ORIGINAL ARTICLE

# Effects of maternal lipids on the fetal growth in gestational diabetes

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## Abstract

**OBJECTIVE:** The aim of this study was to determine whether there is an association between ultrasound fetal biometry and lipids and glucose profiles at the beginning of gestational diabetes (GDM) treatment.

**METHODS:** In 98 women with GDM plasma glucose and lipid profile were measured between 27–32 weeks' of gestation. The association between the biochemical parameters and the measurements and percentiles of the biparietal diameter (BPD), femur length (FL) and abdominal circumference (AC), estimated fetal weight (EFW) and the actual birthweight (BW) were analyzed.

**RESULTS:** There was no significant association between fetal and neonatal biometry measurements and maternal glucose concentrations. Highly significant positive correlation was found between triglicerydes and fetal biometry at the beginning of GDM treatment: AC, BPD, FL and EFW ($p$=0.007, $p$=0.018, $p$=0.018, $p$=0.013, respectively), as well as between total cholesterol and bi-parietal diameter ($p$=0.04). Associations between maternal plasma lipids and birthweight or birthweight percentile were not evident.

**CONCLUSIONS:** These data suggest that maternal lipids and carbohydrates metabolic disturbance are an important determinant for fetal growth in pregnancy before gestational diabetes is diagnosed.

**Abbreviations :**

| | |
|---|---|
| AC | - abdominal circumference |
| BMI | - body mass index |
| BPD | - bi-parietal diameter |
| EFW | - estimated fetal weight |
| FFA | - free fatty acids |
| FL | - femur length |
| GCT | - glucose challenge test |
| GDM | - gestational diabetes mellitus |
| HDL | - high density lipoproteins cholesterol |
| LDL | - low density lipoproteins cholesterol |
| OGTT | - oral glucose tolerance test |
| TG | - triglycerides |

## INTRODUCTION

Gestational Diabetes Mellitus (GDM) affects up to 10% of pregnancies, being the most frequent metabolic disorder happening during this time (Gabbe, 1986). It has an important implications for mothers, who are in a greater risk of developing diabetes mellitus in the future, and their offspring that is likely to develop adverse perinatal outcomes, such as macrosomia, with all it's possible implications. Increased incidence of fetal death, prematurity, preeclampsia and respiratory distress syndrome are just a few of them. GDM is a result of insulin resistance and altered compensatory insulin secretion. It effects in impaired glucose utilisation by peripheral tissues (e.g. skeletal muscles), decreased inhibition of liver glucose release, increased lipolysis due to downregulated insulin inhibitory effect and reduced amino – acid turnover (Catalano *et al.* 2003). As a result the excess of glucose, lipids and amino-acids is found in maternal blood, which obviously contributes to it's higher concentration in fetus. When combined with increased fetal production of growth – promoting factors (like insulin), it makes possibility of increased birth weight more likely.

There is also a strong clinical evidence that in addition to perinatal outcomes some adulthood-acquired metabolic disorders, like hyperlipidemia and obesity may be related to inappropriate fetal conditions, especially in diabetic pregnancies (Eriksson *et al.* 2002). That's why keeping fetal growth under control is a goal that all the clinicians struggle to achieve. Coping with GDM – related hyperglicemia, although in most cases relatively easy and – with the abundance of diet and insulin – based strategies – straightforward , has proven not to be effective enough in fighting accelerated fetal growth, especially in obese patients (Langer *et al.*,2005).

The aim of our study was to determine whether maternal lipids and serum glucose level are related to fetal biometry and actual birth weight. Maternal lipids and glucose profiles were measured at the beginning of GDM treatment. Proper diabetes management maintained good glycemic status until delivery.

## MATERIAL AND METHODS

Ninety eight pregnant women with singleton pregnancy and gestational diabetes mellitus have been enrolled in the study, recruited from patients who attended outpatient's clinic of the 1st Clinic of Obstetrics and Gynaecology, Warsaw Medical University. The authors obtained approval of the Ethical Committee of Warsaw Medical University and all the patients signed the approved informed consent form.

GDM was originally diagnosed after standard glucose tests currently recommended by Polish Gynaecology Association: fasting glucose for first trimester, 50g glucose challenge test (GCT) and 75 g oral glucose tolerance test (OGTT) for pregnancies between 24 and 28 weeks of gestation. Results consistent with diagnosis of GDM were: fasting glucose above 124 mg/dl, recorded twice, glycemia of 200 mg/dl or above in GCT or at least one out of three of the following results in OGTT: fasting glucose greater than 100 mg/dl, 1-hour glycemia of 180 mg/dl or above and 2-hour glycemia of 140 mg/dl or above. If fasting glucose in first trimester was between 100–124 mg/dl, OGTT was performed as a case of urgency. For cases with 1-hour glycemia between 140–199 in GCT, OGTT was performed equally fast. Glucose measurements were based on venous blood samples. Once GDM was diagnosed women were advised to continue on diabetic diet: 40% carbohydrates, 40% fat and 20% protein. Equipped with glucometers (Optium Xido, Abbott), patients were monitoring capillary glucose 4 times daily – fasting and 1 hour after each main meal. Once a week they were asked to monitor glycemia more frequently: fasting, 1 and 2-hours after each meal, at midnight and at 3.00 AM. The need for insulin therapy was established and adjusted according to glucose profile: fasting >100 mg/dl and 1-hour postprandial >140 mg/dl was an indication for insulin therapy commencement.

After GDM was diagnosed women were hospitalized in our Clinic for further investigations. Blood samples were obtained and fetal ultrasound performed with BK Medical ultrasound system. Lipid ( cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride) and glucose profiles were recorded. For plasma lipids measurements we used Thermo Electron Corporation diagnostic sets. Glucose profile assessment was based on capillary glucose, measured with glucometer (Optium Xido, Abbott). Standard obstetric ultrasound was performed that also included biparietal diameter (BPD), femur length (FL) and abdominal circumference (AC) measurements as well as estimated fetal weight (EFW) analysis.

Statistical analysis was performed using Statgraphics Centurion software . T- test was used for finding differences between the groups of different AC percentile. To assess associations between variables we used Pearson's correlations.

## RESULTS

The patient's characteristics and OGTT data is presented in Table 1. Table 2 shows fetal biometry measurements and maternal serum lipids concentrations. As for biometry correlations – there was no significant association between biometry measurements and maternal glucose concentrations either fasting, OGTT or derived from glucose profile. No significant correlation was also found when assessing glycemia and birth weight or birth weight percentile. Highly significant positive correlation was found between triglicerydes and fetal biometry at the beginning of GDM treatment: AC, BPD, FL and EFW ($p$=0.007, $p$=0.018, $p$=0.018, $p$=0.013, respectively) (Figure 1), as well as between

**Tab. 1.** Maternal and neonatal characteristics of study population.

| **Maternal data** | |
|---|---|
| Age | 30.88±4.93 |
| Pre-pregnancy BMI | 23.93±3.69 |
| Pre-pregnancy BMI ≥ 30 (%) | 7.95 |
| OGTT fasting glucose (mg%) | 78.91±14.39 |
| OGTT 1 hour glycaemia (mg%) | 171.76±32.1 |
| OGTT 2 hours glycaemia (mg%) | 151.54±33.68 |
| Insulin therapy (%) | 12 |
| **Glucose profiles** | |
| Fasting (mg %) | 84.5±14.51 |
| Postprandial (mean) (mg %) | 129.64±34.79 |
| Neonatal data: | |
| Gestational age at delivery (wks) | 38.52±1.04 |
| Birth weight (g) | 3501.48±461.1 |
| CC percentage | 28 |

**Tab. 2.** Plasma lipids concentration and fetal biometry parameters in women with gestational diabetes mellitus at the beginning of treatment (mean ± SD).

| **Maternal plasma lipids (mg %)** | **(mg/dl)** |
|---|---|
| Total cholesterol | 256±53.9 |
| Triglycerides | 218±76.6 |
| LDL | 146.16±48.2 |
| HDL | 67.98±22.3 |
| **Fetal biometry measurements** | |
| AC (mm) | 254.55±35.8 |
| BPD (mm) | 75.35±7.78 |
| FL (mm) | 55.86±7.38 |
| EFW (g) | 1528.12±543.59 |

total cholesterol and bi-parietal diameter ($p$=0.04). Associations between maternal plasma lipids and birth weight or birth weight percentile were not evident. Comparing groups of pregnancies with and without accelerated fetal growth ( AC ≥ 90 percentile and AC < 90 percentile, respectively), we found mother's weight gain and neonatal birth weight to be significantly different between the groups. No differences in their prepregnancy weight, BMI or lipids and glucose measurements at the time of GDM diagnosis were present (Table 3).

## DISCUSSION

We aimed in this study to determine whether plasma lipids and glucose measurements are correlated with fetal biometry parameters and therefore can be considered as test that can influence GDM management. Ultrasound fetal biometry performed in early third trimester has already been found vital for predicting GDM-related perinatal morbidity (Bochner *et al.* 1987, Landon *et al.* 1987).

Although increased birth weight and macrosomia has been known to relate to maternal hyperglicemia for years, clinical data published to date support theory that pathophysiology of deviated fetal growth is caused by many, rather than a few factors. Langer *et al.* (2005) demonstrated that diet-based GDM management, even if effective enough in maintaining euglicemia, is not efficient in decreasing neonatal morbidity. It has been noted that in case of obese mothers only those on insulin treatment presented the same risk for adverse pregnancy outcomes that normal weight women with good glycemia control. Recent studies pointed out that lipogenesis and lipolysis are vital for fetal metabolic environment and so we focused on serum lipids as tests that can possibly predict increased birth weight and macrosomia independently of serum glucose levels.

**Tab. 3.** Maternal parameters and neonatal birth weight in pregnancies with fetal AC < 90 and ≥ 90 percentile (mean ± SD).

| | | | |
|---|---|---|---|
| Prepregnancy weight (kg) | 64.46±13.43 | 64.56±11.06 | ns |
| Prepregnancy BMI | 23.84±4.52 | 23.13±3.24 | ns |
| Weight gain (till study entry)(kg) | 8.34±3.67 | 11.08±5.18 | 0.013 |
| Total cholesterol (mg/dl) | 251.75±57.2 | 262.03±53.7 | ns |
| Triglycerides (mg/dl) | 224.1±91.05 | 219.59±61.7 | ns |
| LDL (mg %) | 137.41±46.8 | 156.57±50.8 | ns |
| HDL (mg %) | 67.4±15.2 | 65.5±18.5 | ns |
| **Glucose profile** | | | |
| Fasting (mg %) | 87.53±14.47 | 93.11±14.91 | ns |
| Postprandial (mean) (mg %) | 128.64±33.49 | 124.84±25.56 | ns |
| **Neonates** | | | |
| Gestational age at delivery (wks) | 38.69±1.67 | 37.94±1.95 | ns |
| Birth weight (g) | 3328.38±555.7 | 3642.35±459.1 | 0.045 |

The variation of trigliceryde (TG) and cholesterol levels throughout different stages of normal and GDM-affected pregnancy has been well assessed and reported (Montelongo *et al.*,1992, Szymanska *et al.* 2008). Also free fatty acids (FFA) levels were thoroughly investigated and found to be abnormal in women with gestational diabetes, with higher concentrations than in normal controls (Bomba-Opon *et al.* 2006).

We found mother's weight gain to be related to fetal macrosomia. None of the means of the maternal glucose profile was correlated positively with AC or other fetal biometry parameters at the beginning of GDM treatment and actual neonatal birth weight. Nevertheless it is well established that genetic predisposition is highly significant and may be responsible for approximately 15% of fetal weight anomalies, and be even more relevant in early stages of pregnancy (Schaefer-Graf *et al.* 2003). In the study by Schaefer-Graf (2008) maternal lipids have been monitored during third trimester and their correlation to fetal biometry assessed accordingly, as well as to actual birth weight and neonatal fat mass. Authors focused on AC as it's values strongly depend on the thickness of insulin – sensitive subcutaneous fat. The findings of this study are partially consistent with ours, showing strong positive correlation between TG and AC throughout the third trimester, but negative association between TG and actual birth weight (we showed no correlation between these parameters). Apart from the above data our study showed positive and significant TG level correlation with BPD, FL and EFW at the time of GDM diagnosis. To date, maintaining euglicemia is regarded the most effective approach to battle the influence of negative , GDM – related disturbances of fetal endocrine environment. Landon *et al.* (1989) demonstrated accelerated fetal growth in third trimester in women with gestational diabetes, showing significance of AC gain, with no changes in head circumference and femur length grow. It is speculated that hypertriglyceridemia is one of the effects of increased insulin resistance, and may play a role in facilitating macrosomia, as corresponding lipid abnormalities can be found in maternal and infant's blood, especially in obese and poorly controlled GDM cases (Merzouk *et al.* 2000). Supporting theory that lipids do influence fetal growth is the fact, that total lipids content has been found to be decreased in small for gestational age infants born to non – diabetic mothers, especially in newborns with body habit indicating low peripheral fat content, with relatively increased TG, even in constitutionally small infants (Jones *et al.* 1999).

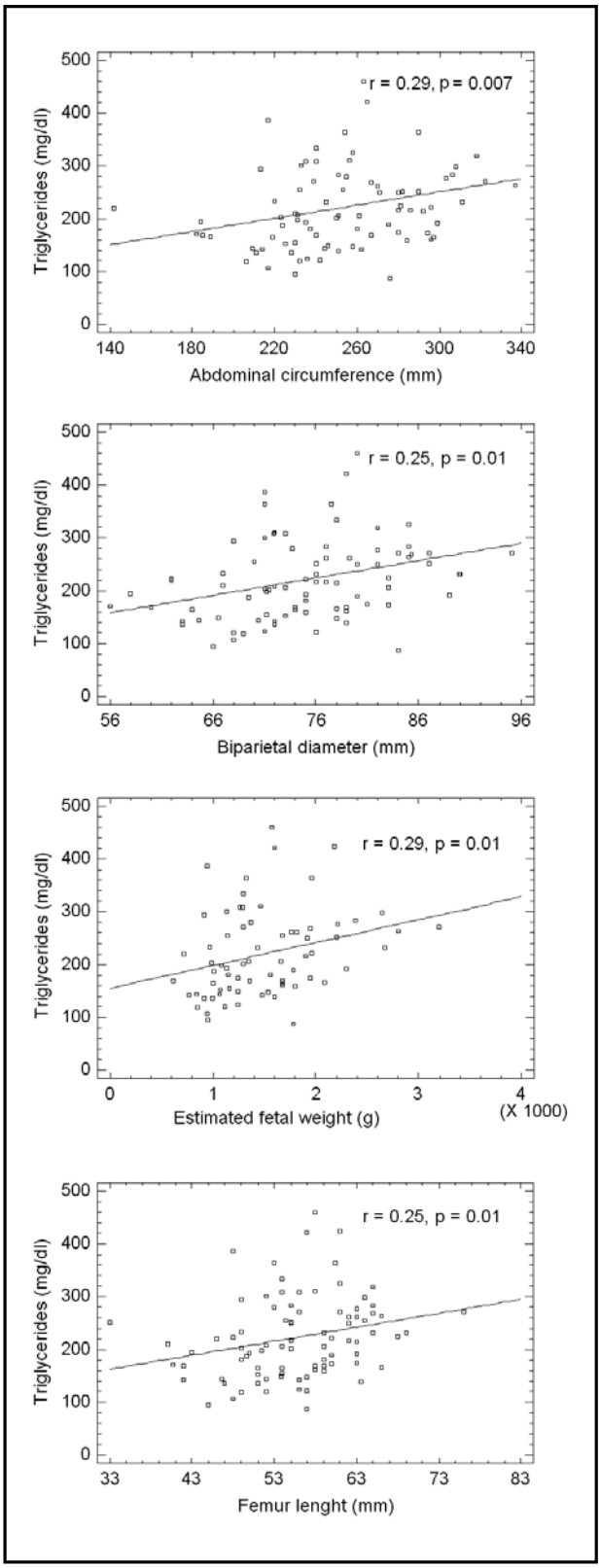


**Fig. 1.** Correlation of TG with fetal biometry measurements.

## CONCLUSIONS

These data suggest that maternal lipids disturbance are an important determinant for fetal growth in pregnancy before gestational diabetes is diagnosed . It seems that treatment of GDM can reduce the lipids influence on the fetal growth.

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