while in women who did not develop GHTN was 287.15 ± 45.40 , 211.76 ± 42.28 , 121.68 ± 12.12 , 52.33 ± 11.08 , 40.36 ± 5.71 . The mean cholesterol, TG, and VLDL among women who developed pre-eclampsia in study group was 320.15 ± 33.95 , 243.23 ± 32.34 , 59.15 ± 5.41 respectively while women who did not develop pre-eclampsia was 282.63 ± 45.68 , 208.87 ± 41.83 , 51.72 ± 11.07 . The mean HDL and LDL among women who developed pre-eclampsia in study group was 42.30 ± 5.76 , 127.76 ± 7.38 respectively with women who did not develop pre-eclampsia women was 39.91 ± 5.86 , 121.27 ± 12.39 . The mean cholesterol, TG, LDL and VLDL among women who developed preterm labor in study group was 324.33 ± 21.48 , 251.25 ± 19.93 , 131.08 ± 8.12 , 61.75 ± 2.76 respectively with women who did not develop preterm labor was 282.48 ± 46.19 , 208.17 ± 41.85 , 120.89 ± 11.99 , 51.45 ± 10.89 . The mean HDL was 40.75 ± 4.24 in women who developed preterm labor with women who did not develop preterm labor was 40.15 ± 6.08 . The mean cholesterol, TG, LDL, VLDL and HDL among women who developed IHCP in study group was 321.03 ± 15.11 , 238.24 ± 19.87 , 129.34 ± 9.57 , 60.20 ± 3.12 , 36.93 ± 5.24 respectively with women who did not develop IHCP was 273.81 ± 47.34 , 203.16 ± 44.72 , 119.16 ± 11.73 , 49.61 ± 11.30 , 41.57 ± 5.61 . The mean cholesterol, LDL, VLDL in women who developed SGA in study group was 317.75 ± 22.03 , 130.37 ± 7.72 , 60.62 ± 1.76 respectively with women who did not develop SGA was 284.88 ± 46.63 , 121.40 ± 12.10 , 52.00 ± 10.97 respectively. The mean TG and HDL was 229.37 ± 30.64 , 43.62 ± 7.65 in women who developed SGA with women who did not develop SGA was 211.94 ± 42.91 , 39.93 ± 5.65 .

Discussion

Certain physiological changes during pregnancy, including lipid metabolism,

support fetal growth and development. The accumulation of adipose cells in the tissues and hepatic lipid synthesis increases and this physiological adaptation is associated with changes in lipid profile during pregnancy. There is increased concentration of TC, TG, LDL-C and decrease in HDL-C during normal pregnancy. Accumulation of lipids in maternal tissues and the development of maternal hyperlipidemia occur in pregnancy. In some cases, a maladaptation occurs and these levels increase over the physiological range leading to dyslipidemia which causes complications like preeclampsia, GDM, and preterm labor.

In our study the mean age of the pregnant women in the study group was 24.89 ± 3.12 years whereas in the control group it was 24.72 ± 3.76 years. The two groups were identical with respect to the age distribution with no statistically significant difference (p value >0.05). Our study was also consistent with the study conducted by Abha singh et al [1] in 2015 where the mean age of the women in the study group was 24.61 years and in control group it was 25.63 years with similar age distribution.

In our study there were 81% primigravida and 19% multigravida. In the control group 80% patients were primigravida and 20% multigravida. On comparison, the two groups showed no statistically significant difference ($p > 0.05$). Our study was consistent with the study conducted by Hong Shen et al in 2014 where the majority of women were primigravida that is 89.4% in study group and 89.2% in control group. [20]

In our study the mean BMI of the pregnant women in the study group was 21.89 ± 1.89 kg/m² whereas in the control group, it was 21.52 ± 1.47 kg/m². The two groups were identical with respect to the BMI with no statistically significant difference (p value >0.05). Our study was consistent with the study conducted by Hong Shen et

al.[20] in 2014 where the mean pre pregnancy BMI was $22.07 \pm 2.93 \text{ kg/m}^2$ AND Wen-Yuan Jin et al [21] in 2010 where the mean pre pregnancy BMI was $20.66 \pm 2.70 \text{ kg/m}^2$.

The Study group showed significant increase in total cholesterol, TG, LDL and VLDL except HDL ($p > 0.05$) when compared to control group and the difference was found to be statistically significant ($p < 0.001$). Study conducted by Mohammed Abdu Helmy et al [22] is also consistent with our study. They included 164 pregnant women in Suez Canal Authority Hospital in Ismailia city, during the period 2018-2019. An association between maternal lipid profile status of the pregnant mother and its fetomaternal outcome were noted. 28 pregnant women developed maternal complications like GDM which was seen in 3.05% of patients. Our study was consistent with the study conducted by Seyedeh Hajar Sharami et al [23] in Al-Zahra hospital, Rasht, Iran in 2016-2017. A total of 539 pregnant women were participated in this study at 28-42 weeks of gestational age. A total of 448 participants (83.1%) had deranged lipid profile and 31% cases had GDM.

The Study conducted by Mohammed Abdu Helmy et al [22] is also consistent with our study. They included 164 pregnant women in Suez Canal Authority Hospital in Ismailia city, during the period 2018-2019. An association between maternal lipid profile status of the pregnant mother and its fetomaternal outcome were noted. 28 pregnant women developed maternal complications like GHTN which was seen in 3.66% of patients.

The Study group among Pre-eclampsia shows significant increase in total cholesterol, TG, LDL and VLDL except HDL ($p > 0.05$) when compared to control group and the difference was found to be statistically significant ($p < 0.001$). Study conducted by Mohammed Abdu Helmy et al [22] is also consistent with our study.

They included 164 pregnant women in Suez Canal Authority Hospital in Ismailia city, during the period 2018-2019. An association between maternal lipid profile status of the pregnant mother and its Fetomaternal outcome were noted. 28 pregnant women developed maternal complications like Pre-eclampsia which was seen in 2.44% of patients.

In the study group, 12% pregnant women developed preterm labor while in control group 18% pregnant women developed preterm labor. No statistically significant difference was observed when the two groups were compared ($p > 0.05$). The Study conducted by Mohammed Abdu Helmy et al.[22] is also consistent with our study. They included 164 pregnant women in Suez Canal Authority Hospital in Ismailia city, during the period 2018-2019. An association between maternal lipid profile status of the pregnant mother and its fetomaternal outcome were noted. 28 pregnant women developed maternal complications in which PTL was seen in 4.27%.

In the study group, 29 % pregnant women developed IHCP while in control group 5% pregnant women developed IHCP. Statistically significant difference was observed when the two groups were compared ($p < 0.001$). A prospective study done by Marcus G. Martineau et al [24] compared metabolic outcomes in cholestatic and uncomplicated singleton pregnancies from 2011–2014. [25] A total of 26 women with IHCP and 27 control pregnancies with no prior history of gestational diabetes mellitus. It was seen that IHCP is characterized by increased fasting triglycerides ($p < 0.005$) and reduced HDL cholesterol ($p < 0.005$). The offspring of mothers with IHCP had significantly larger customized birth weight centiles, adjusted for ethnicity, sex, and gestational age ($p < 0.005$).

Conclusion

Evaluation of lipid profile during 2nd and 3rd trimesters can predict pregnancy associated complications. It may help in counseling the pregnant women to have a modified life style with increased physical activities, dietary modifications and timely interventions when required as the treatment of hyperlipidemia is a challenging issue in pregnancy due to the fact that most of the drugs used for the treatment of dyslipidemia belong to category C or X. As the sample size of our study was small with limited time duration, further studies with a large sample size should be done to make a recommendation.

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