

Association Between Maternal Lipid Profile and Fetal Birth Weight in Type 2 Diabetes Mellitus and Gestational Diabetes Mellitus Pregnancies

Original
Article

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ABSTRACT

Background: Diabetes raises the risk of maternal and neonatal morbidity and mortality. Fetal macrosomia is one of the most common perinatal problems in diabetes pregnancy, particularly in women with poor glycemic control.

Aim: Determine the association between maternal serum lipid levels, particularly TG and TC levels, and newborn BW. Also, the ability of TG and TC levels was tested to predict macrosomia.

Materials and Methods: This observational cohort study was conducted on 150 pregnant women divided into two groups 75 pregnant women with type2 DM and 75 pregnant women with GDM at 3rd trimester GA of 29-40 week. The following lipid parameters were measured.

Results: There is no statistically significant difference between the type 2DM group compared to GDM group regarding age, height, weight, BMI, F.B.G, 2HPP.BG, HbA1c, parity LDL, neonatal weight and gestational age ($p > 0.05$). On the other hand, there was a statistically significant difference between the type 2DM and GDM groups regarding TC, TG, and HDL. By applying Spearman's correlation test, there was a statistically significant positive correlation between neonatal weight and age, TC, TG, and parity in the type 2DM group. Regression analysis defined Neonatal weight development among the type 2DM group as the persistently significant positive predictor for TG.

Conclusion: This research demonstrated the utility of measuring fasting serum TG and TC levels measured at third-trimester pregnancy correlated positively with neonatal BW and may be considered an independent predictor of fetal macrosomia at term in type 2DM and GDM.

Key Words: Fetal birth weight, gestational diabetes mellitus, lipid profiles glycated hemoglobin A.

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INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia due to impaired insulin production, insulin action, or both. Diabetes' persistent hyperglycemia has long-term consequences, including damage, malfunction, and failure of different organs, including the eyes, kidneys, heart, nerves, and blood vessels^[1].

According to the International Diabetes Federation, around 415 million individuals worldwide were diagnosed with diabetes in 2015, with that figure anticipated to rise to 640 million by 2040. It is believed that half of the diabetic patients are uninformed of their illness and, as a result, are more likely to suffer diabetic complications. The expense of coping with diabetes, on the other hand, might be excessive in terms of money spent and lives lost. Diabetes was responsible for around 5.0 million fatalities in 2015, despite that more than 12% of global health

expenditure was devoted to dealing with the illness and its complications in the same year^[2].

The most prevalent metabolic condition that develops during pregnancy is diabetes mellitus. It has two clinical patterns: Pregestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM)^[3].

Neonatal birth weight (BW) is a significant predictor of neonatal and maternal illness and death. As a result, reliable BW prediction might be a helpful tool for deciding future obstetric treatment. Furthermore, preventing BW anomalies would prevent the long-term consequences of the offspring^[4].

Despite the substantial link between macrosomia and the prevalence of diabetes in pregnant women, fetal macrosomia may develop despite maternal euglycemia, and careful glycemic management may occasionally fail to prevent macrosomia^[5]. Other dietary and metabolic

factors other than glucose may play a role in excessive fetal development. Serum lipid levels that exhibit substantial physiological changes during pregnancy may provide such an appealing alternative^[6].

Preterm birth, preeclampsia, and macrosomia have all been linked to abnormal lipid metabolism. Furthermore, it is hypothesised that the “mixture” of maternal nutrients (glucose, lipids, and amino acids) alters the metabolic milieu of the fetuses, with these alterations influencing future diabetes, obesity, and neurocognitive improvement in the offspring (“fuel mediated teratogenesis”)^[7].

AIM OF THE WORK

The study's goal is to see whether there's a link between maternal blood lipids and (fetal and neonatal weight) in pregnant women with type 2 diabetes and gestational diabetes (GDM), focusing on intergroup variations and macrosomia development.

PATIENTS AND METHODS

A cohort study was performed at Fayoum University Hospital between August 2019 and December 2020. The study populations were 150 pregnant women. Patients were classified into two groups.

- Type 2DM: consists of 75 pregnant women diagnosed with type 2DM.

- GDM: consists of 75 pregnant women diagnosed with GDM.

At Fayoum University Hospital, all patients with singleton pregnancies and babies are delivered. Patients were diagnosed with type 2 diabetes after being cured with oral glucose-lowering medication prior to conception, switching to insulin before or during early pregnancy.

OGTT was used to diagnose GDM in the 2nd trimester of pregnancy. The OGTT was carried out in the morning following an overnight fast of 8-12 hours. The OGTT has been carried out in the morning after a fast of 8-12 hours. GDM is diagnosed when at least one unusually high plasma glucose result is obtained during the 75g of OGTT. In addition, the glucose levels in the venous blood were tested. The glucose tolerance is categorized using the most recent International Association of Diabetes in Pregnancy Study Group (IADPSG) guidelines (International Association of Diabetes and Pregnancy Study Groups Consensus Panel).

Following a thorough description of the testing procedures, all patients agreed to participate in the research.

Inclusion criteria:

1. Singleton pregnancies of gestational age (29-40) week.

2. The neonates delivered at Fayoum University Hospital.

3. Type 2 diabetes is diagnosed when an individual has been cured with oral glucose-lowering medications prior to conception, shifted to insulin before or during pregnancy, and has HbA1c less than 6%.

4. OGTT was used to identify GDM in the second trimester of pregnancy.

Exclusion criteria:

1. All conditions possibly associated with fetal growth restriction due to placental insufficiency rather than metabolic factors, eg.

- Women with hypertensive disorders (denoted by blood pressure follow up).

- Women with thyroid disorders.

- Women with systemic lupus erythematosus.

- Women with the anti-phospholipid syndrome.

2. Women who delivered before the 37th-week gestation.

3. Cases of congenital fetal malformations (suspected during pregnancy or detected postpartum) and cases with multiple pregnancies.

4. Cases with familial hyperlipidemia.

5. Cases with BMI more than 30 k/m².

Measurements

Age, BMI, lipid parameters, glycated hemoglobin, parity, gestational age, and infant birth weight were all measured in all pregnant women. Glycosylated hemoglobin was one of the maternal glycemic markers measured (HbA1c). HbA1c was calculated using a reference range of less than 6%^[7].

During the third trimester, both groups were tested for fasting total maternal cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Enzymatic techniques were used to assess total cholesterol and triglycerides. In addition, the polyanion precipitation technique was used to test high-density lipoprotein

cholesterol (HDL-C), whereas the Friedewald formula was used to compute LDL-C^[7].

Immediately after delivery, the baby's birth weight is measured. Macrosomia is defined as a birth weight larger than 4000 g, whereas LGA is defined as a weight larger than the 90th percentile for gestational age and sex.

Statistical method:

The experimental design was cohort case-control, and statistical analysis was performed using SPSS (Social Science version 26.00) statistical software at a significance level of 0.05. Quantitative analyses were obtained using the independent student's t-test to compare continuous variables in the case of normal distribution. Otherwise, non-parametric tests were used Mann Whitney variance analysis with the parametric distribution of Levene's study. Qualitative analyses associations between categorical variables were compared with Chi-square. The confidence interval was established at 95%, while the agreed-upon error margin was established at 5%. Spearman correlation between variables was done. Logistic regression for determining the possibility of using variables in predicting Neonatal weight.

RESULTS

The study populations were 150 pregnant women, and there is no statistically significant difference between the type 2DM group compared to GDM group regarding age, height, weight, BMI, F.B.G, 2HPP.BG, HbA1c and parity ($p > 0.05$) (Table 1).

Table (2) also shows no statistically significant difference between the type 2DM and GDM groups regarding LDL. On the other hand, there was a statistically significant difference between the type 2DM and GDM groups regarding TC, TG, and HDL.

Table (3) shows no statistically significant difference between type 2DM and GDM groups regarding neonatal weight and gestational age ($p > 0.05$).

Figure (1) reported a statistically significant difference between the type 2DM group and GDM group regarding neonatal weight ($p > 0.05$).

By applying Spearman's correlation test, there was a statistically significant positive correlation between neonatal weight and age, TC, TG, and parity in the type 2DM group. In contrast, There was a statistically significant positive correlation between neonatal weight and BMI, HbA1C, TC, TG; at GDM group (Table 4).

Regression analysis (Stepwise method) defined Neonatal weight development among the type 2DM group) as the persistently significant positive predictor for TG, while excluded the other variables as predictors for development (Table 5). In contrast, the regression analysis (Stepwise method) defined Neonatal weight development among GDM group) as the persistently significant positive predictor for T.C and TG while excluded the other variables as predictors for development (Table 6).

Table 1: Basic characteristics of women with type 2DM and women with GDM.

Basic characteristics		Type2 DM (N=75)		GDM (N=75)		P-value
Age(years)		29.00		28.00		0.231* (NS)
BMI (Kg/m ²)		28.00		27.30		0.196* (NS)
F.B.G (mg/dl)		124		120		0.487* (NS)
2HPP.BG (mg/dl)		161		156		0.170* (NS)
HbA _{1c} (%)		5.90		5.90		0.61* (NS)
		N	%	N	%	P-value
Parity	Primigravida	21	28.0%	18	24.0%	0.577** (NS)
	Multipara	54	72%	57	76%	

Ns = non-significant at p value > 0.05 . * = Mann Whitney as median, **= chi square

Table 2: Comparison between type 2DM group and GDM group as regarding TC, TG, HDL, and LDL

		Type 2 DM (N=75)	GDM (N=75)	Significant test	P-value
TC (mg/dl)	Mean ±SD	209.56±39.03	224.67±41.61	2.294*	0.023 (S)
TG (mg/dl)	Median (IQR)	202.0 (158.0-238.0)	220.00 (180.0-270.0)	2163.50#	0.015 (S)
HDL (mg/dl)	Median (IQR)	49.00 (42-65)	43.0 (37.00-54.00)	1929.500 #	<0.001 (VHS)
LDL (mg/dl)	Median (IQR)	113.00 (95.00-132.00)	118.00 (100.0-165.0)	2318.00 #	0.063 (NS)

* t test, # Mann-Whitney test

Ns = non-significant at *p* value > 0.05, V HS = highly significant at *p* value < 0.001

Table 3: Comparison between type 2DM and GDM groups regarding GA, and neonatal weight.

		Type 2 DM (N=75)	GDM (N=75)	P-value
Gestational age (GA) (week)	Median (IQR)	38.10	39.00	0.154 (NS)
Neonatal weight (g)	Mean ±SD	3664.53±563.72	3486.0±555.59	0.053 (NS)

* t test, # Mann-Whitney test

Ns = non-significant at *p* value > 0.05.

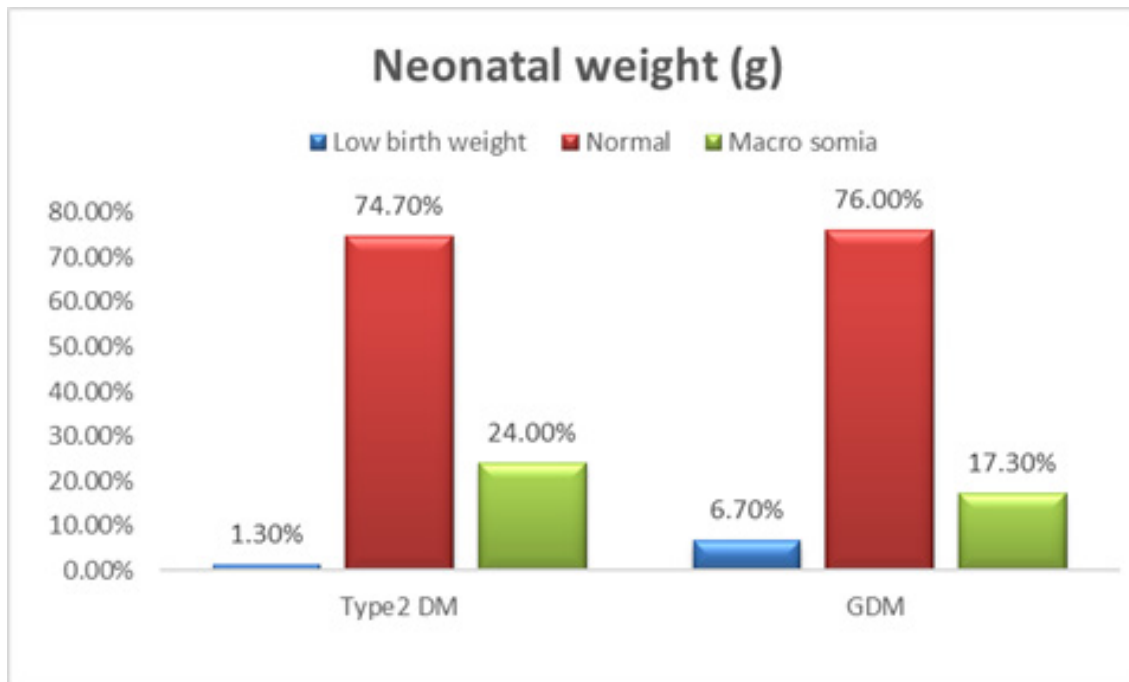


Fig. 1: comparison between type 2DM group and GDM group as regarding neonatal weight.

Table 4: Correlation between neonatal weight and age, BMI, FBS, 2HPP.BS, HbA1C, TC, TG, HDL, LDL, GA, and parity in both groups (Type 2DM, GDM).

	Neonatal weight			
	T2DM		GDM	
	r	p	r	p
Age (years)	0.313*	0.006	-0.031	0.794
BMI (Kg/m ²)	0.105	0.370	0.361**	0.001
F.B.S (mg/dl)	-0.214	0.065	0.223	0.054
2HPP.BS (mg/dl)	0.062	0.600	0.226	0.051
HbA1C (%)	0.025	0.831	0.273*	0.018
T.C (mg/dl)	0.410**	0.001	0.290*	0.012
T.G (mg/dl)	0.277*	0.016	0.247*	0.033
HDL (mg/dl)	0.082	0.485	0.044	0.706
LDL (mg/dl)	0.143	0.220	0.207	0.075
GA (week)	0.035	0.767	0.020	0.866
Parity	0.244*	0.035	0.215	0.063

r =Spearman's correlation. Statistically non significant ($P > 0.05$). *= Statistically significant ($P < 0.05$).

Table 5: Logistic regression for determining the possibility of using TG in predicting Neonatal weight at type 2DM.

Neonatal weight among type 2DM	Unstandardized Coefficients		t	Sig.
	B	Std. Error		
(Constant)	1128.035	11930.330	0.095	0.925
T.G	2.278	.874	2.605	0.012

Table 6: Logistic regression for determining the possibility of using TC, TG in predicting Neonatal weight at GDM group.

Neonatal weight amongtype GDM	Unstandardized Coefficients		t	Sig.
	B	Std. Error		
(Constant)	-92.743-	836.596	-0.111	0.912
T.C	2.916	1.255	2.323	0.023
T.G	2.030	0.949	2.139	0.036

DISCUSSION

There is some disagreement on the beneficial impact of strict glycemic control during pregnancy on fetal BW management. While some studies have shown that nutritional counseling and home blood glucose monitoring minimize the prevalence of macrosomia^[8], others have shown that stringent glucose management has little efficacy in preventing rapid development and may even result in growth restriction^[9]. Another viewpoint is that aggressive glycemic management is only helpful if started before 32 weeks of pregnancy, not later^[10].

Addressing a range of variables linked with metabolic syndrome, done throughout pregnancy, and evaluating their personalized and combined effects on BW are necessary, according to Brisson *et al.*^[6].

In non-pregnant women, hypertriglyceridemia is a prominent feature of insulin resistance syndrome. In

addition, hyperlipidemia, including hypertriglyceridemia, was identified in diabetic women throughout pregnancy and was related to impaired insulin sensitivity, obesity, and, as a result, infant BW with a greater chance of developing macrosomia^[11,12]. Inhibiting TG synthesis, therefore, provides a viable treatment method for human obesity, diabetes and may be effective in regulating newborn BW in diabetic moms in addition to strict glucose management^[8].

The present study investigated the association between maternal serum fasting lipids including; TG, TC, LDL, and HDL cholesterol concentrations at 3rd trimester at GA 29-40 week and neonatal BW.

In this cohort study of pregnant women with type 2 diabetes and gestational diabetes, we discovered that maternal cholesterol and triglyceride levels in the 3rd trimester of pregnancy were significant predictors of macrosomia, independent of maternal BMI and HbA1c, maternal age, parity, previous history of delivering

macrosomic newborns, and serum HDL levels in pregnant women with controlled DM values.

Moreover, In a retrospective study, Son *et al.*^[12] concluded that maternal fasting TG at 24-28 weeks' gestation is an independent predictor for term LGA in mothers with GDM ($p=0.002$). They could identify a different cut-off value of 295 mg/dl with a sensitivity of 48% and a specificity of 83.5%.

Gobl *et al.*^[13] found a positive association between TG in the third trimester and LGA infants, especially in type I DM, after adjusting maternal age and HbA1C. Vrijkotte *et al.*^[11] in a large cohort of non-diabetic mothers (n=2502), reported that higher maternal TG in the first trimester was associated with higher BW.

The present study showed no correlations between neonatal BW and maternal serum, neither HDL nor LDL, and these findings are similar to the results of^[11,12,14].

As regards the positive correlation between pregnancy BMI and neonatal BW, Son *et al.*^[12] reported similar results. However, they concluded that this correlation is independent, which was not present in the present study.

According to both groups of type 2DM and GDM patients, our data demonstrated a significant connection between maternal serum TC, TG, and infant birth weight, irrespective of maternal weight growth and glucose, partially attributable to "good" glycemic management^[15]. Furthermore, we discovered no link between HbA1c and fetal macrosomia in a group of type 2 diabetics in recent research. It implies that HbA1c is not a sensitive predictor of macrosomia or that strict glycemic control may fail to stop macrosomia. The result of our investigation revealed that lipids impact fetal development in addition to maternal glucose levels.

Our study focused on lipids in the 3rd trimester in pregnant women with 2DM and GDM. Lipid parameters, type 2 diabetes, GDM, and fetal macrosomia were all important factors. The GDM patients had higher total cholesterol levels (224.67±41.61mg/dl) than the DM2 patients (209.56±39.03mg/dl). Furthermore, the multivariate analysis revealed a favorable relationship between neonatal birth weight and maternal cholesterol levels. Maternal cholesterol levels were found to be a reliable predictor of macrosomia. This is consistent with the findings of Rey *et al.*^[16], who discovered a favorable relationship between newborn birth weight in the 3rd trimester and maternal cholesterol levels. In contrast to glucose, lipids have been shown to have a substantial influence on newborn weight^[15,17]. The most consistent lipid alteration is a triglyceride, which increases steadily from the 1st to the 2nd to the 3rd trimester in all studies^[13].

Yang *et al.*^[14] discovered a negative connection between newborn birth weight and HDL-C levels in their research. In the current research, we identified a negative connection between HDL-C and LGA in infants ($r=-0.17$, $p<0.05$), while no independent effects on LGA when additional lipid content were included.

The HDL-C levels in both groups were within the normal range, according to the National Cholesterol Education Program 2002. However, both diabetes mellitus pregnant women had LDL-C levels higher than the normal range, and linear multiple regression analysis demonstrated no predictive value for LGA babies. Lipids have certain negative impacts on mother. Women with preeclampsia have elevated serum lipids during pregnancy. Hyperlipidemia may encourage the generation of lipid peroxides and disrupt the equilibrium of vasoactive chemicals, resulting in endothelial dysfunction and vasoconstriction. Patients with GDM are at the same risk as pregnant women who are insulin-resistant and have 2DM; our data will support this assertion. Patients with type 2 diabetes tended to be obese and older. GDM patients had been fat, and their lipid profiles were poor. Infants born to type 2 diabetes mothers were heavier than babies born to GDM patients.

However, not that all GDM moms were given insulin. Lower birth weight in GDM pregnancies compared to type 2DM pregnancies may be due to improved gestational diabetes management. Download Without Authentication^[7].

Diabetes mellitus during pregnancy, as well as insulin treatment, began before or during pregnancy.

Regardless, minor hypercholesterolemia and hypertriglyceridemia were discovered, while HDL-C values were within the normal range, as per the National Cholesterol Education Program 2002. Obesity is a major risk factor for type 2 diabetes and gestational diabetes, and it has been linked to fetal size and poor postnatal outcomes. 2DM patients were obese in this research, whereas GDM patients were fat. Nowadays, most research indicates that infant macrosomia is caused by obesity^[7].

CONCLUSION

This research demonstrated the utility of measuring fasting serum TG and TC levels measured at third-trimester pregnancy correlated positively with neonatal BW and may be considered an independent predictor of fetal macrosomia at term in type 2DM and GDM.

Maternal serum TG and TC levels measured in maternal blood during the 3rd trimester of pregnancy could help in the identification of women who will give birth to LGA babies. In addition, we can prevent macrosomia in type 2DM and GDM pregnancies by properly regulating the lipid profile.

CONFLICT OF INTEREST

There are no conflicts of interests.

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