ORIGINAL ARTICLE

Evaluation of left ventricular function in children and adolescents with type 1 diabetes

Sawsan Ali Hussein, Basil Metti Hanoudi

Abstract

Objective: To assess the effect of type I diabetes mellitus on cardiac systolic and diastolic functions in children and adolescent patients.

Method: The case-control study was conducted from January 1 to December 31, 2017, at Child's Central Teaching Hospital, Baghdad, Iraq, and comprised patients with type 1 diabetes and healthy controls aged 5-18 years for 3 years or more, Clinical evaluation, laboratory investigations, conventional echocardiography and Doppler assessment were done for each individual. Data was analysed using SPSS 25.

Results: Of the 96 subjects, 48(50%) were cases; 19(39.6%) males and 29(60.4%) females. The remaining 48(50%) were the controls; 22(45.8%) males and 26(54.2%) females. The mean age and gender distribution between the groups was not significantly different ($p>0.05$). Among the cases, 37(77.1%) had glycated haemoglobin ≥7.5%, and 28(58.3%) had diabetes for 7 years or more. The cases had significantly longer isovolumic relaxation time than the controls ($p=0.002$). The cases also had significantly lower early diastolic filling velocity ($p=0.022$) and early diastolic filling velocity/late diastolic filling velocity ratio ($p=0.047$) than the controls. Patients with uncontrolled diabetes had significant changes in left atrial and ventricular diameters, left ventricular mass and mass index, and in early diastolic filling velocity compared to those with controlled diabetes ($p<0.05$). Also, patients with duration of diabetes ≥7 years had higher myocardial performance index and longer isovolumic contraction time than those with shorter duration ($p<0.05$).

Conclusion: Subclinical alterations in myocardial function induced by type 1 diabetes may start in asymptomatic individuals, and these changes are accelerated with poor glycaemic control and longer duration of diabetes.

Keywords: Diabetes mellitus, Ventricular function, Glycated haemoglobin, Echocardiography.

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Introduction

Asymptomatic children and adolescents with type 1 diabetes mellitus (T1DM) show evidence of subclinical diastolic dysfunction that is correlated with the degree of metabolic control and duration of diabetes.[1] Several studies have established diabetes as a strong risk factor for cardiovascular morbidity and mortality, especially in females.[2] This increased risk cannot be explained only by the high prevalence of comorbidities, such as coronary heart disease (CHD) or arterial hypertension (HTN) in diabetes.[3] This particular form of heart disease in the absence of clinically detectable atherosclerosis and/or coronary artery disease (CAD) has been termed diabetic cardiomyopathy.[4] It is a common but frequently unrecognised pathological process in asymptomatic diabetic patients.[5] It can affect diastolic function, systolic function, or both.[6] A feature of the diabetic cardiomyopathy is the stiffening of the myocardial tissue, resulting in diastolic dysfunction, increased preload and increasing filling pressures.[7]

College of Medicine, Mustansiriyah University, Baghdad, Iraq.

Correspondence: Sawsan Ali Hussein. Email: sawsanali1989@gmail.com

Hyperglycaemia is the main aetiological factor in the development of diabetic cardiomyopathy. It increases the levels of free fatty acids and growth factors and promotes excessive production and release of reactive oxygen species, which induces oxidative stress (OS) leading to cardiomyocytes apoptosis.[8] Other risk factors include insulin resistance (IR), HTN, dyslipidaemia and obesity.[9]

The most frequent echocardiographic finding in asymptomatic T1DM patients is left ventricular (LV) diastolic dysfunction with normal left ventricular ejection fraction (LVEF).[5] Diastolic dysfunction is characterised by increased LV end-diastolic pressure and a decreased LV end-diastolic volume. Prolongation of isovolumic myocardial relaxation time (IVRT) and an increase in atrial filling further confirm a decrease in myocardial diastolic function.[9]

The current study was planned to evaluate the effect of T1DM on cardiac systolic and diastolic functions in children and adolescent patients, and to assess its correlation with the duration and control of diabetes.

Patients and Methods

The case-control study was conducted from January 1 to

December 31, 2017, at Child's Central Teaching Hospital, Baghdad, Iraq, which is one of the referral centres for childhood endocrinopathies in the capital city. The patients were randomly selected from among those attending the paediatric diabetes outpatient clinic. Age-matched controls comprised healthy individuals with no evidence of cardiovascular disease by history, physical examination, electrocardiogram (ECG) and echocardiography. The study protocol was approved by the hospital scientific- ethical committee.

Those included were aged 5-18 years with duration of T1DM ≥3 years who were asymptomatic with no clinical evidence of heart failure, and having regular cardiac rhythm and normal blood pressure (BP). Also, the patients had no evidence of congenital heart diseases or HTN, or other endocrine and systemic diseases except T1DM, and having no diabetes-related complications, like nephropathy, retinopathy or neuropathy.

Those excluded were patient with a history of smoking, cases with abnormal BP readings, abnormal renal function, irregular rhythm on ECG, and cases with valvular or congenital heart diseases discovered incidentally by echocardiography. Also excluded were those with LVEF ≤ 55%, or any regional wall motion abnormality, and individuals who were lost to follow-up.

After taking informed verbal consent from each individual and/or parents, the participants were subjected to detailed history and clinical examination, which included complete cardiovascular examination and measurements of weight, height, body surface area (BSA) and body mass index (BMI), ECG, laboratory investigations, including glycated haemoglobin (HbA1c) and renal function test, and echocardiography. Cases with diabetes were then divided into HbA1c <7.5% ≥7.5% subgroups, and T1DM duration <7 years and ≥7 years subgroups. Informed verbal consents were obtained from each individual in the study population and/or their parents.

Echocardiographic studies were done by a paediatric cardiologist at the Paediatric Cardiology Department of Ibn Al-Nafees Cardiac Centre, using GE Vivid E9 machine with 3-5 MHz phased array imaging transducer with pulsed and continuous wave Doppler and colour flow imaging capabilities. All cases were examined in supine and left lateral recumbent position.

Data was analysed using SPSS 25. Data was expressed as mean, standard deviation, range, frequencies and percentages, as appropriate. Two-tailed independent t-test was used to compare the continuous variables between the groups. P<0.05 was considered significant.

Results

Of the 96 subjects, 48(50%) were cases; 19(39.6%) males and 29(60.4%) females. The remaining 48(50%) were the controls; 22(45.8%) males and 26(54.2%) females. The mean age and gender distribution between the groups was not significantly different (p>0.05). Among the cases, 37(77.1%) had HbA1c ≥7.5%, and 28(58.3%) had diabetes for 7 years or more. The cases had significantly longer isovolumic relaxation time than the controls (p=0.002). The cases also had significantly lower early diastolic filling velocity (p=0.022) and early diastolic filling velocity/late diastolic filling velocity (E/A) ratio (p=0.047) than the controls. Patients with uncontrolled diabetes had significant changes in left atrial and ventricular diameters, left ventricular mass and mass index, and early diastolic filling velocity compared to those with controlled diabetes (p<0.05) (Table-1). Also, patients with duration of diabetes ≥7 years had higher myocardial performance index and longer isovolumic contraction time (IVCT) than those with shorter T1DM duration (p<0.05) (Table-2).

Table-1: Echocardiographic parameters according to glycaed haemoglobin (HbA1c) levels.

Echocardiographic parameters	HbA_{1c} Level		P- value
	< 7.5 Mean ± SD N= 11	≥ 7.5 Mean ± SD N= 37	
LVEDD (cm)	3.03 ± 0.32	3.48 ± 0.6	0.025
LVESD (cm)	2.05 ± 0.46	2.14 ± 0.5	0.604
LVPWD (cm)	0.47 ± 0.09	0.65 ± 0.14	0.001
VTI (cm)	20.45 ± 4.66	19.43 ± 3.66	0.451
LVOT (cm)	1.41 ± 0.47	1.47 ± 0.25	0.634
SV (ml)	40.2 ± 35.93	34.97 ± 15.01	0.480
CO (L)	3.81 ± 3.09	3.12 ± 1.22	0.268
EF%	67.63 ± 5.53	68.32 ± 4.91	0.694
FS%	37.09 ± 5.46	37.78 ± 4.14	0.654
LV Mass (gm)	35.62 ± 10.59	63.98 ± 29.1	0.003
LV Mass Index (gm/m^2)	41.77 ± 6.23	56.19 ± 15.51	0.004
TEI index	0.75 ± 0.51	0.64 ± 0.24	0.341
IVCT (msec)	99.27 ± 79.24	85.4 ± 39.89	0.433
IVRT (msec)	55.63 ± 15.16	59.94 ± 18.45	0.484
LVET (msec)	220.45 ± 27.66	228.97 ± 38.98	0.504
E (cm/sec)	111.18 ± 11.01	99.45 ± 11.01	0.027
A (cm/sec)	74.09 ± 18.27	73.56 ± 19.67	0.938
E/A	1.54 ± 0.24	1.39 ± 0.25	0.102

LVEDD: Left ventricular end diastolic diameter, LVESD: Left ventricular end systolic diameter, LVPWD: Left ventricular posterior wall diameter, VTI: Velocity time integral, LVOT: Left ventricular outflow tract diameter, SV: stroke volume, CO: Cardiac output, EF: Ejection fraction, FS: Fractional shortening, LV: Left ventricular, TEI: Total ejection isovolumic index, IVCT: Isovolumic contraction time, IVRT: Isovolumic relaxation time, LVET: Left ventricular ejection time, E: Peak flow velocity of the left ventricle in early diastole, A: Peak flow velocity of the left ventricle in late diastole with atrial contraction.

Table-2: Echocardiographic parameters among diabetic patients according to the duration of type 1 diabetes mellitus (DM).

Echocardiographic parameters	Duration of DM (Years) < 7 Mean ± SD N= 20	Duration of DM (Years) ≥ 7 Mean ± SD N= 28	P- value
LVEDD (cm)	3.31 ± 0.5	3.42 ± 0.63	0.493
LVESD (cm)	2.1 ± 0.46	2.13 ± 0.51	0.788
LVPWD (cm)	0.59 ± 0.17	0.63 ± 0.14	0.414
VTI (cm)	19.24 ± 3.81	19.97 ± 3.98	0.529
LVOT (cm)	1.39 ± 0.31	1.5 ± 0.3	0.241
SV (ml)	32.54 ± 20.7	38.76 ± 21.66	0.323
CO (L)	3.08 ± 1.77	3.42 ± 1.84	0.521
EF%	67.75 ± 5.1	68.46 ± 5.01	0.632
FS%	36.95 ± 4.6	38.1 ± 4.31	0.378
LV Mass (gm)	53.07 ± 26.77	60.63 ± 29.91	0.372
LV Mass Index (gm/m^2)	54.43 ± 14.84	51.78 ± 15.57	0.556
TEI index	0.55 ± 0.2	0.74 ± 0.37	0.044
IVCT (msec)	70.95 ± 33.55	101.17 ± 57.63	0.027
IVRT (msec)	54.70 ± 18.36	62.0 ± 16.87	0.168
LVET (msec)	228.0 ± 36.83	226.32 ± 37.1	0.878
E (cm/sec)	102.3 ± 14.34	102.03 ± 16.74	0.955
A (cm/sec)	73.4 ± 18.51	73.89 ± 19.96	0.931
E/A	1.39 ± 0.38	1.38 ± 0.52	0.94

LVEDD: Left ventricular end diastolic diameter, LVESD: Left ventricular end systolic diameter, LVPWD: Left ventricular posterior wall diameter, VTI: Velocity time integral, LVOT: Left ventricular outflow tract diameter, SV: Stroke volume, CO: Cardiac output, EF: Ejection fraction, FS: Fractional shortening, LV: Left ventricular, TEI: Total ejection isovolumic index, IVCT: Isovolumic contraction time, IVRT: Isovolumic relaxation time, LVET: Left ventricular ejection time, E: Peak flow velocity of the left ventricle in early diastole, A: Peak flow velocity of the left ventricle in late diastole with atrial contraction.

Discussion

The current isovolumic relaxation time (IVRT) was significantly higher in the cases than the controls, indicating early changes of LV diastolic dysfunction in diabetic patients. This is in line with Fattouh et al.,[10] in contrast with Abd-El Aziz et al.[11] The current study also showed that the mean E wave was significantly lower in the cases than the controls, and the finding is similar to literature.[11,12]

The E/A ratio was significantly lower in the cases than the controls, which indicate that there is a diastolic dysfunction in diabetic patients. The finding is in accordance with some studies,[3] while others[13] found no significant differences probably because of the longer duration of T1DM in the current study. There were non-significant differences between the cases and the controls regarding LV diameters, stroke volume (SV), cardiac output (CO), total ejection isovolumic index (TEI), ejection fraction percentage (EF%) and fractional shortening (FS), which are similar to earlier results.[11,13-15] These results indicate that there is no overt clinical heart failure in diabetic patients.

Concerning LV mass and LV mass index, there was non-significant differences between the cases and the controls, which is similar to the results of Salem et al.[14] and Labombarda et al.,[16] but different from the results obtained by Hodzic et al.[15] This could be attributed to the significantly higher weight and BMI in diabetic patients taken by Hodzic et al,[15] while in the current study there was no significant differences in these parameters between the groups.

Regarding echocardiographic findings, the current study showed significant effect of poor glycaemic control on LV and E wave. Abd-El Aziz et al.[11] and Hodzic et al.[15] found no significant association between glycaemic control and echocardiographic parameters, while Salem et al.[14] found that HbA1c correlated positively with peak flow velocity of LV in late diastole with atrial contraction (A wave) and negatively with E/A ratio. These differences could be attributed to variation in sample sizes, general characteristics, and that single HbA1c reading may not be sufficient to reflect the overall glycaemic control.

TEI and IVCT were significantly higher in patients with duration of T1DM ≥7 years. There was no comparable study found regarding these parameters. Besides, all other echocardiographic parameters had no significant association with T1DM duration, which is closer to earlier findings.[6,10,13,15]

The limitation of the current study is that the sample size was not scientifically calculated, and that can cause a decrease in the power of the study.

Conclusion

Subclinical alterations in myocardial function induced by T1DM may start in asymptomatic individuals, and these changes are accelerated with poor glycaemic control and longer duration of T1DM.

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References

1. Wojcik M, Rudzinski A, Starzyk J. Left ventricular diastolic dysfunction in adolescents with type 1 diabetes reflects the long- but not short-term metabolic control. J Pediatr Endocrinol Metab 2010;23:1055-64. doi: 10.1515/jpem.2010.167.
2. Devereux RB, Roman MJ, Paranicas M, O'Grady MJ, Lee ET, Welty TK, et al. Impact of diabetes on cardiac structure and function: the

strong heart study. Circulation 2000;101:2271-6. doi: 10.1161/01.cir.101.19.2271.0; 101:2271–2276.
3. Suys BE, Katier N, Rooman RP, Matthys D, Op De Beeck L, Du Caju MV, et al. Female children and dolescents with type 1 diabetes have more pronounced early echocardiographic signs of diabetic cardiomyopathy. Diabetes Care 2004;27:1947-53. doi: 10.2337/diacare.27.8.1947.
4. Hill MF. Diabetic Cardiomyopathy: Cardiac Changes, Pathophysiological Mechanisms, Biologic Markers, and the Available Therapeutic Armamentarium. In: Veselka J, eds. Cardiomyopathies: From Basic Research to Clinical Management. Rijeka, Croatia: IntechOpen, 2012; pp 487-512. DOI: 10.5772/27855.
5. Miki T, Yuda S, Kouzu H, Miura T. Diabetic cardiomyopathy: pathophysiology and clinical features. Heart Fail Rev 2013;18:149-66. doi: 10.1007/s10741-012-9313-3.
6. Brunvand L, Fugelseth D, Stensaeth KH, Dahl-Jørgensen K, Margeirsdottir HD. Early reduced myocardial diastolic function in children and adolescents with type 1 diabetes mellitus a population-based study. BMC Cardiovasc Disord 2016;16:103. doi: 10.1186/s12872-016-0288-1.
7. Yazici D, Yavuz DG, Toprak A, Deyneli O, Akalin S. Impaired diastolic function and elevated Nt-proBNP levels in type 1 diabetic patients without overt cardiovascular disease. Acta Diabetol 2013;50:155-61. doi: 10.1007/s00592-010-0235-z.
8. Falcão-Pires I, Leite-Moreira AF. Diabetic cardiomyopathy: understanding the molecular and cellular basis to progress in diagnosis and treatment. Heart Fail Rev 2012;17:325-44. doi: 10.1007/s10741-011-9257-z.
9. Voulgari C, Papadogiannis D, Tentolouris N. Diabetic cardiomyopathy: from the pathophysiology of the cardiac myocytes to current diagnosis and management strategies. Vasc Health Risk Manag 2010;6:883-903. doi: 10.2147/VHRM.S11681.
10. Abd-El Aziz F, Abdelghaffar S, Hussien E, Fattouh A. Evaluation of cardiac functions in children and adolescents with type 1 diabetes. J Cardiovasc Ultrasound. 2017;25:12–9.
11. M Abd-El Aziz F, Abdelghaffar S, M Hussien E, M Fattouh A. Evaluation of Cardiac Functions in Children and Adolescents with Type 1 Diabetes. J Cardiovasc Ultrasound 2017;25:12-19. doi: 10.4250/jcu.2017.25.1.12.
12. Abdaziz W, Sultan G, El Zayat R, Maagouz H. Detection of early left ventricular dysfunction in type 1 diabetes mellitus by strain and strain rate imaging. J Mol Cell Cardiol 2015;6:3690–701.
13. Kim EH, Kim YH. Left ventricular function in children and adolescents with type 1 diabetes mellitus Korean Circ J 2010;40:125-30. doi: 10.4070/kcj.2010.40.3.125.
14. Salem M, El Behery S, Adly A, Khalil D, El Hadidi E. Early predictors of myocardial disease in children and adolescents with type 1 diabetes mellitus. Pediatr Diabetes 2009;10:513-21. doi: 10.1111/j.1399-5448.2009.00517.x.
15. Hodzic A, Ribault V, Maragnes P, Milliez P, Saloux E, Labombarda F. Decreased regional left ventricular myocardial strain in type 1 diabetic children: a first sign of diabetic cardiomyopathy? J Transl Int Med 2016;4:81-7. doi: 10.1515/jtim-2016-0025
16. Labombarda F, Leport M, Morello R, Ribault V, Kauffman D, Brouard J, et al. Longitudinal left ventricular strain impairment in type 1 diabetes children and adolescents: a 2D speckle strain imaging study. Diabetes Metab 2014;40:292-8. doi: 10.1016/j.diabet.2014.03.007