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Original Research Article

An Analytical Assessment of the Lipid Levels by Trimester between Patients with GDM and Normal Pregnant Women

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Abstract

Aim: The aim of the present study was to determine the longitudinal lipid levels by trimester and compare the differences between patients with GDM and normal pregnant women.

Methods: This analytical study was conducted at Department of Obstetrics & Gynecology, Madhubani Medical College & Hospital, Madhubani, Bihar, India. A total of 1000 women who attended regular prenatal health care and delivered their babies in Department of Obstetrics & Gynecology, Madhubani Medical College & Hospital, Madhubani, Bihar, India during the period of 6 month were included in this study. Among them, 200 pregnancy women who were diagnosed as GDM in the 2nd trimester according to the American Diabetes Association (ADA) 2010 criteria were classified as patients with GDM, while 800 healthy pregnant women were included in the control group.

Results: Among the 1000 mothers in the present study, the maternal age in the GDM group was 32.65±3.92 years, while that of the control group was 31.53±3.68 years, with significantly statistical difference between the 2 groups. The prepregnancy BMI in the GDM group was 23.22±3.49kg/m^2, which was significantly higher than that of the control group (21.87±2.97kg/m^2), P<.001. The mean age at delivery was 39.20±1.01 weeks in the GDM group and 39.43±1.21 weeks in the control group, with statistical difference between the 2 groups. There were no significantly statistical differences on the birth weight, the rate of primiparous, the rate of caesarean section, and the rate of macrosomia between the 2 groups.

Conclusion: Overall, in a large longitudinal cohort study, we found that TG, TC, LDL-C concentrations, and TG/HDL-C ratio increased progressively throughout pregnancy; meanwhile, HDL-C amounts increased from the 1st to the 2nd trimester with a slight decrease in the 3rd trimester. Lipid profiles were dramatically different between the GDM group and the control group, except of serum TC and LDL-C concentrations.

Keywords: Gestational Diabetes Mellitus, Lipid Profiles, Triglycerides To High-Density Lipoprotein Ratio

Introduction

Gestational diabetes mellitus (GDM), defined as glucose intolerance first diagnosed during pregnancy, is the most common metabolic condition during pregnancy and is increasing in prevalence worldwide. [1] Up to 22% of all pregnancies are affected by GDM, and this prevalence may be higher under new diagnostic criteria. [2] This is a growing concern as women with GDM are at increased risk of developing diabetes post pregnancy, in addition to hypertension, hyperlipidaemia and coronary heart disease. [3–5] The offspring of women with GDM are also more likely to develop diabetes and metabolic syndrome in childhood or adulthood. [6,7] More immediate consequences of GDM include fetal macrosomia, preeclampsia and cesarean delivery. [8,9] Although older maternal age and ethnicity are risk factors for GDM, maternal obesity is the strongest known risk factor. [10]

Physiological insulin resistance underlies all pregnancies beginning around 24–28 weeks of gestation and progressing through the third trimester. Altered maternal lipid metabolism is also common in pregnancy with modest increases in lipids early in pregnancy and significant elevations of lipids later in pregnancy, specifically, triglycerides and to a lesser extent phospholipids and cholesterol. [11,12] In women with GDM, the physiological changes in insulin and lipids are exaggerated and may indicate underlying metabolic dysfunction that transiently manifests during pregnancy. [13]

Circulating lipid patterns in GDM versus normal pregnancy have been extensively studied, with most studies observing higher triglyceride levels across all trimesters of pregnancy in women with GDM. Results are less consistent for the other circulating lipid measures, with most studies focusing on the third trimester. [11] There is significant debate in the literature as to whether lipid patterns differ in women with GDM early in pregnancy and whether these early patterns are potential markers of preexisting insulin resistance. [14] In this study, we sought to perform a systematic review and meta-analysis of observational studies comparing measurements of total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and non-HDL-C in the first, second and third trimesters of pregnancy in women who develop GDM and those who remain glucose tolerant.

In this study, we sought to perform an observational study to compare the concentrations of total cholesterol (TC), triglycerides (TGs), low-density lipoprotein cholesterol (LDLC), high-density lipoprotein cholesterol (HDL-C), and TG/HDL-C ratio (TG to HDL-C ratio) in the 1st, 2nd, and 3rd trimesters of pregnancy in normal pregnant women and women with GDM. We aim to determine the longitudinal lipid levels by trimester and compare the differences between patients with GDM and normal pregnant women.

Methods

This retrospective cohort study was conducted at Department of Obstetrics & Gynecology, Madhubani Medical College & Hospital, Madhubani, Bihar, India. A total of 1000 women who attended regular prenatal health care and delivered their babies in Department of Obstetrics & Gynecology, Madhubani Medical College & Hospital, Madhubani, Bihar, India during the period of 6 month were included in this study.

Among them, 200 pregnancy women who were diagnosed as GDM in the 2nd trimester according to the American Diabetes Association (ADA) 2010 criteria

[15] were classified as patients with GDM, while 800 healthy pregnant women were included in the control group.

Inclusion criteria

Singleton pregnancy; had integrated medical records.

Exclusion criteria

Multiple pregnancies; type 1 or type 2 diabetes mellitus before pregnancy, inherited metabolic diseases, cardiovascular disease, thyroid or liver dysfunction before pregnancy; use of drugs that could affect lipid levels, including corticosteroids, etc.

Methodology

The information of maternal age, height, parity, prepregnancy body mass index (BMI), delivery mode, gestational age, birth weight, etc, were recorded. Prepregnancy BMI was derived as the weight (kg) divided by the square of the height (m), and the patients were classified as low weight (<18.5kg/m^2), normal weight (18.5–24.9kg/m^2), overweight (25.0–29.9kg/m^2), or obese (≥30.0kg/m^2) on the basis of World Health Organization BMI classification. [16] Macrosomia is defined as birth weight ≥4000g.

Biochemical analyses

Longitudinal lipid assessments were carried out during three periods: 6 to 8 gestational weeks (GWs) (the 1st trimester, T1), 24 to 28 GWs (the 2nd trimester, T2), and 32 to 34 GWs (the 3rd trimester, T3). TG/HDL-C ratio was calculated accordingly by trimester. Blood samples were collected at the outpatient clinic by a trained nurse after a 10- to 12-hour fasting period. Serum TC, LDL-C, HDL-C, TG, and glucose concentrations were measured on an automatic biochemical analyzer (Beckman Coulter Co. Ltd., Tokyo, Japan) and monitored by a well-trained inspector. The inter- and intra-assay coefficients of variation were <1.6%, 0.6% (TC); <1.7%, 1.1% (TG); <1.1%, 0.6% (HDL-C); and <1.6%, 1.1% (LDL-C), respectively.

Statistical analysis

In our study, descriptive statistics included means and standard deviation (SD) for continuous variables, and numbers and percentages for categorical variables. First, we used 2-way repeated measures analysis of variance to estimate whether serum TC, TG, LDL-C, HDL-C concentrations, and TG/HDL-C ratio increased by trimesters (P for trend) and explore the differences in serum lipids concentrations in the 1st, 2nd, and 3rd trimesters between pregnant women with and without GDM (P for difference). Then, we used backward stepwise logistic regression analysis to test whether serum lipids measured in the 1st trimester could predict the risk of GDM in the 2nd trimester, and the candidate predictor variables included maternal age, prepregnancy BMI, and parity as confounding variables. Finally, to test robustness of our main results, we performed additional propensity-based subgroup analyses. Pregnant women with and without GDM were matched (1:1) on maternal age, prepregnancy BMI, and parity, using the Greedy matching macro. [17] All the analyses were performed with SPSS version 20.0 for Windows (SPSS Inc, Chicago, IL). P values <.05 were defined as statistically significant.

Results

Table 1: Characteristics of study population

	Control group (n=800)	GDM (n=200)	P Value
Maternal age, yrs	31.53±3.68	32.65±3.92	< 0.001
Prepregnancy BMI, kg/m^2	21.87±2.97	23.22±3.49	< 0.001
< 18.5, n	64	10	
18.5–24.9, n	640	140	
25.0–29.9, n	88	40	< 0.001

≥ 30.0, n	8	10	
Caesarean section, n (%)	120 (15%)	40 (20%)	0.11
Primiparous, n (%)	520 (65%)	120 (60%)	0.18
Delivery gestation, wks	39.43±1.21	39.20±1.01	< 0.001
Birth weight, g	3357.35±414.31	3381.60±420.93	0.37
Macrosomia, n (%)	64 (8%)	20 (10%)	0.10

Table 1 presents maternal and neonatal characteristics of our study population. Among the 1000 mothers in the present study, the maternal age in the GDM group was 32.65±3.92 years, while that of the control group was 31.53±3.68 years, with significantly statistical difference between the 2 groups. The prepregnancy BMI in the GDM group was 23.22±3.49kg/m^2, which was significantly higher than that of the control group (21.87±2.97kg/m^2), P<.001. The mean age at delivery was 39.20±1.01 weeks in the GDM group and 39.43±1.21 weeks in the control group, with statistical difference between the 2 groups. There were no significantly statistical differences on the birth weight, the rate of primiparous, the rate of caesarean section, and the rate of macrosomia between the 2 groups.

Table 2: Maternal lipid profiles by trimester

Lipids	**Total (n=1000)**	**F**	**P Value**
TC (T1), mmol/L	4.04±0.70	2413.462	<0.001
TC (T2), mmol/L	5.76±0.96		
TC (T3), mmol/L	6.16±1.07		
TG (T1), mmol/L	0.94±0.52	2107.747	<0.001
TG (T2), mmol/L	2.29±0.98		
TG (T3), mmol/L	3.14±1.29		
LDL-C (T1), mmol/L	2.15±0.56	832.370	<0.001
LDL-C (T2), mmol/L	3.02±0.78		
LDL-C (T3), mmol/L	3.30±0.92		
HDL-C (T1), mmol/L	1.42±0.27	1171.205	<0.001
HDL-C (T2), mmol/L	1.85±0.35		
HDL-C (T3), mmol/L	1.71±0.33		
TG/HDL-C (T1)	0.70±0.46	956.019	<0.001
TG/HDL-C (T2)	1.33±0.84		
TG/HDL-C (T3)	1.96±1.17		

Table 2 shows maternal lipid profiles by trimester. Serum TG, TC, LDL-C concentrations, and TG/HDL-C ratio increased progressively throughout pregnancy (all P for trend < 0.001). However, HDL-C amounts increased from the 1st to the 2nd trimester with a slight decrease in the 3rd trimester. All the lipid parameters of the 3rd trimester were higher than those of the 1st and 2nd trimesters, except HDL-C. Similarly, the levels of lipids increased by increasing trimesters in both GDM and control groups (all P Value < 0.001).

Table 3: Maternal lipid profiles of the different trimesters in the 2 groups

Lipids	GDM (n=200)	Control (n=800)	F	P Value
TC (T1), mmol/L	4.07±0.67	4.04±0.70	2.715	0.100
TC (T2), mmol/L	5.65±1.00	5.79±0.94		
TC (T3), mmol/L	6.04±1.07	6.18±1.07		
TG (T1), mmol/L	1.08±0.57	0.91±0.50		

TG (T2), mmol/L	2.57±1.13	2.23±0.93	25.502	<0.001
TG (T3), mmol/L	3.36±1.51	3.08±1.23		
LDL-C (T1), mmol/L	2.21±0.55	2.14±0.56	2.128	0.145
LDL-C (T2), mmol/L	2.96±0.82	3.05±0.77		
LDL-C (T3), mmol/L	3.16±0.89	3.33±0.92		
HDL-C (T1), mmol/L	1.37±0.26	1.43±0.27	24.856	<0.001
HDL-C (T2), mmol/L	1.75±0.33	1.87±0.35		
HDL-C (T3), mmol/L	1.64±0.30	1.73±0.33		
TG/HDL-C (T1)	0.84±0.54	0.66±0.44	30.652	<0.001
TG/HDL-C (T2)	1.58±0.96	1.27±0.80		
TG/HDL-C (T3)	2.20±1.45	1.90±1.08		

Compared with the control group, the GDM group showed higher TG concentrations and higher TG/HDL-C ratio throughout pregnancy, while lower HDL-C concentrations throughout pregnancy (P<0.05). However, there were no significant differences in TC and LDL-C concentrations in the 1st, 2nd, and 3rd trimesters between the GDM group and the control group (P>0.05).

Discussion

Gestational diabetes mellitus (GDM) and maternal obesity are independently associated with adverse maternal and neonatal outcomes. [18,19] Both share common metabolic characteristics such as increased insulin resistance, hyperglycemia, and hyperinsulinemia, and GDM may impart distinct effects on clinical outcomes independent of obesity alone. The same is true for maternal obesity, although differences in metabolism may also exist among certain ethnic groups. [20]

It is already well known that both obesity and GDM are relative risk factors for adverse maternal and neonatal outcomes, being related to an increased occurrence of Large for Gestational Age (LGA) fetuses and macrosomia (defined as neonates birthweight over 4000 g). Although macrosomia can be influenced by both genetic and environmental factors, the rapid increase in prevalence is mainly attributable to environmental causes. [21] Among these, maternal overweight and the related metabolic changes such as diabetes mellitus type 2 and GDM, seem to be crucially important.

Lipid metabolism is essential for a healthy pregnancy development. [22] The plasma lipid profile including the levels of TC, HDL-C, LDL-C, and TG changes apparently during normal pregnancy. [23] Plasma lipid concentrations increase markedly during pregnancy due to estrogen stimulation and insulin resistance. [24] During the 1st two-thirds of gestation, there is an increase in maternal fat accumulation, associated with both hyperphagia and increased lipogenesis. [25] In the last 3rd trimester of gestation, however, as a result of increased lipolytic activity and declined lipoprotein lipase activity, maternal fat storage decreases or even ceases. [26] These changes are reflections of maternal physiologic adaptation to energy demand of the fetus, also they are necessary preparations for delivery and lactation. [22]

Consistent with Shen's study, we also found the similar lipid profiles throughout the pregnancy. And this indicated that the elevation of lipid concentrations is a physiologic requirement for maintaining stable energy storage for the fetus. However, it is difficult to ascertain which level of lipid elevation is physiologic or pathologic and there are no worldwide standard criteria of lipid levels during pregnancy due to the heterogeneity of the population and territory. Moreover, the

TG/HDL-C ratio was proved to be a good and sensitive indicator to identify insulin-resistant individuals of North American aboriginal, Chinese, and European. [27] The TG/ HDL-C ratio was considered as an atherogenic index. [28] In our study, we found that the TG/HDL-C ratio increased significantly throughout the pregnancy, which indicated progressive insulin resistance during normal pregnancy. A recent meta-analysis [29] showed that serum TG was significantly elevated among GDM women and the increase persisted across all the 3 trimesters of pregnancy. They also found that serum HDL-C levels were significantly lower in women with GDM in the 2nd and 3rd trimesters of pregnancy compared with women without insulin resistance. However, no elevated serum TC and LDL-C levels were found between women with GDM and women without insulin resistance in the study.

Similar to the results of the recent meta-analysis, [29] in our study, we found that compared with the control group, the GDM group showed higher TG concentrations, TG/HDL-C ratio, and lower HDL-C concentrations throughout pregnancy. In the matched-pairs analysis, after adjusting age and prepregnancy BMI, we found significant difference on HDL-C concentrations, but no significant difference on TG concentrations between the 2 groups. The phenomena may be probably because of the relatively small sample size, or because serum TG had a closer correlation with age and prepregnancy BMI, and serum HDL-C concentrations maybe more related to GDM than serum TG. But further studies with lager sample size in matched-pairs analysis will be needed. This study indicated that lipid profiles were dramatically different between the GDM group and the control group and GDM women had more serious dyslipidemia and insulin resistance in pregnancy. Meanwhile, we found that there were no significant differences in TC and LDL-C concentrations in the 1st, 2nd, and 3rd trimesters between the 2 groups. However, the exact mechanism was unknown and further studies should be conducted to explore the role of dyslipidemia in the pathogenesis of GDM.

To examine whether lipid abnormalities in the 1st trimester have potential clinical utility for identifying women at risk for subsequently developing GDM, we analyzed the relationship between maternal lipid profile in the 1st trimester and GDM. Logistic regression analysis showed that maternal age, prepregnancy BMI, and TG/HDL ratio were associated with an increased risk of GDM. This indicated that TG/HDL-C ratio in the 1st trimester in combination with maternal age and prepregnancy BMI could be good markers to predict the risks of GDM. Similarly, Wang et al [30] found that TG/HDL-C ratio in combination with HbA1c and prepregnancy BMI were good markers to predict the risk of GDM and delivering large for gestational age infant. [31]

In the future, more research is needed to establish the lipid standard during pregnancy according to local maternal characteristics such as inheritance, ethnicity, region, etc. More studies will be needed to explore the correlation between dyslipidemia and the pathogenesis of GDM. Also for women with elderly maternal age, high prepregnancy BMI, elevated TG/HDL-C ratio in the 1st trimester, close surveillance and monitoring, necessary weight control, and diet management should be carried out to reduce the incidence of GDM as much as possible.

This study yielded 3 main findings: maternal TG, TC, LDL-C concentrations, and TG/HDL-C ratio increased progressively throughout pregnancy; and HDL-C concentrations increased from the 1st to the 2nd trimester with a slight decrease in the 3rd trimester; Lipid profiles were dramatically different between the GDM group and the control group. Compared with the control group, the GDM group showed higher TG concentrations, TG/HDL-C ratio, and lower HDL-C concentrations throughout pregnancy. However, there were no significant differences in TC and LDL-C concentrations in the 1st, 2nd, and 3rd trimesters, between the GDM group and the control group; Maternal age, prepregnancy BMI, and TG/HDL ratio in the 1st trimester were associated with an increased risk of GDM and could predict the risk of GDM at an early stage.

Conclusion

Overall, in a large longitudinal cohort study, we found that TG, TC, LDL-C concentrations, and TG/HDL-C ratio increased progressively throughout pregnancy; meanwhile, HDL-C amounts increased from the 1st to the 2nd trimester with a slight decrease in the 3rd trimester. Lipid profiles were dramatically different between the GDM group and the control group, except of serum TC and LDL-C concentrations. Maternal age, prepregnancy BMI and TG/HDL ratio in the 1st trimester could predict the risk of GDM at an early stage.

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