Increased Carotid Artery Intima-Media Thickness in Pregnant Women with Gestational Diabetes Mellitus

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Original Article

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Abstract

Background: Pregnant women with previous gestational diabetes mellitus are at increased risk of progressive carotid artery disorders. The current study evaluated carotid intima-media thickness (IMT) in pregnant women with gestational diabetes at two time points of mid-term and full-term pregnancy to determine whether gestational diabetes mellitus causes increased IMT.

Methods: This cross-sectional study carried out at Afzalipour Hospital (Kerman, Iran) between 2009 and 2010, recruited 50 women who were at high risk of gestational diabetes during pregnancy and had an oral glucose challenge test (OGCT) as screening for gestational diabetes. B-mode ultrasound scans were performed at baseline and at two time points of mid-term pregnancy (20 to 24 weeks) and full-term pregnancy (36 to 38 weeks) on all the participants. The mean IMT of common carotids and internal carotid arteries from two walls (near and far walls) at four different angles was assessed.

Results: An overall comparison between the impaired OGCT test group and the control group revealed significant differences in carotid IMT in the mid-term (0.65 ± 0.07 vs. 0.59 ± 0.06 mm; p value = 0.002) and full-term (0.65 ± 0.05 vs. 0.59 ± 0.04 mm; p value < 0.001) pregnancy; however, the trend of the changes in carotid IMT during mid to full-term pregnancy was insignificant in each group (p value > 0.05).

Conclusion: Carotid IMT was significantly higher in the women with gestational diabetes than that in the normoglycemic group in different trimesters. This finding denotes that atherosclerosis might start years before the diagnosis of gestational diabetes in vulnerable women.

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Keywords: Pregnancy • Diabetes mellitus • Carotid arteries

Introduction

Screening for gestational diabetes mellitus is routinely programmed to prevent complications caused by elevated blood glucose levels in pregnancy, including macrosomia, Cesarean delivery, shoulder dystocia, neonatal metabolic problems, perinatal mortality, and pre-eclampsia. Diabetes mellitus during pregnancy also appears to be associated...
with an increased risk of cardiovascular diseases even in later life. Moreover, this underlying co-morbidity is an independent risk factor for subsequent coronary artery disease. In this context, diabetes mellitus during pregnancy has been identified as a major etiology for atherosclerosis in large elastic arteries.

One of the main indicators for assessing atherosclerotic lesions during this period is the increased intima-media thickness (IMT) of carotid arteries. It has been well known that, as opposed to the blood flow through the other arteries of the maternal organs, the blood flow through the carotid artery is decreased during pregnancy, which has been attributed to pregnancy-mediated increased responsiveness of the carotid artery to vasoconstrictors and decreased responsiveness to vasodilators. Also, the endothelial hypertrophy of the carotid artery can be a common finding, leading to changes in the carotid blood flow and its complications. Thus, increased carotid IMT can be deemed a validated endothelial dysfunction surrogate endpoint during pregnancy.

Some studies have recently shown that pregnant women with previous gestational diabetes mellitus are at increased risk of carotid artery disorders. Be that as it may, the scarcity of research into this hypothesis means that it is still unknown whether or not gestational diabetes mellitus causes increased IMT. The current study was performed to evaluate carotid IMT in diabetic pregnant women with gestational diabetes and to ascertain if an impaired oral glucose challenge test (OGCT) correlates with the development of increased IMT.

**Methods**

This cohort study included 50 women ranging from 18 to 35 years of age at high risk of diabetes during pregnancy. Gestational diabetes mellitus was screened with a one-hour 50 g oral glucose challenge test (OGCT). Abnormal results were, thereafter, confirmed with a three-hour 100 g oral glucose tolerance test (OGTT). Eligible women were nulliparous with a singleton pregnancy, had a normal blood pressure at the time of recruitment, and gave informed consent. Women with any of the following were excluded: family history of cardiovascular disorders; history of hypertension; anti-hypertensive and cholesterol medication use; hyperlipidemia; overt diabetes or fasting plasma glucose (FPG) > 125 mg/dl according to the American Diabetes Association (ADA) definition; chronic renal or hepatic diseases; malignancies; recent hormonal medications; cigarette smoking; severe obesity (body mass index [BMI] > 35 kg/m²); and history of infertility or polycystic ovarian disease. Those with the status of plaques/shadowing (≥ 1.0 mm) at any carotid site were also excluded. The study protocol was approved by the Research and Ethics Committees at Kerman University of Medical Sciences.

Baseline demographic variables were collected either from the women’s medical records or self-completed questionnaires at trial entry and comprised maternal age, height, weight, BMI, smoking status, and blood pressure at trial entry. Complete baseline data were available for all the women. All lipid and lipoprotein measurements were made at a central laboratory. Total cholesterol was measured enzymatically with standard methods and total triglyceride was measured via standard spectrophotometric techniques. After the precipitation of low-density lipoprotein (LDL) particle with phosphotungstic acid, high-density lipoprotein (HDL) cholesterol was measured enzymatically in the supernatant by a modification of the method for total cholesterol.

B-mode ultrasound scans were performed at baseline and at two time points of mid-term pregnancy (20 to 24 weeks) and full-term pregnancy (36 to 38 weeks) on all the participants. Carotid ultrasound scans were carried out by a single trained sonographer unaware of the study protocols and methodology. B-mode ultrasound images were equipped with a 7.5-MHz linear array transducer and captured with a GE log 200 ultrasound machine. The ultrasonic variable used in the statistical analysis was the mean of the IMT of common carotids and internal carotid arteries from two walls (near and far walls) at four different angles.

The mean of carotid IMT was compared between the women with impaired OGCT and those who screened normal on OGCT at the two study time points. For the statistical analyses, the statistical software SPSS version 19.0 for Windows (SPSS Inc., Chicago, IL) was used. The continuous variables, if normally distributed, were analyzed using the Student-test and presented as mean differences, while the Mann-Whitney test was employed for skewed data. A p value of 0.05 or less was considered to indicate statistical significance.

**Results**

The baseline characteristics of the pregnant women with impaired OGCT tests are presented in Table 1. The two groups were similar in terms of pregnancy age, height, weight, BMI, and baseline laboratory parameters. There were no significant associations between carotid IMT and maternal indices, including the demographic variables and laboratory parameters.

An overall comparison between the impaired OGCT test group and the control group via the Mann-Whitney U test revealed significant differences in carotid IMT in the mid-term and full-term pregnancy (Table 2). The trend of the changes in carotid IMT during the mid-term to full-term pregnancy was, however, insignificant in each group.
**Discussion**

An increased carotid IMT can be observed not only in long-standing type II diabetic but also in newly detected type II diabetic patients. Especially in pregnant women, carotid IMT gradually increases from the first to the third trimester of normal pregnancy and regresses in the postpartum period. Nevertheless, the trend of the increase in pregnant women with gestational diabetes is still unclear. In our study, with the aid of carotid ultrasound, arterial examination was performed at mid-term and full-term pregnancy and both controls and the women with an impaired OGCT test were assessed and compared with regard to the changes in carotid IMT. We showed that although carotid IMT was more increased in those with impaired OGCT, the trend of this change was similar between the impaired and normal OGCT groups. Furthermore, we observed that carotid IMT was significantly higher in the diabetic group than in the normoglycemic group in different trimesters, but the trend of these gradual changes from the first to the third trimester was similar in both groups. Totally, effective glycemic control seems to be helpful for the prevention of increased carotid IMT.

During the pregnancy period, peripheral vascular resistance is physiologically paralleled by improved macrovascular compliance. Some researchers have shown that 2-4 years after previous gestational diabetes mellitus, a significantly higher arterial stiffness can be found compared with reference women without a history of diabetes. Pregnancies complicated by diabetes not only are associated with increased carotid IMT but also can lead to increased maternal arterial stiffness.

This study demonstrates increased IMT of the carotid artery in a group of women who had a pregnancy complicated by impaired OGCT. This finding is in line with the literature confirming that women with a history of gestational diabetes have a higher risk of developing increased carotid IMT. This change can potentially lead to cardiovascular diseases in later life. There are some explanations for this phenomenon. One of the first steps in the development of atherosclerosis is endothelial activation, followed by endothelial dysfunction. Thus, in diabetes mellitus, vascular endothelial activation or dysfunction is considered to play a key role in the development of many of the clinical manifestations related to carotid artery disease, several years after delivery.

Association between parity and carotid artery disease can be affected by some underlying factors. Some epidemiological studies have found positive associations between parity and risk of carotid artery plaques in elderly women and, therefore, age of pregnancy can be a trigger for this phenomenon. Also, multi-gravidity and previous history of coronary diseases have been also identified to be related to the appearance of carotid artery plaques. Folate deficiency during pregnancy is another probable triggering factor for progressing carotid IMT. Folate deficiency is linked with hyperhomocysteinemia, which is associated with accelerated progression of atherosclerosis and, thereby,
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