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CHANGES IN MATERNAL SERUM LIPID PROFILE AND APOLIPOPROTEIN A IN PREGNANCIES WITH FETAL GROWTH RESTRICTION :A CASE CONTROL STUDY

Obstetrics & Gynaecology

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ABSTRACT

Background: Fetal growth restriction is a condition where a fetus is unable to achieve its genetic growth potential and is one of the leading causes for perinatal morbidity and mortality. There are immense changes in maternal lipid profile during pregnancy to meet the increasing need for energy of the developing fetus. The transfer of lipidsfrom mother to the fetus is imperative for brain growth, production of steroid hormones and synthesis of cell membrane. Any abnormalities in maternal lipid metabolism are associated with various complications like fetal growth restriction. Objective: To study the changes in maternal serum lipid profile and lipoprotein A in pregnancies with fetal growth restriction. **Materials and method:** A prospective case-control study was conducted at Rohilkhand medical college and hospital, Bareilly, Uttar Pradesh where Group A (n=59) having pregnant females with fetal growth restriction (FGR) diagnosed by ultrasound and Group B (n=59) having pregnant females with normal growth fetuses in period of gestation between 28-34 weeks with singleton pregnancies were taken. After at least 10 hours of fasting, venous blood samples were taken and send for serum lipid profile and apolipoprotein A measurements. These values were compared in pregnancies with FGR (Group A) and normal fetal growth pregnancies (Group B).**Results:** In this study, it was observed that the values of total serum cholesterol, LDL- cholesterol, HDL- cholesterol, VLDL-cholesterol, triglycerides and Apolipoprotein A were lower in group with FGR (Group A) than in normal fetal growth pregnancies group (Group B) significantly. Mean +/-SD of total cholesterol was198.67+/-56.54 mg/dl in Group A and 245.80+/-57.76 mg/dl in Group B. Similarly, Mean +/-SD of LDL cholesterol was 100.34+/-23.75 mg/dl in Group A and 134.44+/- 43.64 mg/dl in Group B. Mean +/-SD of HDL was 54.23+/-12.34 mg/dl in Group A and 78.34+/-13.87 mg/dl in Group B. Mean +/-SD of VLDL cholesterol was 42.36+/-12.79 mg/dl in Group A and 64.24+/-11.83 mg/dl in Group B. Mean +/- SD of Triglycerides was 202.96+/-62.19 mg/dl in Group A and 305.24+/-68.80 mg/dl in Group B. Mean +/-SD of apolipoprotein A was 157.76+/-14.84 mg/dl in Group A and 178.34+/-18.38 mg/dl in Group B. **Conclusion:** As total serum cholesterol, LDL- cholesterol, HDL- cholesterol, VLDL-cholesterol, triglycerides and Apolipoprotein A levels are significantly lower in pregnancies with FGR (Group A) than in normal fetal growth pregnancies (Group B), these can be used as marker for FGR.

KEYWORDS

Maternal Lipid Profile, Triglycerides, Fetal Growth Restriction, Serum Cholesterol, Serum Apolipoprotein A.

INTRODUCTION

Lipid metabolism changes significantly during pregnancy. Physiological maternal hyperlipidemia is required for normal fetalgrowth[1-3]. In 1845 Bacqueral and Rodier, first reported these changes but this needs further understanding and explanation[4]. Both hormonal and genetic factors have been shown to be responsible for modifications in lipid and lipoprotein metabolism in pregnancy. Recent studies have shown that intrauterine growth retardation is associated with abnormal lipid metabolism during pregnancy. It has also been postulated that abnormal lipid metabolism in pregnancy is associated with ischemic heart disease (IHD) and atherogenesis in the mother due to changes in maternal microcirculation[1]. Fetal growth restriction causes increased chances of stillbirth and other neonatal complications. It also results in long term health complications like neurodevelopmental disorders and cardiovascular impairment in later life[5,6].

When a fetus fails to achieve its genetic growth potential, it is known as fetal growth restriction. After prematurity, it is the most common cause of perinatal morbidity and mortality[7,8]. It includes those fetuses whose birth weight is below 10thpercentile or is <2 SD below the mean weight appropriate for that gestational age or the abdominal circumference less than 10thpercentile[9].

Depending upon the study population, the incidence lies between 3% and 10%[10].

Pregnancy demands increased energy for the developing fetus and preparation for lactation[11]. In normal uncomplicated pregnancy maternal lipids increase progressively. Serum cholesterol increases by 25-50 % in the third trimester and triglycerides level increase by 2-3 times[12]. During pregnancy,there is increase in female sex hormone, estrogen and human placental lactogen. This results in an increase in lipid synthesis more commonly by the liver and lipid metabolism[13]. In the later gestation, continuously increasing insulin resistance, increasing plasma levels of estrogen and human placental lactogen result in catabolic changes responsible for development of hypertriglyceridemia in the mother[14]. Hyperlipidemia also occurs especially in the last trimester due to increased fat depot breakdown. Since cholesterol and triglycerides are required to meet the increasing energy requirements of the mother and the fetus which is growing rapidly, the physiological basis for hyperlipoproteinemia and hyperlipidemia especially during late gestation is explained to some extent[14].

The transfer of lipids from the mother to the fetus is imperative for fetal development, especially for production of steroid hormones, synthesis of cellular membranes and brain growth[15].

Lipids are necessary substrates not only for energy metabolism but also for structural development of fetus[16]. Placental lipases hydrolyse maternal triglycerides as these cannot cross the placenta directly. This produces fatty acids which are then made available to the fetus[17]. Similarly, cholesterol is required for cell membrane, biliary acids and steroid hormone synthesis[18] Due to any reason if there is disturbance in these processes, which might be due to placental dysfunction or maternal lipid profile derangement, can eventually lead to restricted fetal growth.

Recent evidence has shown that abnormal fetal growth might be linked to abnormal maternal serum lipid profile. Still there is ashortage of studies and literature on establishing the relationship between fetal growth restriction and lipid metabolism in otherwise normal pregnancy. The association between various lipid parameters in the mother and fetal growth restriction has not received much attention and remains controversial till date. Most importantly, utilizing maternal lipid profile and related changes as a marker for fetal growth restriction needs further investigation. Also, specific contribution of each lipid parameter for risk of fetal growth restriction after eliminating confounding factors requires more exploration.

Aim and Objectives

Aim: To study the changes in serum lipid profile and lipoprotein A in pregnancies with fetal growth restriction.

Objectives:

- To analyse the serum lipid profile and apolipoprotein A in pregnancies with fetal growth restriction
- To compare the serum lipid profile and apolipoprotein A in pregnancies with fetal growth restriction with that in normal pregnancies.

MATERIALS AND METHODS

Study place: The study was conducted in Department of Obstetrics and Gynaecology at Rohilkhand medical college and hospital, Bareilly.

Type of study: This was a prospective case control study.

Time period of study: The study was conducted for a period of 1 year from April 2025 to March 2026

Method: After approval from the institutional ethics committee, following method was used for the study.

A written consent was taken from each woman participating in the study after explaining the procedure to the patient in their understandable language. Weight, height and BMI were measured. After at least 10 hours of fasting, venous blood samples were taken and sent for serum lipid profile and apolipoprotein A measurements. These values were compared in pregnancies with FGR and normal pregnancies. Patients were also followed up till delivery for period of gestation at delivery and birth weight of the baby.

Sample size calculation:

A total of 118 pregnant women between 28 – 34 weeks of gestation were recruited out of which 59 cases were diagnosed with FGR by ultrasound and 59 cases with normal fetal growth pregnancy.

A two-sample t- test formula was used for sample size calculation taking a 30 mg/dl mean difference in triglyceride levels with 90% power and 5% level of significance with a pooled standard deviation of 50 mg/dl and ratio of cases to controls is 1:1.This study was a case control study with ratio of cases to controls as 1:1. So the formula used for sample size calculation was

$n = 2 (Z_{\alpha/2} + Z_{\beta})^2 . \Sigma^2 / \Delta^2$

where

n= sample size per group

- $Z_{\alpha/2}$=Confidence level (e.g., 1.96 for 95% confidence).
- Z_{β}=Power (e.g., 1.28 for 90% power).
- Σ=Pooled standard deviation of the outcome variable (50 mg/dl)[24]
- Δ=mean difference in triglyceride levels (30 mg/dl)[24]Keeping the values in the formula $n = 2 \times (1.96 + 1.28)^2 \times 50 \times 50/30 \times 30 = 58.3 \sim 59$ (per group)

Inclusion criteria:

- Antenatal cases with gestational age between 28-34 weeks and singleton pregnancies.
- Estimated fetal weight (EFW) below the 10th percentile for gestational age.
- Absence of structural or chromosomal fetal abnormalities.
- Maternal age 18-40 yrs.

Matching of controls for gestational age was done and EFW for controls was between 10thand 90thpercentiles.

Exclusion criteria:

- Multiple pregnancies
- Any chronic diseases in the mother affecting metabolism of lipids (thyroid disorders, renal disease, liver disease).
- Pre-existing diabetes mellitus or GDM or chronic hypertension or preeclampsia.
- Patients taking lipid lowering drugs or corticosteroids.
- Fetuses with structural or genetic abnormalities.
- History of substance abuse or smoking in mother.

STATISTICAL ANALYSIS: The coding, entry of the data, it's clearing and compiling was done in excel sheets. The data was imported to SPSS (Statistical Package for the Social Sciences) version 23.0 where means and standard deviation was calculated. Appropriate statistical test was applied depending on the type and distribution of data. A p value of less than 0.001 was considered statistically significant.

RESULTS

As shown in Table 1, no significant difference in maternal age and BMI between group 1 and group 2 was seen. Statistically significant difference was observed in gestational age at delivery and birth weight of baby between the two groups

Table 1: Comparison of Demographic factors of mother and other clinical variables in Group A and Group B

Variable	Group A (FGR)	Group B (Normal fetal growth pregnancy)	p- value
Maternal age (Years)	26.56+/-4.55	27.45+/-4.34	0.28
BMI (Kg/m^2)	22.45+/-1.48	22.14+/-1.56	0.27
Gestational age at delivery (weeks)	36.5+/-1.6	39.6+/-1.5	<0.001
Birth weight (Kg)	1.86+/-0.84	2.80+/-0.76	<0.001

Table 2: Comparison of maternal lipid profile and Apolipoprotein A in Group A and Group B

Variable	Group A (FGR)	Group B (Normal pregnancy)	p- value
Total serum cholesterol (mg/dl)	198.67+/-56.54	245.80+/- 57.76	<0.001
LDL-cholesterol (mg/dl)	100.34+/-23.75	134.44+/-43.64	<0.001
HDL-cholesterol (mg/dl)	54.23+/-12.34	78.34+/-13.87	<0.001
VLDL-cholesterol (mg/dl)	42.36+/-12.79	64.24+/-11.83	<0.001
Triglycerides (mg/dl)	202.96+/- 62.19	305.24+/- 68.80	<0.001
Apolipoprotein A (mg/dl)	157.76+/- 14.84	178.34+/- 18.38	<0.001

Statistically significant difference was observed in values of total serum triglycerides, LDL- cholesterol, HDL- cholesterol, VLDL-cholesterol, triglycerides and Apolipoprotein A in group with FGR (Group A) and in normal pregnancies group (Group B).

These values were found to be noticeably low in pregnancies with FGR than in normal fetal growth pregnancies.

DISCUSSION

Recently, a few studies have been done to establish the relationship between FGR and maternal serum lipid profile and Apolipoprotein A. **Contini *et al.* (201G)**[19] conducted a study and found that low maternal cholesterol and LDL levels are more frequently associated with FGR than with control group. Similarly, **Miranda *et al.* (2018)**[20] did a prospective study in which a group of 52 pregnant females with singleton gestation with fetal growth restriction later than 32 weeks of pregnancy were taken as cases. 28 pregnant females with appropriate for gestational age fetuses and low risk pregnancies were taken as control. After delivery, samples were taken from maternal blood and sent for serum lipid profile. Plasma cholesterol, intermediate density lipoproteins (IDL), triglycerides and high-density lipoproteins (HDL) showed notably lower concentrations in mothers having fetal growth restricted fetuses in comparison to controls ($p<0.01$). These findings were also evident from the studies of **Bae *et al.* (200G)**[21] who found that total cholesterol, LDL and triglyceride levels were markedly lower in pregnant females with FGR as compared to control group. But they also concluded that there was nodifference in levels of other lipids. In their study, they inferred that in FGR pregnancies LDL levels do not rise as much as they rise in normal pregnancies and this may be related to pathogenesis of fetal growth restriction.

In contrast, **Satter *et al.* (1GGG)**[22] in their study found that VLDL1, HDL and median triglyceride concentrations were not significantly different in fetal growth restricted and appropriate for gestational age fetuses. But they also observed that concentration of LDL-cholesterol, IDL, LDL, VLDL2 and median cholesterol were quite lower in pregnant women with FGR than those with AGA fetuses ($p<0.01$).

Munoz *et al.* (1GG5)[23] in their study found that plasma triglyceride, total cholesterol, LDL- cholesterol tend to increase as period of gestation increases. This increase is more significant after 25 weeks of gestation. They observed that in FGR group concentration of triglyceride were significantly lower than in AGA group. There was no significant difference in other parameters.

CONCLUSION

As total serum cholesterol, LDL- cholesterol, HDL- cholesterol, VLDL-cholesterol, triglycerides and Apolipoprotein A levels are significantly lower in pregnancies with FGR (Group A) than in normal fetal growth pregnancies (Group B), these can be used as a marker for FGR.

From this study, it can be concluded that levels of maternal serum lipid and Apolipoprotein A need to rise in an appropriatemanner to ensure normal fetal growth and development. Failure of this may lead to FGR and compromise in fetal structural development. To establish these findings more studies are required in a larger population.

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