Journal of Food and Nutrition Research, 2014, Vol. 2, No. 7, 335-339
Available online at http://pubs.sciepub.com/jfnr/2/7/1

DOI:10.12691/jfnr-2-7-1

Lipid Changes and Effect of Diet Therapy only in Gestational Diabetes Mellitus and Normal Pregnancy in Developing Area Southern China

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Received May 06, 2014; Revised June 17, 2014; Accepted June 22, 2014

Abstract Objective: To explore the changes in the feature of serum lipid in different trimester of normal pregnancy and GDM, analysis of the effect of diet therapy on blood lipid level on GDM and the relationship between serum and lipid. Methods: 92 normal pregnant women and 85 GDM women were inclusive in this study. The maternal serum lipid levels, diet intake and newborn weight of both groups were recorded. After diet therapy, GDM group was further divided into two subgroups, one with blood glucose under control and one with poor glycemic control according to the blood glucose monitoring. Results: LDL-C and apoB were significantly increased in GDM group compared to normal group in the first trimester($P < 0.05$); GDM patients consume more energy having higher weight gain/ pregravid BMI compared to normal group till gestational diabetes was confirmed ($P <0.05$). Compared to early trimester, TC,TG, LDL-C, LDL-C,apoA1 and apoB were increased in the normal group in late trimester($P <0.05$); Compared to the control group in late phase, there was higher apoB, but lower TG in glucose control group. There were higher TC, TG and neonatal weight in the poor glycemic group compared to the control group in late phase ($P < 0.05$); There was a positive correlation between TC, TG and newbornweight ($P < 0.05$). Conclusion: With increasing gestational age, there is increasing level of blood lipid profile during pregnancy. Excessive nutrient intake and incidence of GDM may be related. Diet therapy can improve blood lipid status which may help control neonatal weight.

Keywords: *Gestational Diabetes Mellitus (GDM), lipid, nutrition intake, diet therapy, neonatal weight*

Cite This Article: LingLing Huang, Jun Xiong, Gowreesunkur Purvarshi, SuMei Wang, LinLin Zhong, and Hui Tang, "Lipid Changes and Effect of Diet Therapy only in Gestational Diabetes Mellitus and Normal Pregnancy in Developing Area Southern China." *Journal of Food and Nutrition Research*, vol. 2, no. 7 (2014): 335-339. doi: 10.12691/jfnr-2-7-1.

1. Introduction

In pregnant women, there is enhanced intestinal fat absorption capacity to meet the needs of pregnancy, in addition to a variety of hormones in the body, blood lipid levels are gradually increased with increasing gestational age [1]. Gestational diabetes (GDM) is the most common metabolic disorder in pregnancy. The study shows GDM patients with severe dyslipidemia, and this variation has existed in early pregnancy, with the elevated hormone levels and enhanced insulin resistance, dyslipidemia can worsen [2,3]. Studies have shown that GDM incidence is closely related to abnormal regulation of multiple genes and proteins [4,5,6], however, relatively genetic diseases have stable incidence, which cannot be used to explain the significant increased incidence in recent years. This might indicate that lifestyle plays an important role. Research has shown that dietary intake of the irrational structures such as saturated fats and trans-fats increases the risk of type 2 diabetes [7]. GDM in addition to adverse perinatal outcomes of the mother and child also have other long-term adverse effects such as the increased incidence of metabolic syndrome, obesity and diabetes [8].

In fact, controlling the blood sugar levels by diet therapy in patients with GDM leading to improved perinatal outcomes has been widely proven to be an effective method. Therefore, the medical professional organizations have advocated a target of glucose control during pregnancy [9]. However, there are few studies that have investigated the effect of diet on blood lipid levels in specific areas but still no studies have mentioned about different eating habits. This study consists of selected pregnant women in southern China and to analyze the lipid changes during pregnancy in normal pregnant and GDM women, the impact of diet on blood lipids and the impact of lipids on birth weight, expecting to find high-risk factors and solid data in order to guide them about healthy eating during pregnancy.

2. Subjects and Methods

2.1. Patients

Between January 2012 and November 2013, pregnant women were recruited from the outpatient department at the First Affiliated hospital of GuangXi Medical University (China, GuangXi). Inclusion criterion for GDM was impaired glucose tolerance in oral glucose tolerance test (OGTT), as described below. Matched pregnant women with normal oral glucose tolerance test served as controls (Control Group). Exclusion criteria for both groups were: (I) history of concurrent liver, renal or rheumatologic diseases, hypertension, and thyroid disease. (II) medications that could affect glucose homeostasis during pregnancy or 12 months pre-pregnancy (sibutramine, orlistat, rimonabant, corticosteroids); (III) insulin using. (IV) multiple pregnancy. (V) family history. Family history of diabetes was defined as a history of diabetes in biological relatives, including parents, siblings, and grandparents. (VI) preterm delivery. After the inclusion and exclusion criteria were applied, a total of 175 women were included in the current analysis. Gestational age was determined by using the first-trimester ultrasound assessment. GDM patients were managed throughout pregnancy with diet alone. According to their glucose levels, GDM pregnant women were divided into two groups, blood glucose control group and poor glycemic control group.

Signed informed consent was obtained from all participants, and the study was approved by Research Ethics Board of the First Affiliated hospital of GuangXi Medical University.

2.2. Methods

Baseline assessment included age, gravidity, pregravid body mass index (BMI) calculation. Newborn weights were recorded. Lipid data were recorded from GDM group and normal group of pregnant women in the 12^{th} ~ 14^{th} and 34^{th}-35^{th} weeks of pregnancy, Morning fasting peripheral venous blood was obtained for determination of serum lipid levels, including serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), lipoprotein (a) [LP (a)], apolipoprotein A1 (apoA1) and apolipoprotein B (apoB).

All women who met the inclusive criteria performed OGTT at 24~28 gestational weeks. According to the criteria proposed by the International Association of Diabetes and Pregnancy Study Groups (IADPSG) [10], the diagnosis of GDM was established when at least one glucose value during a 75 g OGTT was equal or exceeding the following thresholds: fasting, 5.1 mmol/L (92 mg/dL); 1 h, 10.0 mmol/L (180 mg/dL); and 2 h, 8.5 mmol/L (153 mg/dL). Once diagnosis of GDM was established, the patients were given individualized dietary guidance from our hospital nutrition clinic department. The control target postprandial blood glucose was fasting state<5.3 mmol/L, 2hr postprandial< 6.7 mmol/L. According to the glucose monitoring results, the GDM group was divided into 2 groups, those with blood glucose under control and those with poor glycemic control. The inclusion criterion for poor glycemic is three times of blood glucose monitoring results exceeding 10% of the normal range or HbA1>6.5% for one time. These patients refused to use insulin because they did not follow the doctor's advice to control the diet intake as required.

Dietary intake was collected by using an FFQ, which was originally developed by Block et al [11,12]. The modified Block FFQ was designed to capture dietary intakes used in the current study to ask women to recall usual intake during the time between 12^{th} week of gestation to the date of performing OGTT. A paper copy of the FFQ was completed before the pregnant women can know about the result of the OGTT.

Participating women were asked about the frequency and amount of each food and beverage item consumed. Night frequency categories ranging from "never" to "every day" could be selected for most food items. The portion size consumed could be selected from a list of common food serving units, photographs representing 3-dimensional bowl and plate portions ranging from 10mL to 500ml was included. The questionnaire was designed to take 20 minutes to complete. Study personnel checked for the completeness of each FFQ question during the study visit and reminded the participants to fill in any unanswered questions. The FFQs were scanned and analyzed by EpiData software [13] using a food list developed from Chinese Center for Disease Control and Prevention diet and nutrient content database.

2.3. Statistical Analysis

All statistical analyses were carried out with the SPSS statistical software version 16.0. Data were expressed as mean ± standard deviation. Intergroup differences were compared using a two-tailed Student's t test. Correlation analysis using Spearman rank correlation analysis as appropriate. P value of < 0.05 was considered statistically significant.

3. Results

3.1 Characteristics of the participants with and without GDM are presented in Table 1. There were no statistically significant difference in age, parity, pregravid BMI, TC, TG, HDL-C, apoA1, LP between the control group and GDM (P >0.05). A higher apoB, LDL-C in GDM group(P <0.05).

Table 1. Baseline Characteristics and lipids of the participants with and without GDM in first trimester

	Control (n=90)	GDM (n=85)	t	P
Age(y)	28.28±3.71	29.23±3.66	-1.704	0.092
Gravidity	1.93±1.12	1.83±1.03	0.614	0.541
Pregravid BMI(kg/m2)	21.66±2.37	21.32±2.33	0.956	0.341
TC(mmol/L)	4.42±0.70	4.62±0.82	-1.738	0.086
TG (mmol/L)	1.48±0.66	1.39±0.46	1.041	0.300
HDL-C (mmol/L)	2.27±0.41	2.34±0.56	-0.947	0.345
LDL-C (mmol/L)	2.54±0.72	2.88±0.84	-2.880	0.005
apoA1(g/L)	1.54±0.46	1.71±0.73	-1.854	0.067
apoB(g/L)	0.74±0.16	0.88±0.21	-4.977	0.000

Data are mean±SD values

3.2 Assessment of nutrition intake among the participants. Nutrient intake of the participants to the OGTT day (24-28 weeks) with and without GDM is presented in Table 2. Energy, carbohydrate intake in women with normal pregnancy were lower than that in patients with GDM (P <0.05). The pregnancy weight gain

to OGTT did not have statistically significant difference between 2 groups. However, when using BMI as a parameter, the control group has a lower weight gain/BMI compared to the GDM group (P <0.05).

Table 2. Nutrition intakes and weight gain to the date of performing OGTT.

	Control(n=90)	GDM(n=85)	t	P
Total energy (kcal/d)	1928.4±155.61	2637.2±275.46	-21.106	0.000
fat (g/d)	60.75±7.22	63.24±9.86	-1.914	0.058
protein(g/d)	88.94±7.14	91.12±8.69	-1.817	0.071
Carbohydrate (g/d)	263.64±29.75	379.62±55.99	-17.244	0.000
Pregnancy weight gain up to OGTT(kg)	5.85±1.12	6.24±1.51	-1.903	0.059
weight gain/ Pregravid BMI	0.27±0.06	0.29±0.07	-2.063	0.041

Data are mean ± SD values

3.3 Lipid changes among the normal pregnancy group in early stage and late stage are presented in Table 3. The level of TG, TC, HDL-C, LDL-C, apoA1, apoB in the third trimester pregnancy were significantly higher than the first trimester pregnancy in the normal group (all P <0.05).

Table 3. Lipids changes in different pregnancy phases among normal pregnancy group

Control(n=90)	Early phase	Late phase	t	P
TC (mmol/L)	4.42±0.70	6.03±1.16	-13.506	0.000
TG(mmol/L)	1.48±0.66	3.79±1.81	14.539	0.000
HDL-C (mmol/L)	2.27±0.41	2.09±0.54	2.696	0.008
LDL-C (mmol/L)	2.54±0.72	3.29±1.00	-6.151	0.000
apoA1(g/L)	1.54±0.46	1.96±0.64	-6.266	0.000
apoB(g/L)	0.74±0.16	1.02±0.23	-13.058	0.000

Data are mean±SD values

3.4 Lipid changes and neonatal weight between the GDM group and control group in the late stage are presented in Table 4. Comparing with the control group in late phase, there was lower TG, but a higher apoB in glucose control group (P <0.05). There were higher TC, TG and neonatal weight in the poor glycemic group compared to the control group in the late phase (P <0.05). There was no statistically significant difference in neonatal weight between control and blood glucose control group (P >0.05).

Table 4. Lipids changes in late trimester and neonatal weight between normal and GDM groups

	Control (n=90) Late phase	GDM Late phase	
		blood glucose control group (n=71)	poor glycemic control (n=14)
TC (mmol/L)	6.03±1.16	6.23±1.06	7.60±2.54*
TG (mmol/L)	3.79±1.81	3.09±1.36*	4.80±1.41*
HDL-C (mmol/L)	2.09±0.54	2.09±0.45	2.19±0.97
LDL-C (mmol/L)	3.29±1.00	3.55±0.94	3.41±1.21
apoA1(g/L)	1.96±0.64	1.91±0.39	2.15±0.80
apoB(g/L)	1.02±0.23	1.10±0.22*	1.00±0.25
Neonatal weigh(g)	3218.0±325.86	3255.2±469.39	3867.3±335.19*

Data are mean±SD values. * comparing with the control, P<0.05.

3.5 The correlation analysis of neonatal birth weight is present in Table 5. using lipid as variables, neonatal birth weight as the dependent variable, the correlation analysis results showed that TG, TC in late pregnancy has a positive correlation with neonatal birth weight (P <0.05).

Table 5. Correlation between birth weight and blood lipids in late trimester

	Newborn weight (m/g)	
	r	P
TC (mmol/L)	0.197	0.009
TG (mmol/L)	0.191	0.011
HDL-C (mmol/L)	-0.075	0.322
LDL-C (mmol/L)	0.112	0.141
apoA1(g/L)	-0.007	0.922
apoB(g/L)	0.089	0.240

4. Discussion

The results of this study showed that compared with normal pregnant women during early pregnancy, apoB, LDL-C concentration is increased in GDM patients, which suggests that when the placenta is formed, dyslipidemia has occurred in GDM patients.

Studies have shown that multiple dysfunctional genes and protein regulation are closely related with gestational diabetes mellitus, however, there is a relatively stable incidence of genetic disease, and therefore the recent significant increase in diabetes cannot be explained. Epidemiological studies prompt that gene difference may not be the determining factor [14]; lifestyle plays an important role in the occurrence of diseases. After the retrospective survey of diet of pregnant women, we found that compared to normal pregnant women, GDM patients daily intake of dietary fat and carbohydrate were statistically significantly increased (P <0.05), the excess nutrient intake also caused a pregnancy excessive body weight gain and diabetes. The excessive carbohydrate intake not only increases blood sugar directly, but also can be transformed into lipids that affect pancreatic beta cell function [15].

Pregnancy is a normal physiological process. To adapt to the progression of pregnancy, there are a series of changes that occur in organs and tissues, including the endocrine system, changes in blood lipid levels which is extremely significant [16]. Our study found that with increasing gestational age, the tendency of blood lipid elevation is more obvious, as in later trimester serum TG, TC, LDL-C, HDL-C, apoA1, apoB levels were increased compared to early pregnancy, the difference was statistically significant (P <0.05), consistent with the relevant reports [17]. Analysis showed that the following factors might be the reasons for the changes. First of all, pregnant women in order to maintain the pregnancy, fetal

growth and postpartum lactation requirements, intestinal fat absorption capacity enhancement causes physiologically elevated lipid levels [18]. Secondly, insulin is an important hormone for metabolism; it has the function of regulating blood lipids [19]. Placental insulin degrading enzymes can accelerate insulin degradation, combined with resistin and leptin produced by the placenta [20], Therefore, pregnant women manifest temporary insulin resistance, causing TG, LDL, free fatty acids to be elevated significantly [21]. Again, protein hormones and steroid hormones are secreted by the placenta that can affect the biological effects of insulin to gradually increase, and reach to the maximum point in late pregnancy, so with increasing gestational age, the indicators of blood lipids increases at different levels. Even though, TG, TC, LDL-C, apoB can act as inducing endothelial injury factors, apoA1 as anti-vascular disease factors, when both are in dynamic equilibrium, hyperlipidemia in the normal pregnant women is also unlikely to cause vascular diseases which can lead to pregnancy complications.

Compared to the control group in the third trimester, good glycemic control group has a lower serum TG concentration, while in the poor glycemic control group lipid metabolism has a further aggravated tendency. Comparing the positive nutritional therapy to the GDM patients, normal pregnant women lack the professional dietary guidance, which might be the cause for some parts of lipid levels being higher than in the control. The result is similar with Velaquez-Lopez's research [22]; consumption of unsaturated fatty acids not only decreases the lipid concentration, but also helps to control the blood glucose in GDM patients [23]. Dietary soy isoflavones have the efficacy of lowering blood TC, TG, LDL-C level [24]; dietary fiber can reduce the absorption of sugar and fat, and promote excretion [25]; Combining all these information, pregnant women in addition to controlling the daily intake of carbohydrates, also have to pay attention to the structure of the diet.

Neonatal weight is influenced by nutrition, maternal factors, and genetic factors. Our study shows that neonatal weight has a positive correlation with TG, TC. Triglycerides are not directly available through the placenta, but it is available in a simple way through the placental barrier diffusion after decomposition to free fatty acids by lipoprotein lipase in the placenta, involved in the synthesis of fetal fat [26]. Endothelial cells and placental syncytiotrophoblast transport large amounts of TC to fetal circulation [27].

In conclusion, increased lipid levels exist in pregnant women. Lipid loads in GDM women are higher than normal pregnant women in early and late pregnancy, which indicate there might be Dyslipidemia in GDM. Lifestyle, such as excessive intake of inappropriate nutrition, is one of the reasons for the rise of gestational diabetes mellitus. Diet therapy can be used not only to control the blood glucose, but also to control serum lipid. Neonatal birth weight and lipid levels are closely related, through diet guidance, we expect to decrease the neonatal birth weight in GDM. Considering the reality in developing countries or regions, it is suggested that our future research will be carried out on pregnant women on how to perform a more effective health education and an acceptable dietary guidance to increase patient compliance.

Acknowledgements

Acknowledgement for financial support, the Medical and Health Foundation of GuangXi, China (MHZ2010020, Z2010354).

Author Disclosure Statement

No competing financial interests exist.

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