Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

# ASSOCIATION OF MATERNAL TRIGLYCERIDES LEVEL WITH NEONATAL MACROSOMIA IN NON-OBESE NON-DIABETIC PREGNANT WOMEN

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**ABSTRACT:**

INTRODUCTION: Maternal dyslipidemia experts potential and adverse impacts on pregnant women and newborns. However, the association between maternal serum triglycerides level and the risk of macrosomia has not yet been clearly studied.We did this study for association between the maternal serum triglycerides level and risk of macrosomia among the non-diabetic and non obese pregnant women.

OBJECTIVE: To find the associations of maternal triglyceride levels with neonatal macrosomia in non-obese and pregnant women without Diabetes Mellitus . SETTING: SCB Medical College, Cuttack, Odisha, India. MATERIAL AND METHOD: This was a escriptive cross-sectional study of 100 pregnant patients with BMI less than 30. The medical records of 100 non obese and non-diabetic pregnant women at term were prospectively analyzed. Maternal fasting serum triglyceride levels were measured during late pregnancy. Scatter diagram was used to analyze the variables associated with the risk of macrosomia.RESULTS:Maternal TG level was higher in patient with macrosomia babies (333.00 ± 51.62) compare to those without macrosomia (253.15 ± 81.02). This difference in mean was statistically significant (P value = 0.001) (Table 5). There was a positive correlation between birth weight and maternal triglyceride level which was statistically significant with correlation coefficient value of 0.278 (r) and p value of 0.005. CONCLUSION:Our findings highlight the importance of maternal lipid metabolism in fetal overgrowth and may have implications for the etiology and primary prevention of macrosomia. However, further prospective investigations involving larger population and basic research studies are necessary to fully evaluate their clinical value and the mechanisms

**Key words:** Maternal triglyceride, Macrosomia

## INTRODUCTION

Macrosomia is defined as a fetal birth weight equal to or greater than 4000g irrespective of gestational age, has a serious impact on maternal and fetal perinatal outcomes[1] .For decades, the occurrence of macrosomia has been attributed to high maternal blood glucose. With regards to the Pedersen hypothesis, excess maternal glucose transfers through the placenta and stimulates islet cells and hyperinsulinemia,

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

resulting in macrosomia[2].Maternal dyslipidemia experts potential and adverse impacts on pregnant women and newborns. However, the association between maternal serum triglycerides level and the risk of macrosomia has not yet been clearly studied.

We did this study for association between the maternal serum triglycerides level and risk of macrosomia among the non-diabetic and non obese pregnant women.

Macrosomia is associated with important neonatal complications such as birth trauma, hypoglycemia, and hematologic and respiratory complications[3]. Macrosomia is a major risk factor for obesity and type 2 diabetes mellitus in adolescence and young adulthood.

Even though fetal macrosomia occurs more often in pregnancies of diabetic mothers, considerable numbers of infants with macrosomia are born from non-diabetic mothers (8–14%)[4]. Clausen et al in 2005 have assessed the risk of macrosomia in relation to early second trimester maternal serum lipids[5]; In the current study, we have focused on maternal serum lipids during the first weeks of the third trimester of pregnancy. This is because the possibility of developing a late impaired glucose metabolism after the screening time in some of the mothers could not be excluded.

There are also known risk factors for macrosomia, including maternal fasting glycemia, body mass index (BMI) prior to pregnancy, and HbA1c[6]. In the current study, we used healthy non-diabetic, non-obese and normotensive pregnant women to focus on the remaining risk factors after restricting our study to such normal mothers. Growth of the fetus depends on nutrients such as glucose, lipids, and amino acids.[4]

Therefore, in this study we evaluated the association between metabolic characteristics, especially serum triglyceride levels of the healthy non-diabetic and non-obese pregnant women in the first weeks of the third trimester of the pregnancy and its association with delivering macrosomic or large-forgestational-age (LGA) neonates.

Maternal abnormal lipid profile can also induce excessive fetal growth[7]. The changes in lipid metabolism during pregnancy are characterized by fat accumulation in maternal depots during early pregnancy and development of hyperlipidemia later[8]. Recently, some maternal lipid parameters have been identified as independent risk determinants of fetal overgrowth, especially in pregnancies complicated by GDM or with DM3[7]. Several studies have demonstrated that in non-diabetic pregnancies, birth weight and the risk of macrosomia or large for gestational age (LGA) were positively associated with maternal serum triglyceride (TG) levels[9], and while other studies failed to find any association. Studies have shown that patterns of maternal dyslipidemia and the prevalence of macrosomia vary across populations and ethnic groups[10]. While a few studies have explored the relationship between maternal serum lipids and neonatal birth weight in Chinese population, their sample sizes were relatively small[11].In the present study, we sought to evaluate the association between maternal serum triglyceride levels at late gestation and the risk of macrosomia among a large group of women without DM.

**The National Cholesterol Education Program has set guidelines for triglyceride levels[12]**

| **Level** | | **Interpretation** |
|---|---|---|
| **(mg/dL)** | **(mmol/L)** | |
| < 150 | < 1.70 | Normal range – low risk |
| 150–199 | 1.70–2.25 | Slightly above normal |
| 200–499 | 2.26–5.65 | Some risk |
| 500 or higher | > 5.65 | Very high – high risk |

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

The hypertriglyceridemia that occurs during pregnancy is due to both the increased production of triglyceride rich lipoproteins and the decreased clearance of triglyceride rich lipoproteins. The increased production of triglyceride rich lipoproteins by the liver is due to the increased lipolysis of triglycerides that occurs in adipocytes, which results in an increase in free fatty acids that are transported to the liver. In the liver, these free fatty acids are used in the synthesis of triglycerides, which are then packaged into VLDL and secreted by the liver. The high estrogen levels in the third trimester stimulate lipogenesis and VLDL production in the liver. The decrease in clearance of triglyceride rich lipoproteins is due to a decrease in lipoprotein lipase and hepatic lipase[13]. The decrease in hepatic lipase is due to the elevated estrogen levels, while the decrease in lipoprotein lipase is likely due to a combination of factors including insulin resistance and elevated estrogen levels. The triglyceride enrichment of LDL and HDL is due to an increase in CETP activity resulting in the transfer of triglyceride from VLDL to LDL and HDL and a decrease in hepatic lipase, which decreases the removal of triglycerides from these lipoprotein particles[14].

Maternal dyslipidemia is linked to adverse perinatal outcomes. In animal studies, mice fed a hypercholesterolemic diet had increased rates of abortion, mortality, small litter sizes and lower birth weights of offspring. The offspring of hypercholesterolemic mothers also showed growth impairment and reduced renal function, effects only partially reversed by being fed a standard diet after delivery[15] .. Variations in maternal lipid metabolism have an impact on fetal growth. In pregnancies of non-diabetic mothers, maternal triglyceride levels are correlated with fetal birth weight. Concentration of triglycerides in the third trimester is a stronger predictor of birth weight than glucose parameters[16.]

Maternal lipid metabolism is vital determinant of fetal development and growth. . Maternal lipid profile at early and midpregnancy gestation is significantly associated with neonatal birth weight, and with the risk of macrosomia. .Maternal serum TG does not directly cross the placenta, but the presence of lipoprotein receptors, various fatty acid-binding proteins, and lipase activity in the placenta enables the release of free fatty acids (FFAs) from TG and their efficient transport to the fetus. It is speculated that the increased hydrolysis of maternal TG by placental lipoprotein lipase to FFAs and the excessive delivery of fatty acids to the fetus may be partly responsible for the increased risk of macrosomia among women with hypertriglyceridemia.

## OBJECTIVE:

To find the associations of maternal triglyceride levels with neonatal macrosomia in non-obese and pregnant women without DM.

## STUDY DESIGN

 Descriptive cross-sectional study of 100 pregnant patients with BMI less than 30.

## INCLUSION CRITERIA

1) Healthy pregnant women without diabetes and without obesity.
2) Pregnant mothers of BMI 18-29
3) live-born singleton pregnancy
4) delivery at 37–42 gestational weeks
5) naturally conceived

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

6) had integrated medical records and a clear gestational age.
7) Macrosomic babies.Materials and Methods

**EXCLUSION CRITERIA**

1) Preterm labour prior to 37 weeks of gestational age.
2) Any abnormality or disorder in fetus or neonates.
3) pre-gestational DM or gestational diabetes mellitus (GDM) or type 2 DM
4) Multiple pregnancies
5) Pregnant mothers with BMI≧30

**METHODS**

In this study, the cases were taken from those who attended the antenatal clinics of the O&G department of SCBMCH. Cuttack or were admitted to the same department during the period October 2019 to September 2020 .AII the cases had antenatal check up in the antenatal period and they were advised for delivery and postpartum check up here. During the visit women were informed about the present study and the consent were taken. A detailed clinical assessment of the patient was performed in the outpatient department including history (diabetes, BMI & socioeconomic status, etc), general physical examination and obstetrical examination. Routine investigations were done during antenatal visits. Serum triglyceride levels of non-obese and non-diabetic pregnant women who fulfilled inclusion criteria after 8-10 hours of fasting in late gestation. All women are generally healthy pregnant women carrying a single fetus having BMI between 18 kg per $m^2$ and 29 kg per $m^2$ without a history of diabetes prior to or in previous pregnancies and with a negative result from the diabetes screening test in the current pregnancy. Also took a blood sample of blood sugar level(GCT) to rule out PGDM/type2 DM/ GDM assessed 2hours after administering 75gms of oral glucose. The main outcome was measurement of neonatal birth weight.

The medical records of 100 non obese and non-diabetic pregnant women at term were prospectively analyzed. Maternal fasting serum triglyceride levels were measured during late pregnancy. Scatter diagram was used to analyze the variables associated with the risk of macrosomia.

**Statistical analysis**

All the data collected were entered into the Microsoft Excel 2007 software and further analyzed in SPSS version 24 (IBM Inc. Chicago). All the categorical variables were expressed in terms of number/frequency and percentages. Association between two categorical variables were obtained by using Chi-squared test/Fischer Exact test. All the continuous variables were expressed in terms of mean and standard deviation. Significance level in comparison of means were obtained by independent sample t-test test. Histograms and box plots were used to describe the continuous variables. Bar and pie charts were used to describe the categorical variables. Correlation between two continuous variable was measured by person correlation coefficient and scatter plot was used to depict the correlation. A p value less than 0.05 was considered statistically significant.

**RESULTS:**

The current study aims to findout the associations of maternal triglyceride levels with neonatal macrosomia in a total of 100 non-diabetic and non-obese women. The mean

ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

age of the study participant was 26.21 ± 3.42 years which ranged from a minimum of 19 years to a maximum of 38 years. Mean weight gain during pregnancy was 11.08 ± 1.29 kilograms with a minimum of 8 kgs and a maximum of 14 kgs. Mean BMI of the study participants was 24.56 ± 2.03 Kg/m2 . Mean 2-hour GCT after giving 75 grams of glucose was 100.81 ± 14.10 with a minimum of 75 and a maximum of 132 (Table-1)

Mean maternal triglyceride level was 254.5 ± 79.25 with a minimum of 100 to a maximum of 434 (Table 2). Mean birth weight was 3.85 ± 0.20 with a minimum of 3.6 to a maximum of 4.8. Similarly, RBS was 66.74 ± 15.60 with a minimum of 42 to a maximum of 99 (Table 3)

Fetal outcome among the patient was given in table 4.. Macrosomia was present in 13% of the subjects . Total 22 neonates needed NICU admission. Neonatal compilation like hypoglycemia and jaundice was seen in 11% each .

Maternal TG level was higher in patient with macrosomia babies (333.00 ± 51.62) compare to those without macrosomia (253.15 ± 81.02). This difference in mean was statistically significant (P value = 0.001) (Table 5). There was a positive correlation between birth weight and maternal triglyceride level which was statistically significant with correlation coefficient value of 0.278 (r) and p value of 0.005 (figure 1). We did not find any statistical significant difference with respect to BMI, RBS of newborn, weight gain in pregnancy, SBP and DBP.

**DISCUSSION:**

Here in our study, mean height of the subjects in the study was 156.39 ± 5.35 centimeters and the mean weight was 59.96 ± 5.03 kilograms. Mean weight gain during pregnancy was 11.08 ± 1.29 kilograms with a minimum of 8 kgs and a maximum of 14 kgs. Mean BMI of the study participants was 24.56 ± 2.03 Kg/m2.

**Blood sugar level & Blood pressure of the patients**

Here in our study, mean 2-hour GCT after giving 75 grams of glucose was 100.81 ± 14.10 with a minimum of 75 and a maximum of 132 to exclude GDM/Type 2 DM. Mean systolic blood pressure was 112.52 ± 9.18 while the mean diastolic blood pressure was 74.38 ± 5.63.On reviewing literature, association of maternal serum lipids at late gestation with the risk of neonatal macrosomia in women without diabetes mellitus by Xiangxiang Wang et al145 in 2018,the mean SBP in mmhg was 120.07 ± 12.25, mean DBP in mmHg was 76.63 ± 9.33.

**Triglyceride levels & newborn birth weight:**

Here the mean maternal triglyceride level was 254.5 ± 79.25 with a minimum of 100 to a maximum of 434 . Mean birth weight was 3.85 ± 0.20 with a minimum of 3.6kg to a maximum of 4.8kg. Study of Association of maternal serum lipids at late gestation with the risk of neonatal macrosomia in women without diabetes mellitus by Xiangxiang Wang et al in 2018 showed the median of serum TG levels in the macrosomia group was much higher than that in the control group (3.52 mmol/L vs. 3.09 mmol/L, $p < 0.001$)[17].

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**Prevalence of macrosomia**

Here macrosomia was present in 13% of the subjects . Total 22 neonates needed NICU admission. Neonatal compilation like hypoglycemia and jaundice was seen in 11% each . "Study of Association of maternal serum lipids at late gestation with the risk of neonatal macrosomia in women without diabetes mellitus" by Xiangxiang Wang et al in 2018 showed that the overall prevalence of macrosomia was 10.0%[17].

**Association of macrosomia with Maternal triglyceride levels:**

In our study maternal TG level was higher in patient with macrosomia babies (333.00 ± 51.62) compare to those without macrosomia (253.15 ± 81.02). This difference in mean was statistically significant (P value = 0.001) . There was a positive correlation between birth weight and maternal triglyceride level which was statistically significant with correlation coefficient value of 0.278 (r) and p value of 0.005 (figure 1). We did not find any statistical significant difference with respect to BMI, RBS of newborn, weight gain in pregnancy, SBP and DBP. "Study of Association of maternal serum lipids at late gestation with the risk of neonatal macrosomia in women without diabetes mellitus" by Xiangxiang Wang et al in 2018 showed that maternal serum triglyceride (TG) and highdensity lipoprotein cholesterol (HDL-C) levels were related to macrosomia; each 1 mmol/L increase in TG resulted in a 27% increase in macrosomia risk, while each 1 mmol/L increase in HDL-C level resulted in a 37% decrease in macrosomia risk, even after adjusting for potential confounders[17].

**Conclusion**

Our results revealed that high maternal serum TG concentrations in late pregnancy and neonatal macrosomia are associated. Maternal TG level was higher in patient with macrosomia babies (333.00 ± 51.62) compare to those without macrosomia (253.15 ± 81.02). This difference in mean was statistically significant (P value = 0.001) . There was a positive correlation between birth weight and maternal triglyceride level which was statistically significant with correlation coefficient value of 0.278 (r) and p value of 0.005 . The combination of hypertriglyceridemia and low HDL-C levels was a stronger predictor of macrosomia than either alone. Our findings highlight the importance of maternal lipid metabolism in fetal overgrowth and may have implications for the etiology and primary prevention of macrosomia. However, further prospective investigations involving larger population and basic research studies are necessary to fully evaluate their clinical value and the mechanisms involved.

**Funding: None**

**Conflict of Interest: None**

**This study was approved by institutional ethics committee.**

**TABLE:1 Blood sugar level and blood pressure of the study participants**

| | | | | |
|---|---|---|---|---|
| Blood sugar level (2hr GCT)(mg/dl) | Minimum | Maximum | Mean | SD |
| | 75 | 132 | 100.81 | 14.10 |
| Systolic BP(mmHg) | 100 | 130 | 112.52 | 9.18 |
| Diastolic BP(mmHg) | 64 | 90 | 74.38 | 5.63 |

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**Table:2 Maternal triglyceride level**

| | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| Triglyceride level(mg/dl) | 100 | 434 | 254.52 | 79.25 |

**Table:3 Newborn birth weight and sugar level**

| | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| Birth weight in Kg | 3.60 | 4.80 | 3.85 | 0.20 |
| RBS(mg/dl) | 42 | 99 | 66.74 | 15.60 |

**Table 4: Newborn outcome in the study population**

| Out comes | | Number | Percentage |
|---|---|---|---|
| Macrosomia | Present | 13 | 13 |
| | Absent | 87 | 87 |
| NICU Admission | Needed | 22 | 22 |
| | Not needed | 78 | 78 |
| Neonatal complications | hypoglycemia | 11 | 11 |
| | Jundice | 11 | 11 |
| | None | 78 | 78 |

**Table 5: Association of macrosomia with Maternal triglyceride and other factors**

| Variables | Macrosomia present | | Macrosomia absent | | P value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| Matrnal TG | 253.15 | 81.02 | 333.00 | 51.62 | 0.001 |
| BMI | 24.67 | 2.00 | 23.81 | 2.13 | 0.926 |
| RBS of newborn | 67.57 | 15.24 | 61.15 | 17.47 | 0.654 |
| SBP | 101.95 | 14.21 | 93.15 | 10.85 | 0.347 |
| DBP | 112.18 | 9.09 | 114.77 | 9.88 | 0.878 |

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ISSN: 0975-3583, 0976-2833 VOL 12, ISSUE 04, 2021

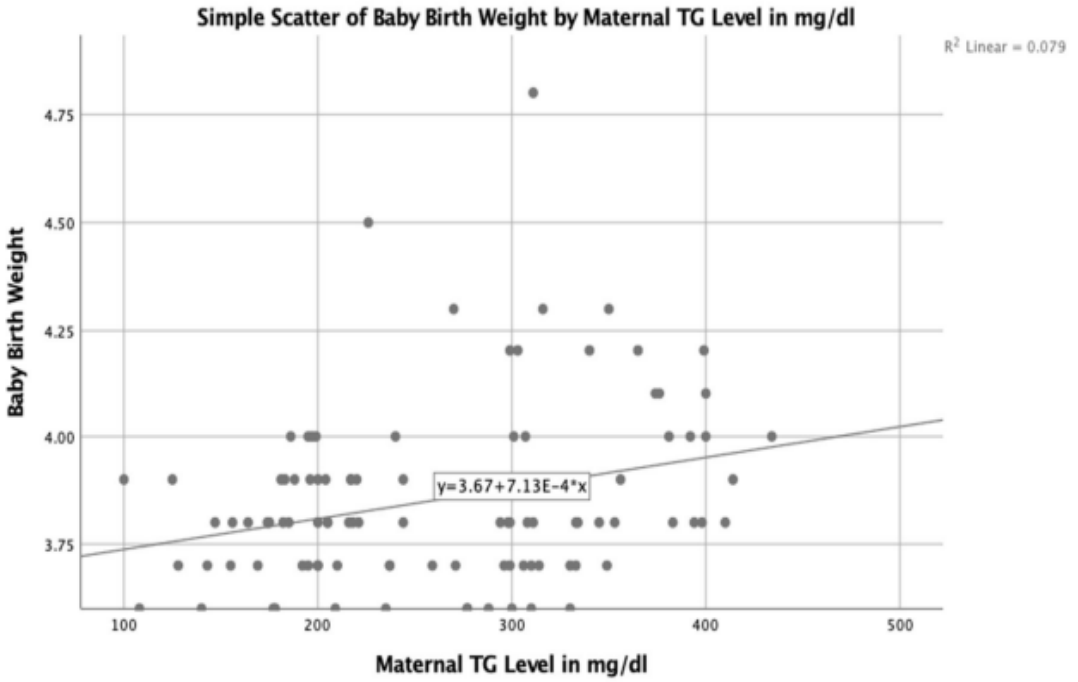


**Figure 1: Correlation between birthweight and maternal triglyceride level**

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