ORIGINAL ARTICLE

Eastern Journal of Medicine

East J Med 28(4): 618-623, 2023
DOI: 10.5505/ejm.2023.57778

Comparison of Carotis İntima Media Thicknesses İn Gestational Weeks 24-26 and 36-38 İn Pregnant Women With Gestational Diabetes

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ABSTRACT

The aim of this study is to investigate the differences between carotid intima media thickness (CIMT) of patients with gestational diabetes mellitus (GDM) and healthy pregnant women.

METHODS: In this prospective study, 30 patients diagnosed with GDM and 30 healthy pregnant women were included. Serum HDL, LDL, TG, HbA1C and CRP levels, body mass indexes (BMI), and CIMT were measured for all participants included in the study. Measurements were repeated at 36-38 weeks of gestation. The difference between the second and third trimester measurements of both groups was compared.

Second trimester CIMT measurements of GDM and healthy pregnant women were 5.483 ± 0.825 mm and 4.866 ± 0.642 mm, respectively, and the difference between the measurements of the two groups was statistically significant. Third trimester CIMT measurements of GDM and healthy pregnant women were 5.516±0.748 mm and 4.983 ±0.724 mm, respectively, and the difference between the measurements of the two groups was statistically significant (p=0.016). The difference between the second and third trimester CIMT measurements of the patients in the GDM group was not statistically significant (p=0.326). The difference between the second and third trimester CIMT measurements of the patients in the control group was not statistically significant (p=0.09).

GDM patients are at risk for atherosclerosis. In treated GDM patients, the increase in CIMT can be prevented. These findings may indicate that with early diagnosis and treatment of GDM, our patients can be protected from the atosclerotic consequences of hyperglycemia.

Keywords: Atherosclerosis, Carotid intima media thickness, diabetes mellitus, gestational diabetes mellitus

Introduction

Diabetes mellitus (DM) is characterized by hyperglycemia, resulting inadequate effect for a variety of etiological reasons. Chronic hyperglycemia in diabetes may cause damage to many organs, such as the eyes, nerves or heart (1). Gestational Diabetes Mellitus (GDM) is glucose intolerance occurring or diagnosed at any stage of gestation (2, 3). Pregnancy-induced DM brings with it various fetal and maternal risks. Perinatal complications with serious morbidity and mortality risk have been associated with GDM (4, 5). Patients with GDM are at risk for type 2 DM after pregnancy (6, 7).

The importance of diagnosis and treatment of cardiovascular risk factors in diabetic patients can be more clearly understood when it is considered that cardiovascular diseases play a role of Type 2 diabetic patients (8). The measurement of carotis intima media thickness (CIMT) is an increasingly common method for the diagnosis of atherosclerosis. This method is easy to implement and is predictive of future cardiovascular diseases. Increased CIMT is associated with cardiovascular risks (9-11).

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Received: 11.03.2023, **Accepted:** 15.08.2023

In this study, it was aimed to determine the differences of CIMT in pregnants with and without GDM. Additionally, the differences of CIMT values at second and third trimesters also investigated.

Material and Methods

The study included 30 pregnant women (study group) who presented at the antenatal clinic between 01.07.2012 and 01.07.2013 during gestational weeks 24-28 and were diagnosed with GDM by 75 gr OGTT and 30 pregnant women (control group) who did not have GDM. Approval for this prospective study was granted by the Clinical Research Ethics Committee of Recep Tayyip Erdogan University (Decision No: 2012/107). Informed consent was obtained from all the patients and the participants in the control group. For OGTT, blood samples were obtained from patients after 8 hours fasting. The IADPSG criteria were used for GDM diagnosis (fasting glucose :> 92 1st hour>180 and 2nd hour>153). Body mass index (BMI), HbA1C(hemoglobin A1C), HDL(High-density lipoprotein), LDL(Low-density lipoprotein), TG (triglyceride), micro CRP (C- reactive protein) levels and CIMT of the patients included in the study were measured. Pregnant women diagnosed with GDM were referred to the Endocrinology Polyclinic for the necessary treatment. These patients were recalled between gestational weeks 36 and 38, and CIMT was measured again. The CIMT levels of the GDM patients and the control group were compared with the baseline levels. Statistical analysis was applied to determine significant differences between the control group and the study group in all the parameters studied. Inclusion criteria were GDM-diagnosed pregnancy with 75 gr OGTT at 24-28 gestational weeks for the study group and a healthy pregnancy with no GDM with 75 gr OGTT at 24-28 gestational weeks for the control group. Those included in both groups had not been diagnosed with coronary heart disease or fetal anomaly. Exclusion criteria were the presence of any known atherosclerotic or inflammatory disease, type 1 or type 2 DM, smokers, or a diagnosis of GDM in a previous pregnancy. Patients who gave birth pre-term and those who developed pre-eclampsia or hypertension were withdrawn from the study after the research had started.

CIMT was measured by an experienced radiologist using the same device and method. Patients were examined in the supine position with the head in mild extension. The intima and media layers of the vessel wall 1 cm proximal from carotid bulb of the right and left common carotid arteries were measured at three different points with longitudinal scanning. The arithmetic mean of the obtained data was calculated. The radiologist measuring the CIMT was blinded to the patient groups.

The study performed according to The Principles of Helsinki Declaration.

Statistical Analysis: Statistical analyses were made using SPSS 17.0 software. While evaluating the study data, in addition to descriptive statistical methods (mean, standard deviation) in the comparison of quantitative data, the Paired sample T Test was used in the comparison of the parameters with normal distribution. Normality of the data was evaluated with Kolmogorov-Smirnov test. The Mann-Whitney U test was used in the evaluation of the data without normal distribution. A value of $p<0.05$ was considered statistically significant.

Results

The average age of all the participants in the study was 30.67 ± 5.937 years. No statistically significant difference were determined between the groups in respect of the average age, (p=0.459). The mean gestational week of all the pregnant women included in the study was 26 weeks ± 7 days. The mean gestational weeks of all pregnant women during the third trimester were 38 weeks ± 7 days. The mean number of pregnancies of the whole sample was 2.32 ± 1.32. The mean BMI of all the study participants was 27.76 ± 5.47 kg/m^2. No statistically significant difference were determined between the groups in respect of the average age, second trimester gestational week, third trimester gestational week, mean number of pregnancies and BMI (p=0.459, p=0.091, p=0.058, p=0.262 and p=0.626). The demographic data of the study and control groups are shown in Table 1.

The mean CIMT measured during the second trimester of the pregnant women in the study was found to be 4.866± 0.642 mm. The difference between the two groups were statistically significant (p=0.003). The mean CIMT measured during the third trimester of the pregnant women in the study were found to be 4.525± 0.778 mm. The difference between the two groups were statistically significant (p=0.016). In the GDM group, no statistically significant difference was determined between the CIMT values at the second and third trimester (p=0.326). In the control group, no statistically significant difference was determined between the CIMT values at the second and third trimester (p=0.09). Comparisons of mean CIMT values measured during the first and second control examinations of the two groups has shown at table 2.

Table 1: Demographic Data of The Study and Control Groups (Mann Whitney U test)

	GDM(mean ± SD)	Control(mean ± SD)	p
Age (years)	31.23±6.678	30.10±5.142	0.459
BMI (kg/m2)	25.05±5.05	27.47±5.93	0.626
Second trimester gestational weeks	26 .2 weeks ± 8 days	25 .5 weeks± 6 days	0.091
Third trimester gestational weeks	37.6 weeks± 7 days	38 .2weeks± 8 days	0.058
Gravida	2.57±1.54	2.07±1.01	0.262

Table 2: Comparisons of Mean CIMT Values Measured During The First and Second Control Examinations of The Two Groups (row: Mann Whitney U test, Column: Paired Sample T Test)

	Second Trimester CIMT measurement (mm) (mean ± SD)	Third trimester CIMT measurement(mm) (mean ± SD)	p
GDM	5.483±0.825	5.516±0.748	0.326
Control	4.866 ±0.642	4.983 ±0.724	0,09
p	0.003	0.016	

Table 3: Comparison of Biochemical Parameters of the GDM and Control Groups (Mann Whitney U test)

	GDM (mean ± SD)	Control (mean ± SD)	Total (mean ± SD)	p
HDL mg/dl	67.17±17.722	69.47±13.928	68.47±15.568	0.667
LDL mg/dl	139.12±46.802	148.03±41.026	143.98±43.56	0.654
Cholesterol mg/dl	248.14±56.422	256.1±47.168	252.26±51.536	0.809
TG mg/dl	218.54±105.465	192.87±66.118	205.26±87.523	0.474
HBA1C %	5.03±0.528	4.876±0.219	4.953±0.406	0.172
CRP mg/dl	1.062±1.184	0.565±0.355	0.795±0.874	0.116

HDL: High-density lipoprotein, LDL; Low-density lipoprotein, TG; Triglyceride, HBA1C; hemoglobin A1C, C-reactive protein

There were no statistically significant difference observed between the two groups in terms of HDL, LDL, total cholesterol, triglyceride, HbA1C and CRP levels (p=0.667, p=0.654, p=0.809, p=0.474, p=0.172 and p=0.116). The comparison of biochemical parameters of both groups is shown in Table 3.

Discussion

In the United States (USA), the prevalence of DM is estimated to be 9.5% on average (12). However, due to DM-related complications, this disease accounts for 14% of all healthcare costs in the USA and at least half of these complications arise from vascular pathologies (13). DM-induced morbidity is due to both macrovascular (atherosclerosis) and microvascular (retinopathy, nephropathy and neuropathy) diseases. Since the onset of these diseases is insidious, the diagnosis is usually delayed. As a consequence, when DM is diagnosed, microvascular complications of diabetes may have already developed. Therefore, early diagnosis of DM is of great importance for preventing or at least delaying the occurrence of such insidious and dangerous diseases (14, 15).

GDM is a very common medical disorder of pregnancy. The degree of glucose intolerance, i.e. treatment with diet or insulin, does not affect the diagnosis. The prevalence of GDM has been reported to be between 2% and 10% (2, 16).The prevalence of GDM varies according to the screening method used and the region scanned. However, there has been a recent increase in the prevalence of GDM (2). Possible factors that may be responsible for the increased prevalence are the aging population, urbanization, and increasing obesity worldwide. This increase in the prevalence of GDM and the risk of serious maternal/fetal complications reveals the importance of diagnosis and treatment of this disease (17).

CIMT measurement is a non-invasive method used as an indicator of subclinical atherosclerosis (18).The thickness of the intima and media layers can be measured in combination with high resolution B mode USG. CIMT is a valid method for predicting the risk of mortality and morbidity of vascular diseases. Increased CIMT also indicates an increased risk of cardiovascular disease in patients with diabetes. In patients with type 1 DM, the CIMT is greater than in the normal population. A study involving 1309 patients with type 1 DM showed that the CIMT of common carotid artery of these patients were weakly associated with cardiovascular events (19). This study is important in terms of demonstrating the relationship between DM and CIMT.

Since GDM occurs especially in the 2nd trimester due to the effect of diabetogenic hormones, if CIMT is increased due to chronic hyperglycemia, the CIMT values measured during these weeks should theoretically not be different in GDM and non-GDM groups. Again, theoretically, the CIMT values of patients with chronic hyperglycemia may be expected to further increase in later gestational weeks. However, if the CIMT is increased due to atherosclerosis before pregnancy or there is a genetic or metabolic predisposition to diabetes, the CIMT values of GDM patients should again theoretically be higher than those of non-GDM patients at any time during the pregnancy.

The results of the study showed that the CIMT of GDM pregnancies were higher than those of the control group. It was also shown that there was no increase in CIMT in appropriately-treated GDM pregnancies during progressive gestational weeks. Another finding of the study was that the CIMT measurement of non-GDM pregnancies did not show any significant difference in the second and third trimesters. This can be interpreted as the fact that uncomplicated pregnancy does not constitute a risk for atherosclerosis.

Studies in literature on subclinical atherosclerosis in GDM patients have shown that the thickness of the CIM in GDM patients is higher than that of patients with healthy pregnancies (20). Our findings were consisted to the literature. We also found that after appropriate treatment of GDM patients the CIMT measurements is not different from healthy pregnants in third trimester. These findings underlying the significance of screening and treatment of GDM.

Hyperglycemia is the main cause of microvascular complications in diabetic patients and may also blame of macrovascular complications (21). GDM is considered to be a prediabetic condition. Although most women with GDM have normal glucose tolerance after delivery, there is a risk of developing type 2 diabetes in the future. Patients with GDM have an increased risk for atherosclerosis and coronary heart diseases in addition to constituting a risk for type 2 diabetes and hypertension (22).

Between the first trimester and the third trimester of pregnancy, CIMT gradually increases, and then decreases after delivery (23). In the current study, the second and third trimester CIMT measurements of the control group pregnancies were compared. The third trimester CIMT values of these cases showed a slight increase compared to the second trimester, but not at a statistically significant level. These findings were consistent with literature.

There is a known relationship between blood lipids and CVD. In cases of increased insulin resistance, the production of very low-density lipoprotein (VLDL) from the liver increases inappropriately (24). These abnormalities may explain the dyslipidemia observed in diabetic patients (25). In this study, the difference between the blood lipids of the case and control groups was not statistically significant. The similar blood lipid levels, BMI and CRP in both groups indicate that the increase in CIMT in this study was not caused by atherosclerosis due to dyslipidemia or metabolic characteristics.

HbA1C is an indicator of chronic hyperglycemia. In particular, it is used to predict the blood glucose level during the last three months. In the current study, the HbA1C levels of the two groups with and without GDM were not statistically different. This showed that the hyperglycemic state of GDM patients included in our study was newly initiated and the CIMT increase was not due to chronic hyperglycemia.

Study Limitations: There are some weaknesses and strengths of this study. The pregnant women in the case and control groups being equivalent in terms of known risk factors for CVD, such as chronic hyperglycemia, blood lipids, age, CRP, and BMI, supports the notion that the risk factor for atherosclerosis in the CIMT measurements of both groups is GDM. The CIMT increase identified in the pregnant women with GDM in this study can be considered to be a GDM-dependent increase, independent of other factors. However, the limited number of pregnant women in the study group makes it difficult to apply the results to the general population. Furthermore, since anti-diabetic treatment was given to the pregnant women diagnosed with GDM, it is not possible to comment on CIMT increase in untreated GDM patients.

The results obtained in this study showed that the second trimester CIMT measurements in pregnant women with GDM were higher than those of healthy pregnancies. This can be interpreted as pregnant

woman with GDM having a predisposition to atherosclerosis even before the onset of diabetes. If pregnant women with GDM are appropriately treated, an increase in CIMT can be avoided. So these findings may suggest that early detection and treatment of GDM may prevent our patients from the atherosclerotic consequences of hyperglycemia.

Conflict of interests: The author(s) have no conflicts of interest relevant to this article.

References

1. American Diabetes Association. (2) Classification and diagnosis of diabetes. Diabetes Care. 2015; 38 Suppl: S8-S16.
2. Hillier TA, Pedula KL, Ogasawara KK et al. A Pragmatic, Randomized Clinical Trial of Gestational Diabetes Screening. N Engl J Med. 2021; 384(10):895-904.
3. Sellers EA, Dean HJ, Shafer LA, et al. Exposure to gestational diabetes mellitus: impact on the development of early-onset type 2 diabetes in Canadian first nations and non–first nation's offspring. Diabetes care, 2016; 39(12), 2240-46.
4. Choudhury AA, Devi Rajeswari V. Gestational diabetes mellitus - A metabolic and reproductive disorder. Biomed Pharmacother. 2021; 143:112183.
5. Ye W, Luo C, Huang J, et al. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. BMJ. 2022; 377:e067946.
6. Moon JH, Jang HC. Gestational Diabetes Mellitus: Diagnostic Approaches and Maternal-Offspring Complications. Diabetes Metab J. 2022; 46(1):3-14.
7. Noctor E, Dunne FP. Type 2 diabetes after gestational diabetes: the influence of changing diagnostic criteria. World journal of diabetes, 2015; 6(2), 234.
8. Parikh NI, Gonzalez JM, Anderson CAM, et al. Adverse Pregnancy Outcomes and Cardiovascular Disease Risk: Unique Opportunities for Cardiovascular Disease Prevention in Women: A Scientific Statement from the American Heart Association. Circulation. 2021; 143(18):e902-e16.
9. Kayastha P, Paudel S, Gurung G, et al. Mean Carotid Intima-Media Thickness in Patients with Type 2 Diabetes Mellitus Attending Tertiary Care Center: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2021; 59(244):1243-1246. Published 2021 Dec 11.
10. Ren L, Cai J, Liang J, Li W, Sun Z. Impact of cardiovascular risk factors on carotid intima-media thickness and degree of severity: a cross-sectional study. PloS one, 2015; 10(12), e0144182.
11. Wang X, Dalmeijer GW, Den Ruijter HM, et al. Clustering of cardiovascular risk factors and carotid intima-media thickness: The USE-IMT study. PloS One, 2017; 12(3), e0173393.
12. International Diabetes Federation. IDF Diabetes Atlas, 10th edn. Brussels, Belgium: International Diabetes Federation, 2021
13. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. Diabetes Care. 2013; 36(4):1033-46.
14. Immanuel J, Simmons D. Screening and treatment for early-onset gestational diabetes mellitus: a systematic review and meta-analysis. Current diabetes reports, 2017; 17(11), 1-11.
15. Gilbert MP. Screening and treatment by the primary care provider of common diabetes complications. Medical Clinics, 2015; 99(1), 201-19.
16. Zhu WW, Yang HX, Wang C, Su RN, Feng H, Kapur A. High prevalence of gestational diabetes mellitus in Beijing: effect of maternal birth weight and other risk factors. Chinese medical journal, 2017; 130(09), 1019-25.
17. Szmuilowicz ED, Josefson JL, Metzger BE. Gestational Diabetes Mellitus. Endocrinol Metab Clin North Am. 2019; 48(3):479-93.
18. Katakami N, Kaneto H, Shimomura I. Carotid ultrasonography: a potent tool for better clinical practice in diagnosis of atherosclerosis in diabetic patients. Journal of diabetes investigation, 2014; 5(1), 3-13.
19. Polak JF, Backlund JC, Budoff M et al. Coronary Artery Disease Events and Carotid Intima-Media Thickness in Type 1 Diabetes in the DCCT/EDIC Cohort. J Am Heart Assoc. 2021; 10(24):e022922.
20. Cortés YI, Catov JM, Brooks M et al. Pregnancy-related events associated with subclinical cardiovascular disease burden in late midlife: SWAN. Atherosclerosis. 2019; 289:27-35.
21. Roumeliotis A, Roumeliotis S, Panagoutsos S, et al. Carotid intima-media thickness is an independent predictor of all-cause mortality and cardiovascular morbidity in patients with diabetes mellitus type 2 and chronic kidney disease. Ren Fail. 2019; 41(1):131-8.

22. Hod M, Kapur A, Sacks DA et al. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care. International journal of gynecology and obstetrics: the official organ of the International Federation of Gynecology and Obstetrics, 2015; 131, S173-S211.
23. Kärkkäinen H, Saarelainen H, Valtonen P et al. Carotid artery elasticity decreases during pregnancy-the Cardiovascular Risk in Young Finns study. BMC pregnancy and childbirth, 2014; 14(1), 1-7.
24. Özdogan E, Özdogan O, Altunoglu EG, Köksal AR. Tip 2 Diyabet Hastalarinda Kan Lipid Düzeylerinin Hba1c ve Obezite ile Iliskisi. Şişli Etfal Hastanesi Tip Bülteni, 2015; 49(4), 248-254.
25. Schofield JD, Liu Y, Rao-Balakrishna P, Malik RA, Soran H. Diabetes dyslipidemia. Diabetes therapy, 2016; 7(2), 203-19.