Lipid Concentration at 13-23 Weeks of Pregnancy and the Risk of Abnormal Glucose Challenge Test (GCT)

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Received: 16 July 2015

Accepted: 25 September 2015

Published in December 2015

Abstract

Objective: The aim of this study was evaluating the relationship between maternal serum lipid measured at 13-23 weeks of pregnancy and subsequent glucose intolerance.

Materials and Methods: In a prospective study, 624 pregnant women prior to 23 weeks were eligible for the study. Primarily, serum levels of total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride were measured. Women were grouped according to tertiles determined by the distribution of maternal serum lipid concentration among the entire cohort. Then, all patients at 24-28 gestation weeks were screened with a 50gr oral glucose test. The prevalence of abnormal GCT was compared among the lipid profile tertiles.

Results: The number of women with abnormal GCT was less in the group with TG concentration in lower tertile in comparison with the groups with TG concentrations in the higher and middle tertile (P<0.001, P=0.004 respectively) .

Conclusion: Triglyceride levels early in pregnancy are associated with abnormal GCT.

Keywords: Lipid concentration, Pregnancy, Glucose challenge test

Introduction

In normal pregnancy, there is a major alteration in maternal lipid profile. Pregnancy may increase 300% triglyceride (TG) level, 25-50% increase in total cholesterol (TC), high density cholesterol (HDL) and low density lipoprotein (LDL) (1,2). In gestational diabetes, exaggerated hypertriglyceridemia has been found in the first, second and third trimesters of pregnancy compared to normal pregnant women, although there are studies which show no changes in plasma lipid levels of diabetic compared to non-diabetic pregnant women (3-7). In general, the case control and prospective studies findings have been unreliable. These studies have been limited by their relatively small sample size and no adjustment for potential confounding factors.

Gestational diabetes mellitus (GDM), complicated 3-5% of pregnancies. The disorder is associated with high maternal and fetal morbidity (9-11). Insulin resistance during pregnancy generally appears in the second trimester or later, so that GDM is often overlooked and undiagnosed at the first trimester. It has been suggested that not

significant increase of glucose intolerance during pregnancy in women without gestational diabetes are related tohigh incidence of macrosomia, cesarean section, preeclampsia, and increase need for NICU admission, as well as greater length of maternal and neonatal hospital inpatient care (12-16).

In the present study, we studied the relationship between maternal serum lipid measured at 13-23 weeks y and subsequent glucose intolerance while adjusting for the confounding factors.

Materials and methods

A prospective study of 624 pregnant women, between Jan 2010 to Feb 2011 was performed. The pregnant women were chosen from prenatal clinics in City of Ray- Iran. Women who initiated prenatal care before 23 weekswere eligible for the study. Women with diabetes mellitusor other endocrine or metabolic disorders, cardiovascular diseases, renal or any chronic diseases, multiple pregnancies and fetal anomalies, and smokers were excluded. They were entered the study after completing an informed consent.

Initial data including maternal age, pregnancy weight, parity, gestational age, weight, height and medical histories were recorded. Gestational age was calculated based on the last menstrual period and was confirmed by diagnostic ultrasonography performed before 20 weeks of gestation.

Primarily, serum levels of total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride were measured. Then, the women were observed once every other week until 24-28 weeks of gestational age. We applied the same method of screening to our patients. All patients at 24-28 weeks of gestation were screened with a 50gr oral glucose. The blood glucose value ≥140 mg/dl one hour after the glucose load was considered abnormal and was followed by 100gr oral glucose tolerance test. GDM was determined based on the American Diabetes Association (ADA) criteria (17).

Cholesterol and TG were determined by enzymatic colorimetric methods (Pars Azmoon Kits Inc Tehran, Iran).The LDL and HDL cholesterol plasma levels were estimated with LDL,HDL-Cholesterol direct methods (BIOLABO REAGENTS Kits). Glucose was measured by enzymatic colorimetric method (glucose oxidas) by commercial kit (Pars Azmoon Inc Tehran, Iran). Blood samples were taken 12 h after an overnight fasting. Laboratory determination was carried out on the day of blood sampling.

Women were grouped according to tertiles determined by the distribution of maternal serum lipid concentrations among the entire cohort. The prevalence of abnormal challenge test was compared among the lipid profile tertiles. Frequency distributions of maternal medical and reproductive history were examined within each tertiles if it was necessary.

The procedures were approved by the ethic committee of the TarbiatModares University.

Statistical analysis

The one way analysis of variance (ANOVA, Tukey post hoc) and χ^2 test were used for the comparison of maternal data among the women with different tertiles of lipid profile .For logestic regression analysis (forward method), correlation between the dependent and independent factors were calculated. A *P*-value of <0.05 was considered statistically significant. All confident intervals were calculated at the 95 percent.

Results

A total of 624 healthy pregnant women were enrolled in this study. Fifty women were excluded from analysis, 22 women delivered before 28 weeks of gestation, and 28 women loss to follow up.Finally 574 women completed the study.

There were 93 women (16.2%) who had an abnormal GCT. GDM was confirmed by GTT in 22 women (22/574, 3.83%).

Women with abnormal GCT were less in the group with TG concentration in lower tertile in

comparison with the groups with TG concentrations in the higher and middle tertile (*P*<0.001, *P*=0.004 respectively). There were not significant differences in the number of women with abnormal GCT in the other serum lipid tertile concentrations groups (table 1).

Characteristics of our cohort members according to maternal serum TG concentrations measured in 13-23 weeks of gestation was shown in table 2. Those with TG concentration in the higher tertile were significantly older, had higher body mass index (BMI) before pregnancy, higher parity and had been measured for lipid profile later in comparison with lower lipid profile tertile (table 2).

In logestic regression analysis, there was significant association between TG concentration, maternal age and BMI before pregnancy as independent factors and abnormal GCT as dependent one (*P*<0.01, *P*<0.001, *P*<001). There was no significant association between other serum lipid profiles and GCT results (table 3).

Post hoc analysis of our data indicated that triglyceride concentrations ≥ 142 mg/dl was defined as a cut-off point for a positive screen for subsequent abnormal GCT in our population. The sensitivity, specificity positive and negative predictive values would be 61.3%, 60.1%, 73.1% and 74.6%, respectively.

Discussion

Gestational diabetes mellitus is associated with maternal and fetal morbidity. Although controversy exits regarding the specific protocols to apply, screening for GDM by glucose tolerance testing in pregnancy has become a standard method of obstetrical care. Diabetic women are treated with therapeutic regime or insulin to reduce glucose levels in pregnancy and improve obstetrical outcome. Previous studies have demonstrated that increasing carbohydrate intolerance in women without overt gestational diabetes was associated with a significantly increased incidence of pregnancy complications (12-16).

Table 1. Comparison of abnormal GCT among the three tertile lipid concentrations

Parameters	Low tertile	Mid tertile	High tertile	*P*-value
Total cholesterol (mg/dl)	<165	165-213	>213	
Abnormal GCT (n)	19	42	32	N.S
LDL cholesterol (mg/dl)	<80	80-114	>114	
Abnormal GCT (n)	21	41	31	N.S
HDL cholesterol (mg/dl)	<49	49-65	>65	
Abnormal GCT (n)	24	51	18	N.S
Triglyceride (mg/dl)	<109	109-174	>174	
Abnormal GCT (n)**	10	48	35	<0.001

* χ2test, Fisher´s Exact test

**plow tertile versus mid tertile =0.004, plow tertile versus high tertile<0.001.

Table2. Characteristics of study cohort members according to maternal TG concentrations

Parameters	Low tertile	Mid tertile	High tertile	P1	P2	P3
Maternal age (years)* mean±SD	24.30±4.51	26.14±4.40	27.19±4.37	<0.001	<0.001	0.05
BMI before pregnancy* (kg/ml) mean±SD	22.74±3.93	24.78±4.54	26.48±4.69	<0.001	<0.001	0.001
Parity n (%)**						
Primipar	87(60.8)	132(46.0)	51(35.4)	0.009	<0.001	N.S
Multipar	56(39.2)	155(54.0)	93(64.6)			
Gestational age at lipid measurement*(weeks) mean±SD	16.39±3.13	17.61±3.42	18.64±3.78	0.002	<0.001	0.01

*ANOVA Test (Tukey), ** χ2 test

P1: plow tertile versus mid tertile, P2: plow tertile versus high tertile, P3: pmid tertile versus high tertile.

Table3. Odds Ratio of abnormal GCT: multiplelogestic regression model (TG concentration, maternalage, BMI before pregnancy, parity and gestational age at lipid measurementas independent factors)

Predictive variable	OR	95%CI	*P*
TG concentrations	1.005	(1.001-1.010)	0.008
maternal age	1.174	(1.106-1.246)	<0.001
BMI before pregnancy	1.101	(1.045-1.160)	<0.001

OR=odds ratio, CI=confidence interval

*No significant association between gestational age at lipid measurement and parity with abnormal GCT.

Insulin resistance is associated with a clustering of interrelated plasma lipid abnormalities. Dyslipidemia has also been noted in women with GDM in various control studies. But, their findings were not similar (3-7). In addition, maternal serum lipid concentrations were determined after the diagnosis of GDM, thus making it difficult to identify whether dyslipidemia is a pathogenic risk factor or a consequence of the disorder. Few investigations have measured maternal plasma lipids in early pregnancy in relation to subsequent risk of GDM (18,7).

We evaluated the relationship between maternal plasma lipid in early pregnancy, and subsequent abnormal GCT while adjusting for confounding factors. We found a positive association between increasing levels of TG and increased risk of abnormal GCT. Associations between the other lipids and the risk of developing abnormal GCT were not evident. We apply a logestic regression model with variables, including maternal age, BMI before pregnancy ,parity and gestational age at lipid measurement as independent factors and abnormal GCT as dependent factor, to test whether maternal hypertriglyceridemia associate with the risk of having an abnormal GCT, independent of confounding factors. In thelogestic regression model hypertriglyceridemia at 13-23 weeks, maternal age and BMI before pregnancy had significant association with abnormal GCT.

Results from our study suggest that hypertriglyceridemia early in pregnancy may be predictive of abnormal GCT. However, our findings suggest that elevated serum TG level may not be sufficient for identifying women at high risk of developing abnormal GCT.

Some studies findings have not been consistent with our findings. (3,7,18,19). We considered abnormal GCT as a primary outcome but the previous studies have been conducted to assess lipid profiles in early pregnancy and subsequent risk of GDM. Additionally, these differences may be due to difference in study design, confounding factors, fasting or non-fasting blood samples collection and variations in population characteristics.

In our study, we used multivariate procedures to adjust confounders. In addition, we collected blood samples early in pregnancy to avoid concerns about the effect of past-diagnostic glucose control. On the other hand, the high rate of enrolled women and follow up reduced the selection bias.

Our study, however, had some limitations. First, a single measurement of serum lipid levels may cause misclassification of maternal lipid status. Second, maternal pre-gestational status was based on self-report, and chances of undiagnosed diabetes were likely.

Our findings suggest that hypertriglyceridemia early in pregnancy may be predictive of abnormal GCT. Some investigators have postulated that dyslipidemia may cause pancreatic β-cell dysfunction and suppression of insulin gene expression (20).Demonstrating an association between increasing of TG and risk of abnormal GCT in our study can further strengthen this thesis.

Future longitudinal study with serial lipid levels measurement in all three trimester is recommended. Additionally, etiological studies are also suggested to consider the relationship between insulin resistance and dyslipidemia.

Acknowledgment

This study was carried out with the kind cooperation of the participating patients. Our

study had no conflict of interest and was funded by Tarbiat Modares University.

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