Annals of Case Reports and Clinical Studies

Research Article

Gestational Diabetes: A Temporary Condition may Deteriorate Maternal Cardiac Functions and Structure?

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Citation: *Mehdi Karasu, Ozkan Karaca, Şeyda Yavuzkir, Kader Uğur. Gestational Diabetes: A Temporary Condition may Deteriorate Maternal Cardiac Functions and Structure?. Ann Case Rep Clin Stud. 2022;1(1):1-8.* Doi: https://doi.org/10.5281/zenodo.7023554

Received Date: 31 July, 2022; **Accepted Date:** 17 August, 2022; **Published Date:** 19 August, 2022

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1. ABSTRACT

1.1. Objective: Gestational Diabetes Mellitus (GDM) is associated with premature cardiovascular disease and adverse cardiovascular outcomes in the mother. Subclinical cardiac functional changes in the left ventricle have been reported during pregnancy using conventional echocardiography but results are inconsistent. The aim of this study is to determine whether there is deterioration in cardiac functions and cardiac structure during pregnancy in patients with gestational diabetes compared to normal pregnancies, and thus to provide a chance for early intervention.

1.2. Methods: A total of 60 pregnant patients, 30 of whom had gestational diabetes and 30 of whom did not have gestational diabetes, were included in the study. Diagnosis of GDM was made by performing the two-step approach recommended by National Institute for Health and Care Excellence (NICE) guidelines. The protocol included standard parasternal and apical views as per American Society of Echocardiography (EAE/ASE) guidelines. Height, weight, gestational age, gestational week, blood pressure, heart rate information were recorded.

1.3. Results: In the GDM group, compared to controls, there were no difference according to maternal age, weight, height, gestastional week, number of gestations and bmi, heart rate and blood pressure. At 20 to 40 weeks' gestation, women with GDM, compared to controls, had no significant difference according to bazal cardiac measurements. There were no statistically significant difference in terms of filling pressures, left and right ventricular mpi, TAPSE, tissue doppler evaluation of left and right ventricule and left and right atrium area.

1.4. Conclusion: At time of pregnancy there is no difference between GDM and non-GDM in terms of cardiac systolic and diastolic parameters and cardiac structure. It is possible that the effects of high plasma glucose on

cardiac functions have not been fully elucidated, and studies with different imaging methods and biomarkers are needed in larger patient groups that can exclude the effect of independent variables.

2. Keywords: Gestational diabetes; Myocardial performance index; Diastolic functions

3. INTRODUCTION

Clinical diabetes is one of most prevalent diseases in the world and is considered an independent risk factor for cardiovascular complications and a leading cause of morbidity and mortality.

Gestational diabetes mellitus (GDM) is any degree of glucose intolerance, recognized or diagnosed for the first time during pregnancy.[1] Gestational diabetes mellitus (GDM), occurs in 5% to 10% of pregnancies. It is important to evaluate risk for development of CVD in women with GDM. Follow-up of these women and the use of established biochemical and hemodynamic markers for cardiovascular morbidity might lead to a decreased risk and severity of cardiovascular events.

In addition to disorders involving glucose metabolism, pregnancy is also characterized by significant changes in the cardiovascular system.

There has been growing evidence that women with a history of certain common pregnancy complications such as preeclampsia and gestational diabetes, confer an increased risk for later development of CVD.[2] GDM increases the risk for the development of CVD.[3] Women with a history of GDM develop subclinical atherosclerosis,[4] an increased risk of cardiac dysfunction,[5] and increased markers of endothelial dysfunction.

Although cardiac morphometric changes due to pregnancy are well known and documented by means of echocardiography, particularly in relation to systolic parameters and ventricular morphology,[6,7] diastolic function parameters are controversial, due to different methodologies and to the fact that some measurements remain within the normal range.[8]

Left ventricular diastolic function plays an important role in determining left ventricular filling and stroke volume. Abnormal diastolic function has been recognized in many cardiovascular diseases and is associated with worse outcomes, including total mortality and hospitalizations due to heart failure. Using echocardiography, it is possible to diagnose the presence of diastolic dysfunction and the pathophysiologic mechanisms involved as they affect left ventricular and left atrial structure and function.[9]

The presence of diastolic dysfunction by Doppler echocardiography is common in the general population.[10] Progression of diastolic dysfunction has been related to the development of heart failure symptoms. In a recent study, a simple marker of diastolic dysfunction, e′ velocity, was shown to be a significant predictor of fatal and nonfatal cardiovascular events in the general population.[11,12]

The initial step in diastolic function assessment is the evaluation of mitral annular e′ velocity. This is done in conjunction with LA volume measurements. Patients with impaired diastolic function usually have a septal e′ velocity <8 cm/s and a lateral e′ <10 cm/s, and, LA volume index may be increased ($\geq$ 34 ml/m^2). However, tissue Doppler annular velocities are not reliable for evaluation of LV relaxation in patients with primary mitral valve disease, patients with LBBB, paced rhythms, or prosthetic valves or rings; and patients with constrictive pericarditis.

The American Society of Echocardiography/European Association of Echocardiography (ASE/EAE) guidelines use three grades of diastolic dysfunction: grade I (mild), grade II (moderate), and grade III (severe).[9] The

separation into three grades is primarily based on the mitral inflow pattern. Important measurements of mitral inflow Doppler signal include peak early filling velocity (E), late diastolic filling velocity (A), the E/A ratio of the early filling velocity, and the time interval between the aortic closure and mitral valve opening called isovolumic relaxation time (IVRT).

The aim of this study is to determine whether there is deterioration in cardiac functions and cardiac structure during pregnancy in patients with gestational diabetes compared to normal pregnancies, and thus to provide a chance for early intervention.

4. MATERIALS AND METHODS

A total of 60 pregnant patients, 30 of whom had gestational diabetes and 30 of whom did not have gestational diabetes, were included in the study. Pregnant patients over 20 weeks of age with impaired fasting blood sugar after admission to the obstetrics clinic were referred to the endocrine outpatient clinic. Patients diagnosed with gestational diabetes in the endocrine outpatient clinic were referred to the cardiology outpatient clinic. Diagnosis of GDM was made by performing the two-step approach recommended by National Institute for Health and Care Excellence (NICE) guidelines.[13] The protocol included standard parasternal and apical views as per American Society of Echocardiography (EAE/ASE) guidelines.[14] Left ventricular systolic functions, valve morphology, left ventricular diastolic functions with tissue dopplers, and left ventricular filling patterns with mitral valve pw dopplers were examined in patients who underwent echocardiography in the cardiology outpatient clinic. Pulsed tissue Doppler recordings were obtained at the septal and lateral aspects of the basal left ventricle at the junction with the mitral valve annulus in the apical four-chamber view. The E/e′ ratio was calculated using the mean value between septal and lateral peak e′ waves. E/A ratios, lateral and septal e', E/e', IVCT, ET, IVRT were measured, MPI was calculated. The morphology and anatomy of the right ventricle were evaluated. The tricuspid valve was evaluated. TAPSE was calculated. Right ventricular free wall was evaluated with tissue dopplers. Height, weight, gestational age, gestational week, blood pressure, heart rate information were recorded.

4.1. Exclusion criteria

We excluded women with impaired fasting blood sugars before 20 weeks, women with valvular heart diseases, women with prior known cardiovascular disease and gestational or pre-existing hypertensive disorder.

4.2. Inclusion criteria

Women who were between 20 to 40 weeks of age and who were diagnosed with gestational diabetes by the endocrine outpatient clinic and did not have a chronic disease and did not smoke were included in the study.

After the exclusion criteria, the echocardiographic parameters of the remaining 28 gestational diabetes women and 23 non-diabetic women were compared with their sociodemographic characteristics.

The results of the patients were uploaded to the SPSS system and statistical analysis was performed. Baseline echocardiographic values were evaluated with mean and standard deviation. Independent sample t test was used to compare gestational diabetes with echocardiographic values. The effect of gestational diabetes on left and right ventricular MPI was evaluated using simple linear regression analysis. $P<0.05$ was considered statistically significant.

All women provided written informed consent to participate in the study.

5. RESULTS

The characteristics of the study population of 28 women with GDM and 23 women with uncomplicated pregnancy are shown in Table 1. In the GDM group, compared to controls, there were no difference according to maternal age, weight, height, gestastional week, number of gestations and bmi.

At 20 to 40 weeks' gestation, women with GDM, compared to controls, had no significant difference according to bazal cardiac measurements (Table 2).

There were no statistically significant difference in terms of filling pressures, TAPSE, tissue doppler evaluation of left and right ventricule and left and right atrium area (Table 3).

The association and effect of GDM on left and right ventricular mpi were evaluated with independent sample t test and simple linner regretion model respectively and shows that there were no significant difference between groups (Table 4-6).

	ges.dia.	N	Mean	Std. Deviation	Two-Sided p
Age	**No**	21	31,6	7,85	0,269
	Yes	28	33,6	4,23	
ges. Week	**No**	23	28,5	4,57	0,931
	Yes	27	28,6	4,63	
ges. num.	**No**	23	2,9	1,62	0,974
	Yes	27	2,9	1,14	
Bmi	**No**	23	27,3	3,86	0,5300
	Yes	27	27,9	2,50	
SBP	**No**	23	122,0	4,06	0,112
	Yes	28	119,6	6,19	
DBP	**No**	23	79,3	5,42	0,338
	Yes	28	77,8	6,20	
HR	**No**	23	76,0	3,37	0,181
	Yes	28	77,8	5,37	

Table 1: Characteristics of study population of 51 pregnancies, according to Gestational Diabetes Mellitus (GDM) status.

	ges.dia.	N	Mean	Std. Deviation	P
aortic root width	**No**	23	26,52	2,484	0,707
	Yes	28	26,21	3,178	
ivs width	**No**	23	9,52	1,310	0,348
	Yes	28	9,82	0,945	
systolic diameter	**No**	23	25,78	3,411	0,657
	Yes	28	25,29	4,353	
diastolic diameter	**No**	23	43,52	4,044	0,824
	Yes	28	43,21	5,459	
right ventricle diameter	**No**	23	19,52	1,928	0,146
	Yes	28	20,36	2,077	
tricuspid gradientt	**No**	22	10,05	4,445	0,286
	Yes	28	11,75	6,275	
EF	**No**	23	60,70	2,285	0,814
	Yes	28	60,54	2,487	

Table 2: Comparison of basic cardiac parameters between women with Gestational Diabetes Mellitus (GDM) and controls.

	ges.dia.	N	Mean	Std. Deviation	P
TAPSE	**No**	23	25,74	2,00	0,262
	Yes	28	26,68	3,53	
LA area	**No**	23	13,70	3,13	0,128
	Yes	28	14,98	2,77	
LV E	**No**	23	0,89	0,19	0,631
	Yes	28	0,92	0,24	
LV A	**No**	23	0,73	0,18	0,391
	Yes	28	0,77	0,12	
LV E/A	**No**	23	1,24	0,25	0,616
	Yes	28	1,20	0,30	
LV E/e'	**No**	23	6,70	1,78	0,871
	Yes	28	6,62	1,66	
medial e'	**No**	23	0,12	0,03	0,487
	Yes	28	0,12	0,03	
medial a'	**No**	23	0,14	0,17	0,318
	Yes	28	0,11	0,02	
RV e'	**No**	23	0,19	0,11	0,244
	Yes	28	0,17	0,03	
RV a'	**No**	23	0,20	0,11	0,091
	Yes	28	0,16	0,04	
RA area	**No**	23	12,32	2,58	0,484
	Yes	28	12,79	2,12	
LV ivct	**No**	23	61,13	11,32	0,494
	Yes	28	58,61	14,26	
LV ET	**No**	23	260,48	29,32	0,155
	Yes	28	244,14	47,30	
LV ivtrt	**No**	23	60,57	9,62	0,651
	Yes	28	62,46	17,97	
RV ivct	**No**	23	60,00	8,72	0,440
	Yes	28	57,14	15,70	
RV ET	**No**	23	247,52	29,63	0,603
	Yes	28	253,18	44,28	
RV ivrt	**No**	23	57,22	12,95	0,749
	Yes	28	55,57	21,49	

Table 3: LV and RV diastolic indices and TAPSE.

	ges.dia	N	Mean	Std. Deviation	P
LV mpi	**No**	23	0,467	0,08369	0,22
	Yes	28	0,515	0,17991	
RV mpi	**No**	23	0,4757	0,09922	0,738
	Yes	28	0,4618	0,17605	

Table 4: Association of GDM with LV and RV mpi.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	**(Constant)**	0,467	0,030		15,461	0,000
	ges.dia.	0,048	0,041	0,166	1,179	0,244

a. Dependent Variable: sol mpi

Table 5: The effect of GDM on LV MPİ.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	0,476	0,031		15,558	0,000
	ges.dia.	-0,014	0,041	-0,048	-0,336	0,738

a. Dependent Variable: sağ mpi.

Table 6: The effect of GDM on RV mpi.

6. DISCUSSION

The purpose of this study was to investigate the presence of early cardiac diastolic and systolic abnormalities in patients with GDM using conventional techniques of TTE and we were able to show that at time of pregnancy there is no difference between GDM and non-GDM in terms of cardiac systolic and diastolic parameters and cardiac structure.

Although. Aguilera J. et al. [15] showed that systolic and diastolic functions were affected with gdm, there was a difference in terms of age, sex, height, weight and bmi.

Freire CMV et al. [16] showed that patients with GDM have a different diastolic function profile, suggesting a mild degree of diastolic abnormality. But also in this study diastolic parameters of filling pressure as E, A, E/A and tissue doppler parameters like e', a' and e'/a' has been evaluated because of deficiency of E/e' the effect of filling pressure on tissue doppler cannot be evaluted.

İn Oliveira AP et al. [17] study also patients with gestational diabetes mellitus seem to have a different diastolic profile as well as a mildly dysfunctional pattern on echocardiogram they have also higher pregestational and gestational body mass index than to control group

Gibbone E et al. [18] used maternal cardiac assessment to identify the women at risk for GDM and they showed that women with GDM have subtle functional and hemodynamic cardiac changes prior to the development of GDM which relates mostly to their demographic characteristics and medical history.

As in our study Oliveira AP et al. [19] showed that there is no statistically significant difference between groups according to diastolic paramaters but this study shows a statisticaly significant difference in terms of sistolic function of left and right ventricule when assessing with specle tracking method but not in 3-D assessment. Also writers showed that with co-variate analysis there is no impact of charecterics of patient on systolic functions of right and left ventricules women with GDM, compared to controls, were older, had higher body mass index and higher systolic blood pressure, delivered earlier and had higher birthweight z-score and they also emphasized that their data would not support the presence of an acute detrimental effect of GDM on maternal cardiac function.

Young women with GDM had a substantially increased risk for CVD compared with women without GDM. Much of this increased risk was attributable to subsequent development of type 2 diabetes.[20]

History of GDM may be a marker for early atherosclerosis independent of pre-pregnancy obesity among women who have not developed type 2 diabetes or the metabolic syndrome.[21] They Show in this study that for long term effect of GDM on atherosclerotic disease progression is obvious but still it is not definite that there is an effect of GDM on cardiac functions on acute phase.

Despite the studies showing that GDM may increase the frequency of cardiovascular events in advancing ages, it is thought that this may be related to type 2 DM and similar metabolic syndromes that develop in patients with

GDM in later years. The effect of metabolic disorders that cause GDM cannot be ignored in cardiovascular diseases that develop in the following years in patients with GDM.

7. CONCLUSION

At time of pregnancy there is no difference between GDM and non-GDM in terms of cardiac systolic and diastolic parameters and cardiac structure. It is possible that the effects of high plasma glucose on cardiac functions have not been fully elucidated, and studies with different imaging methods and biomarkers are needed in larger patient groups that can exclude the effect of independent variables.

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