Changes in the Conventional Echocardiographic Findings due to Lipids Profile Variation in Children with Diabetes Mellitus Type I

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Abstract

Background: Diabetes mellitus type I (DMT1) is a highlighted endocrine and digestive issue that involves the heart organs; with more effect when lipids profiles are considered. The study aimed to assess the variations in echocardiographic findings due to the changes in lipids profiles among children with DMT1.

Methods: This case-control study was performed on 96 DMT1 and 96 healthy children. The DMT1 was confirmed by clinical manifestations and laboratory measures. Both groups underwent conventional echocardiography and HbA1c; diabetic duration and lipids profiles were measured for the children with diabetes. Data was analyzed via SPSS 18.0 and $P < 0.05$ was considered as the significance level.

Results: It was found that the left MPI was higher in patients (p=0.001) than in healthy controls. Patients with poor control had higher levels of LVMI and left deceleration time (p<0.05) compared to optimal controls. Patients with abnormal CHO had higher ejection fraction, fraction of shortening, Left E/A, LAd/Aod, LAs/Aos, left ejection time and PWD while right deceleration time, Aortic diameter in diastole, aortic diameter in systole, left MPI and left deceleration time had lower levels. LDL changes affected aorta diameter in diastole, right deceleration time, aorta diameter in systole, left MPI and left deceleration time, fractional shortening, Left E/A, LAd / Aod, LAs/Aos, aortic ejection time and PWD. Patients with an abnormal HDL, had higher left MPI and lower left ejection time.

Conclusion: It was concluded that more conventional echocardiography involvement is observed in DMT1 children who have abnormal lipids profiles as well as abnormal HbA1c and longer diabetes durations.

Key Words: Children, Conventional Echocardiography, Diabetes mellitus, Lipids profile.

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1- INTRODUCTION

Diabetes Mellitus Type I (DMT1) is a highlighted endocrine and digestion issue (1) and is an insusceptible framework affliction with a solid hereditary part including all ages and races (2) specially children (3). The frequency of Diabetes Mellitus (DM) is evaluated as 387 million people that DMT1 accounted for 5-10% of it, in different areas (4). In Iran, the prevalence extended from 7.7% in 2005 to 8.7% in 2007 and it is proceeding due to issues such as financial weight, lifestyle changes and social protection (5). A strong association exists between DM and Cardiovascular Diseases (CVD) with a predominant reason for mortality (6). CVD death rate in diabetic patients tends to be about twice as much as that of non-diabetic (7) and DM patients with extreme lipids profiles being more at risk in contrast to those with typical lipids profiles. In this regard, Noori et al. (8) revealed that children with DMT1 who had high low-thickness lipoproteins (LDL) cholesterol are most at CVD hazard compared to those with low LDL. Thus, it appears to be essential to focus on lipids variations from the norm so as to diminish cardiovascular disorders at early ages (7). Lipids abnormality, more observed in diabetes patients with poor control, indicated an ordinary level or marginally diminished triglycerides and LDL-cholesterol level. In addition, expanded HDL cholesterol levels decline the danger of CVD (9). In spite of the fact that, the specific results of these changes on the improvement of cardiovascular diseases in diabetes are yet obscure, subjective anomalies of lipoproteins are observed in patients with type I diabetes, even in good glycemic control and these variations from the norm are not completely clarified by hyperglycemia and may be due to the marginal hyperinsulinemia related to the internal course of insulin organization (1). Echocardiography is a basic symptomatic tool and method to show heart utilitarian oddities in chronic diseases such as; thalassemia, diabetes and celiac. The most notable method is the conventional echocardiography which has offered improved quality pictures, and has extended the affectability of echocardiography on the disclosure of subclinical ventricular complications (8). Along these lines, the present examination is expected to survey the progress in regular echocardiographic findings due to changes in lipids profiles in children with DMT1.

2- MATERIALS AND METHODS

2-1. Study design

This case-control study performed on 192 children, including 96 healthy and 96 with diabetes mellitus type I. The investigation was conducted in Ali Asghar Pediatric Hospital, Zahedan, the capital city of Sistan & Baluchestan province, Iran. The examination was run in two centers in collaboration with endocrinology and cardiology between March 2018 and April 2019.

2.2- Sampling

Sample size was calculated from the following formula;

$$n = (\frac{r+1}{r})\frac{\sigma^2(Z_\beta + Z_{\alpha/2})^2}{(d\text{ifference})^2}$$

Where, Z_α=1.96, Z_β=0.84 and r =1. For the parameters of Myocardial Performance Index (MPI), the mean value extracted was 0.29 and 0.27 for the patients and controls, respectively (10). Utilizing the referenced parameters in the mentioned equation gave us 96 subjects in each group.

2-3. Inclusion and Exclusion Criteria

DMT1 patients either symptomatic or asymptomatic were included in the study. The disease of diabetes was confirmed by the clinical manifestations such as polyuria, polydipsia and weight loss along

with the laboratory measures such as fasting blood glucose > 125, random blood glucose>200 mg/dl. Exclusion criteria were the ages higher than 18 years, documented evidence of other cardiac diseases like cardiomyopathy, valvular heart disease, congenital heart disease, and myocarditis, as well as the features of hypothyroidism, uremia, and random blood sugar > 140 mg/dL for both groups.

2-4. Measurements

2-4.1. Echocardiography measures

Both groups went under conventional echocardiography (M mode and 2D) by a cardiologist, using My Lab 60 instrument with 3-8-MHz transducers (made in Italy). The values of all necessary echocardiographic parameters, namely Ejection Fraction (EF), Fractional Shortening (FS), velocity of the blood flow through the heart valves, as well as the Ejection Time (ET), peak A velocity (A), peak E velocity (E), Myocardial Performance Index (MPI), peak E (early mitral and tricuspid valve flow velocity) /peak A (late mitral and tricuspid valve flow velocity) velocity (E/A ratio), isovolumic relaxation time (IVRT), Isovolumic Contraction Time (ICT) of both sides were measured with pulsed Doppler echocardiography. The sample volume was positioned at the tips of the tricuspid and mitral valve leaflets in the apical four chamber view to enable the measurement of (a): the time interval between the start and the end of trans-mitral and trans tricuspid flow. The sample volume was thereafter relocated to the left ventricular outflow tract just below the aortic valve (apical five-chamber view) so as to measure (b): the left ventricular ejection time. The right ventricular outflow velocity pattern was also recorded from the parasternal short-axis view with the Doppler sample volume positioned just distal to the pulmonary valve for the measurement of (b). Myocardial Performance Index (MPI/Tei Index) was

calculated as a-b/b = (ICT + IRT)/ET (11). The left ventricular mass index (LVMI) was calculated by the following formula: LVM (g) = 0.8 (1.04 (((LVDD + PWD + IVSD)^3 -LVDD ^{3}))) + 0.6; and LVMI (g/m^2) = LVM / 2.7 (11) and relative wall thickness was also calculated from RWT = 2 PWD/ LVDD formulae.

2-4.2. Lipids profiles

Patients were tested for their lipids profiles of cholesterol (CHO) mg/dl, high density lipoprotein (HDL) mg/dl, low density lipoprotein (LDL) mg/dl, and triglyceride (TG) mg/dl. Abnormal lipids profile was defined as CHO >200 mg/dl, HDL < 40 mg/dl, LDL >130 mg/dl, and TG >150 mg/dl (1).

2-4.3. Diabetic measures and duration of diabetic state

The cardiac functions in our patients were categorized based on hemoglobin A1c (HbA1c) and duration of diabetic state.

a) HbA1c:

The level of HbA1c reflects glycemic control. HbA1c is the mean blood glucose concentration during the 3 months preceding the measurement. Higher values indicate higher blood glucose levels, and therefore, more poorly controlled diabetes. Laboratory results of HbA1c assays in the blood samples are conducted as part of the patients' regular outpatient visit. The normal range on this assay is 4.0-6.1%. For the purposes of this study, we considered good control to be an HbA1c < 7%, and poor control to be an HbA1c ≥ 7%. (11).

b) Duration of the diabetic state

The diabetic duration is considered as the time between the disease onset based on the diagnosed time by the pediatric endocrinologist and the time of referring to the pediatric cardiologist for performing conventional echocardiography.

The patients were classified into groups according to their diabetic duration based on the cut point of 4 years.

2-4.4. Anthropometric measurements

The height and weight of children were measured by an experienced expert using the standard equipment. The recumbent length for children under 2 years were graded using a flat wooden table; and their weight measurements were performed by the use of the balance weights Mika with the error probability of 100gr, and then their BMIs were calculated [Weight (Kg) / Height (m²)].

2-5. Ethical Considerations

Informed consent was obtained from all individual participants included in the study after the study approval. The study was approved as a project proposed (ID-code: 7230) to the Children and Adolescent Health Research Center by the Ethics Committee of Zahedan University of Medical Sciences, Zahedan, Iran.

2-6. Statistical Analysis

Data was analyzed via SPSS 18.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were presented in mean ±SD. Comparisons between DMT1 subjects and the controls were performed using t-test and Mann-Whitney U test; and when more than two groups were to be compared, the One-way Analysis of Variance and Kruskal –Wallis tests were used based on normality of the variable data distribution. The correlations between the variables were calculated using Pearson's correlation. $P < 0.05$ was considered significant.

3- RESULTS

The study was conducted on 192 subjects composed equally of diabetic and healthy children. The children had a sex distribution of 52.6% and 47.4% for boys and girls, respectively. From among the patients, 47.9% were boys when this rate was 57.3% for controls with similar sex distribution in patients and controls (X^2=1.692, p= 0.193). Mean age of the participants was 10.82± 3.15 years, such that the patients and controls had 10.87±3.46 and 10.77±2.82 years, respectively.

Table 1 demonstrates the normality distribution of study variables among the participants. **Table 2** shows that the right and Left DT, (p<0.001), aorta diameter in diastole (p=0.005) and aorta diameter in systole (p=0.011) were higher in patients when ET (p<0.001), EF (p<0.021), left E/A (p=0.019), LAs /Aos (p=0.001), FS (p=0.014) were higher in controls. MPI was significantly higher in the patients (p=0.001).

Table 3 shows the comparisons between the study variables in diabetic children based on HbA1C groups (cut off point= 7%). Patients with poorly controlled glucose had higher levels in LVMI and left DT significantly (p<0.05).

Table 4 presents the comparisons based on the diabetes duration. In children with longer period diabetes, HbA1c was significantly higher (p=0.008), LA diameter in systole / aortic diameter in systole was significantly lower (p=0.042), LVMI significantly decreased (p=0.005), right AT significantly increased (p=0.047), IVSD significantly decreased (p=0.028), PWD significantly decreased (p=0.036), and right E/A decreased significantly (p=0.050).

Table 5 shows the comparisons based on CHO changes in diabetic children. The changes of CHO were based on the level of 200 mg/dl, in which the normal patients had < 200mg/dl of CHO. In patients with abnormal CHO EF (p=0.015), the levels of FS (p=0.014), Left E/A(p=0.024), LAd/Aod(p=0.008), LAs/Aos(p=0.001), left ET (p<0.001), and PWD(p=0.039) were higher and the echocardiography findings of the right deceleration

time(p<0.001), aortic diameter in diastole(p=0.002), aortic diameter in systole (p=0.013), Left MPI (p=0.001) and left DT(P,0.001) were lower, significantly. Regarding the lipids profile changes, LDL and HDL both increased in patients with an abnormal status of CHO (p<0.05).

Table 6 compares the cardiac findings based on LDL changes in diabetic children. LDL > 130 mg/dl was considered abnormal. In patients who had abnormal values of LDL, the aorta diameter in diastole (p=0.002), right DT (p<0.001), and aorta diameter in systole (p=0.010) were significantly lower. However, the ejection fraction (p=0.010) and fractional shortening (p=0.009) were higher in patients with abnormal LDL values, left MPI (p=0.001) was lower, Left E/A (p=0.026) and LAd / Aod (p=0.017) were higher, LAs/Aos (p=0.001) , left ejection time (p<0.001) and PWD(p=0.047) were higher; and in final, the left deceleration time (p<0.001) was lower, significantly. The lipids profile of HDL increased in patients with an abnormal status of LDL (p<0.001). The results indicated that the echocardiography findings did not change by TG variation in the patients but the CHO increased in patients with an abnormal status of TG levels (p<0.001). Those patients who had abnormal values of HDL, had higher left MPI (p=0.023) when left ejection time (p=0.015) was lower in patients with abnormal HDL. TG increased in patients with a normal status of HDL (p<0.001).

4- DISCUSSION

The results of the study revealed that he left DT, aorta diameter in diastole and aorta diameter in systole were higher in patients, while ET, EF, left E/A, LAs /Aos, and FS were higher in controls. The left MPI was also higher in patients. Patients with poor glycemic control had higher LVMI and left DT. Children with longer periods of diabetes had an increase in HbA1c, right AT, and a decrease in LA

diameter in systole / aortic diameter in systole, LVMI, IVSD, PWD, and right E/A. The results also indicated that patients with an abnormal status of CHO, had higher values of EF, while their FS, left E/A, LAd/Aod, LAs/Aos, left ET, PWD and right DT, aortic diameter in diastole, aortic diameter in systole, Left MPI and left DT had lower values. In addition, the LDL and HDL both increased in patients with an abnormal status of CHO. The diabetic children with an abnormal LDL had lower AoD, right DT, AoS, and left MPI and left DT, while the parameters of EF, ES, left E/A, Lad/Aod, LAs/Aos, left ET, PWD and RWT had higher values. The echocardiography findings did not change by TG variation. The patients with abnormal values of HDL, had higher left MPI while their left ET was lower.

The diabetes cardiomyopathy is defined as the cardiovascular damage in diabetic patients, which is characterized by myocardial dilatation and hypertrophy, as well as a decrease in the systolic and diastolic functions of the left ventricle, and its presence is independent of the coexistence of ischemic heart disease or hypertension (12). DMT1 predicts a broad range of later health problems including an increased risk of cardiovascular morbidity and mortality; and may even begin in childhood (13). Nonetheless, Ferranti et al. (14) expected that cardiac disorders do not occur during childhood, even in the setting of DMT1 with lipids profile abnormalities. Atabek et al. (13) reported that the total cholesterol, triglycerides and LDL-cholesterol were slightly higher in diabetic children than in healthy controls. Endogenous insulin production reduces vascular complications and improves glucose control that may have a beneficial effect on CVD risk in the long period due to a favorable lipids profile. As children enter into adolescence, increasing the good glycemic control may lead to

improvements in lipids levels (15), such that the risk of CVD will decrease (13).

Noori et al. (11) conducted a study on cardiac functions in diabetic children. They found that the left and right DTs

were higher in patients, and the left and right peak E velocity were lower; the left ET decreased in patients and left MPI increased.

Table-1: Test of normality of the study variables in the participants

Variables	All Participants				Diabetes Patients			
	Mean	SD	K.S	P	Mean	SD	K.S	P
Age	10.82	3.15	0.068	0.03	10.87	3.46	0.128	<0.001
Height	145.5	18.02	0.086	0.001	137.45	19	0.074	0.200
Weight	38.78	13.24	0.083	0.003	33.24	11.78	0.076	0.200
Left AT	58.82	8.9	0.157	<0.001	58.64	9.25	0.159	<0.001
Left DT	156.7	45.58	0.107	<0.001	177.6	51.32	0.114	0.003
Right AT	62.28	10.34	0.159	<0.001	62.77	11.17	0.136	<0.001
Right DT	145.38	38.22	0.103	<0.001	162.3	40.96	0.081	0.132
Aod	2.06	0.32	0.098	<0.001	2.13	0.32	0.074	0.200
LAd	2.29	0.37	0.068	0.03	2.31	0.39	0.091	0.048
Aos	1.91	0.31	0.053	0.2	1.97	0.29	0.056	0.200
LAs	1.5	0.29	0.073	0.014	1.48	0.31	0.074	0.200
Left ET	248.57	32.47	0.154	<0.001	240.53	25.61	0.116	0.003
IVSD	0.67	0.13	0.132	<0.001	0.68	0.14	0.132	<0.001
LVDD	3.82	0.46	0.057	0.2	3.8	0.45	0.052	0.200
PWD	0.35	0.06	0.135	<0.001	0.35	0.06	0.139	<0.001
IVSS	0.85	0.15	0.115	<0.001	0.87	0.16	0.135	<0.001
LVDS	2.1	0.32	0.072	0.016	2.12	0.33	0.053	0.200
PWS	0.36	0.05	0.137	<0.001	0.35	0.06	0.136	<0.001
EF	76.57	5.46	0.089	0.001	75.63	5.86	0.083	0.107
FS	44.92	5.06	0.057	0.2	44.03	5.34	0.086	0.079
RWT	0.19	0.09	0.25	<0.001	0.18	0.03	0.12	0.002
Left E / A	1.87	0.46	0.085	0.002	1.78	0.41	0.075	0.200
Right E / A	1.44	0.35	0.116	<0.001	1.4	0.32	0.154	<0.001
Lad / Aod	1.12	0.17	0.063	0.062	1.1	0.17	0.078	0.182
Las / AoS	0.8	0.16	0.084	0.002	0.76	0.16	0.079	0.159
Right ET	255.89	25.91	0.090	0.001	253.98	26.53	0.078	0.183
Left MPI	0.69	0.18	0.042	0.200	0.7374	0.16	0.080	0.153
Right MPI	0.69	0.16	0.076	0.009	0.6794	0.17	0.067	0.200
LVMI	28.9	9.65	0.089	0.001	29.04	10.05	0.09	0.053
Diabetes duration					31.34	23.7	0.174	<0.001
Hb A1c					8.49	2.12	0.112	0.005
TG					124.52	76.17	0.175	<0.001
CHO					155.54	37.52	0.116	0.004
LDL					90.61	23.93	0.212	<0.001
HDL					54.23	11.91	0.17	<0.001

Table-2: Comparing the study variables between the children with Diabetes type I and the controls

Variables	Groups	Mean	SD	Test Value	P value	Variables	Mean	SD	Test Value	P value
Height	Case	137.45	19.00	2362.000	<0.001	LVDS	2.12	0.33	4141.000	0.225
	Control	153.55	12.68				2.07	0.31		
Weight	Case	33.24	11.78	2416.500	<0.001	PWS	0.35	0.06	4225.500	0.318
	Control	44.31	12.31				0.36	0.05		
Left AT	Case	58.64	9.25	4493.500	0.761	EF	75.63	5.86	3723.500	0.021
	Control	59.01	8.58				77.51	4.87		
Left DT	Case	177.60	51.32	1768.500	<0.001	RWT	0.18	0.03	4247.000	0.348
	Control	135.79	25.67				0.20	0.12		
Right AT	Case	62.77	11.17	4314.000	0.438	Left E/A	1.78	0.41	3701.500	0.019
	Control	61.79	9.48				1.96	0.49		
Right DT	Case	162.30	40.96	2011.000	<0.001	Right E/A	1.40	0.32	4093.500	0.181
	Control	128.45	26.08				1.49	0.38		
Right ET	Case	253.98	26.53	4489.500	0.757	LAs/Aos	0.76	0.16	3384.500	0.001
	Control	257.79	25.28				0.83	0.15		
Aod	Case	2.13	0.32	3517.500	0.005	Right MPI	0.68	0.169	4442.000	0.666
	Control	2.00	0.30				0.69	0.153		
LAd	Case	2.31	0.39	4265.000	0.373	LVMI	29.04	10.05	4558.000	0.897
	Control	2.26	0.35				28.77	9.28		
LAs	Case	1.48	0.31	4218.500	0.311	Aos	1.97	0.29	2.571	0.011
	Control	1.52	0.26				1.85	0.31	2.571	
Left ET	Case	240.53	25.61	3187.000	<0.001	LVDD	3.80	0.45	-0.447	0.655
	Control	256.60	36.52				3.83	0.48		
IVSD	Case	0.68	0.14	4302.500	0.426	FS	44.03	5.34	-2.469	0.014
	Control	0.66	0.11				45.81	4.63		
PWD	Case	0.35	0.06	4092.000	0.178	LAd/Aod	1.10	0.17	-1.961	0.051
	Control	0.36	0.05				1.15	0.17		
IVSS	Case	0.87	0.16	3999.000	0.113	Left MPI	0.74	0.163	3.473	0.001
	Control	0.82	0.15				0.65	0.180	3.473	

Table-3: comparing the study variables between the two groups of children with Diabetes type I; Good (45 children) and poor control (51 children)

Variables	Hb A1c (7%)	Mean	SD	Test value	P value	Variables	Mean	SD	Test value	P value
Height	Normal	134.3	18.39	-1.399	0.165	LAs/Aos	0.76	0.14	0.198	0.482
	Abnormal	139.73	19.26				0.76	0.18		
Weight	Normal	31.3	11.09	-1.386	0.169	LVMI	26.79	8.2	-2.09	0.039
	Abnormal	34.63	12.18				31.06	11.19		
Right dt	Normal	154.36	40.91	-1.922	0.058	Left AT	58.77	9.55	1067.5	0.679
	Abnormal	170.25	39.57				58.47	9.16		
Aod	Normal	2.07	0.32	-1.758	0.082	Left DT	167.86	48.05	848.5	0.041
	Abnormal	2.18	0.32				186.76	53.11		
Aos	Normal	1.96	0.28	-0.205	0.838	Right AT	63.2	12.64	1095	0.838
	Abnormal	1.97	0.3				62.76	9.62		
LAs	Normal	1.49	0.28	0.109	0.913	Right ET	252	26.28	1064.5	0.667
	Abnormal	1.48	0.34				255.88	27.09		
LVDD	Normal	3.73	0.39	-1.336	0.185	LAd	2.32	0.36	1094	0.834
	Abnormal	3.86	0.5				2.31	0.42		
LVDS	Normal	2.11	0.3	-0.47	0.64	Left ET	238.77	32.73	1070	0.697
	Abnormal	2.14	0.36				241.86	17.86		
EF	Normal	75.16	5.55	-0.66	0.511	IVSD	0.65	0.13	892.5	0.086
	Abnormal	75.96	6.18				0.7	0.15		
FS	Normal	43.43	4.79	-0.96	0.34	PWD	0.34	0.06	994	0.336
	Abnormal	44.49	5.81				0.36	0.06		
Left MPI	Normal	0.75	0.17	0.599	0.55	IVSS	0.86	0.14	1041.5	0.547
	Abnormal	0.73	0.15				0.88	0.17		
Right MPI	Normal	0.68	0.14	0.169	0.866	PWS	0.35	0.06	980.5	0.288
	Abnormal	0.67	0.19				0.36	0.06		
Left E/A	Normal	1.72	0.44	-1.154	0.251	RWTI	0.18	0.04	1050.5	0.594
	Abnormal	1.82	0.37				0.19	0.03		
LAd/Aod	Normal	1.13	0.14	1.834	0.07	RE.A	1.37	0.28	1008	0.395
	Abnormal	1.07	0.19				1.44	0.34		
Age	Normal	10.11	3.48	824.00	0.026	LDL	159.26	42.20	954.50	0.352
	Abnormal	11.61	3.29				152.34	33.09		
Duration	Normal	35.43	22.51	896.50	0.091	HDL	93.56	26.62	903.50	0.185
	Abnormal	28.43	24.25				88.08	21.30		
CHO	Normal	136.86	88.01	978.00	0.454	TG	54.53	11.07	968.00	0.501
	Abnormal	113.90	63.27				53.96	12.71		

Table-4: comparing the study variables in children with Diabetes type I based on Duration of diabetes

Variables	Duration (years)	Mean	SD	Test Value	P value	Variables	Mean	SD	Test Value	P value
Height	<4	143.50	20.42	1.065	0.29	LAs/Aos	0.86	0.22	2.061	0.042
	>=4	136.74	18.83				0.75	0.15		
Weight	<4	37.70	13.03	1.269	0.208	LVMI	37.31	11.42	2.85	0.005
	>=4	32.72	11.60				28.08	9.5		
Right DT	<4	163.80	41.97	0.122	0.904	Left AT	53.4	8.92	280	0.067
	>=4	162.13	41.09	0.12	0.907		59.24	9.14		
Aod	<4	2.11	0.24	-0.176	0.861	Left DT	165	83.51	340.5	0.282
	>=4	2.13	0.33				179.07	46.74		
Aos	<4	1.88	0.26	-1.006	0.317	Right AT	56	8.86	266.5	0.047
	>=4	1.98	0.29				63.56	11.19		
LAs	<4	1.60	0.41	1.297	0.198	Right ET	256	30.64	390	0.631
	>=4	1.46	0.30				253.74	26.2		
LVDD	<4	3.97	0.44	1.263	0.21	LAd	2.34	0.34	400.5	0.723
	>=4	3.78	0.45				2.31	0.4		
LVDS	<4	2.29	0.30	1.651	0.102	Left ET	234.9	21.98	358	0.386
	>=4	2.11	0.33				241.19	26.04		
EF	<4	74.10	4.56	-0.868	0.388	IVSD	0.8	0.18	247.5	0.028
	>=4	75.80	5.99				0.67	0.13		
FS	<4	42.50	4.14	-0.958	0.341	PWD	0.4	0.08	256.5	0.036
	>=4	44.21	5.45				0.34	0.06		
Left MPI	<4	0.71	0.14	-0.553	0.582	IVSS	0.97	0.2	296.5	0.109
	>=4	0.74	0.17				0.86	0.15		
Right MPI	<4	0.63	0.18	-1.031	0.305	PWS	0.4	0.08	271.5	0.056
	>=4	0.69	0.17				0.35	0.05		
Left E/A	<4	1.77	0.42	-0.052	0.959	RWT	0.2	0.04	284.5	0.081
	>=4	1.78	0.41				0.18	0.03		
LAd/Aod	<4	1.11	0.14	0.275	0.784	Right E/A	1.55	0.36	266.5	0.05
	>=4	1.10	0.18				1.39	0.31		
Age	<4	10.77	2.96	425	0.952	LDL	138.5	33.03	222	0.105
	>=4	10.87	3.38				157.14	37.7		
HbA1c	<4	0.93	3.13	209.5	0.008	HDL	95.13	24.35	326	0.847
	>=4	8.33	1.72				90.19	23.99		
CHO	<4	104.38	53.01	314	0.721	TG	51.14	9.49	268	0.662
	>=4	126.41	77.96				54.48	12.1		

Table-5: Comparing the study variables between the type I diabetic children with normal and abnormal CHO

Variables	CHO Groups	Mean	Std. Deviation	Test Value	P value	Variables	Mean	Std. Deviation	Test Value	P value
Height	Normal	137.56	18.69	-5.98	0	LAs/Aos	0.76	0.16	-3.24	0.001
	Abnormal	151.94	14.64				0.83	0.15		
Weight	Normal	33.15	11.58	-5.73	0	LVMI	28.72	9.97	-0.24	0.811
	Abnormal	43.34	12.78				29.05	9.43		
Right DT	Normal	164.38	41.58	6.93	0	Left AT	58.58	9.54	4460	0.794
	Abnormal	129.95	26.86				59.02	8.39		
Aod	Normal	2.14	0.33	3.14	0.002	Left DT	181.57	51.33	1558.5	<0.001
	Abnormal	2	0.3				136.52	26.97		
Aos	Normal	1.97	0.29	2.5	0.013	Right AT	63.15	11.5	4160	0.291
	Abnormal	1.86	0.31				61.58	9.3		
LAs	Normal	1.48	0.32	-1.07	0.284	Right ET	254.78	27.54	4449.5	0.776
	Abnormal	1.52	0.26				256.78	24.61		
LVDD	Normal	3.8	0.44	-0.42	0.672	LAd	2.3	0.4	4385.5	0.652
	Abnormal	3.83	0.48				2.28	0.34		
LVDS	Normal	2.13	0.33	1.06	0.29	Left ET	240.05	25.85	3122	<0.001
	Abnormal	2.08	0.31				255.48	35.63		
EF	Normal	75.51	5.99	-2.45	0.015	IVSD	0.67	0.14	4474	0.826
	Abnormal	77.42	4.85				0.66	0.11		
FS	Normal	43.93	5.46	-2.48	0.014	PWD	0.34	0.06	3773.5	0.039
	Abnormal	45.73	4.59				0.36	0.05		
Left MPI	Normal	0.74	0.16	3.48	0.001	IVSS	0.87	0.15	4107	0.238
	Abnormal	0.66	0.18				0.83	0.15		
Right MPI	Normal	0.68	0.17	-0.64	0.524	PWS	0.35	0.06	3930.5	0.099
	Abnormal	0.69	0.15				0.36	0.05		
Left E/A	Normal	1.78	0.42	-2.28	0.024	RWT	0.18	0.03	3932.5	0.102
	Abnormal	1.93	0.48				0.20	0.12		
LAd.Aod	Normal	1.08	0.17	-2.69	0.008	Right E/A	1.42	0.32	4412.50	0.704
	Abnormal	1.15	0.17				1.46	0.37		
Age	Normal	10.9488	3.36038	386.00	0.60	LDL	149.40	30.66	0.00	<0.001
	Abnormal	10.1500	4.38463				231.00	33.00		
HbA1c	Normal	8.5302	1.90251	422.50	0.928	HDL	85.91	16.97	10.50	<0.001
	Abnormal	8.1000	3.58484				148.43	21.99		
Duration	Normal	31.5349	23.46045	391.50	0.643	TG	53.73	11.50	210.50	0.197
	Abnormal	29.7000	26.94047				60.29	15.92		

Table-6: Comparing the study variables between the type I diabetic children with normal and abnormal LDL

Variables	LDL group	Mean	Std. Deviation	Test Value	P value	Variables	Mean	Std. Deviation	Test Value	P value
Height	Normal	137.55	18.71	-5.99	<0.001	Las/Aos	0.76	0.16	-3.23	0.001
	Abnormal	151.95	14.61				0.83	0.15		
Weight	Normal	33.15	11.58	-5.73	<0.001	LVMI	28.77	9.94	-0.18	0.858
	Abnormal	43.34	12.78				29.02	9.45		
Aod	Normal	2.14	0.33	3.17	0.002	Left AT	58.85	9.44	4317	0.521
	Abnormal	2	0.3				58.8	8.48		
Right DT	Normal	163.86	41.83	6.69	<0.001	Left DT	181.13	51.82	1632	<0.001
	Abnormal	130.38	27.09				136.88	26.81		
Aos	Normal	1.97	0.28	2.59	0.01	Right AT	63.15	11.5	4160	0.291
	Abnormal	1.86	0.32				61.58	9.3		
LAs	Normal	1.48	0.32	-0.99	0.325	Right ET	254.84	27.55	4435	0.747
	Abnormal	1.52	0.26				256.74	24.61		
LVDD	Normal	3.81	0.44	-0.35	0.725	LAd	2.31	0.4	4272.5	0.456
	Abnormal	3.83	0.48				2.27	0.34		
LVDS	Normal	2.13	0.33	1.2	0.233	Left ET	240.17	25.82	3149.5	<0.001
	Abnormal	2.07	0.31				255.38	35.69		
EF	Normal	75.45	5.96	-2.59	0.01	IVSD	0.67	0.14	4452.5	0.782
	Abnormal	77.47	4.86				0.66	0.11		
FS	Normal	43.87	5.43	-2.63	0.009	PWD	0.34	0.06	3801	0.047
	Abnormal	45.77	4.6				0.36	0.05		
Left MPI	Normal	0.74	0.16	3.42	0.001	IVSS	0.87	0.15	4101	0.232
	Abnormal	0.66	0.18				0.83	0.15		
Right MPI	Normal	0.68	0.17	-0.78	0.435	PWS	0.35	0.06	3959	0.116
	Abnormal	0.69	0.15				0.36	0.05		
Left E / A	Normal	1.79	0.42	-2.24	0.026	RWT	0.18	0.03	3929.5	0.101
	Abnormal	1.93	0.48				0.2	0.12		
LAd /Aod	Normal	1.09	0.17	-2.41	0.017	Right E/A	1.42	0.32	4295.5	0.493
	Abnormal	1.15	0.17				1.47	0.37		
Age	Normal	10.98	3.31	367	0.448	CHO	124.45	72.15	258.00	0.531
	Abnormal	9.85	4.64				125.29	123.29		
HbA1c	Normal	8.52	1.88	426	0.962	HDL	85.36	15.51	0.00	0.000
	Abnormal	8.20	3.72				155.14	10.90		
Duration	Normal	31.80	23.24	349.5	0.332	TG	53.93	11.50	263.50	0.614
	Abnormal	27.40	28.42				57.86	16.89		

Ozdemir et al. (16) found that the left and right MPI were higher, and LV, RV and ET were lower in children with diabetes. Abd-El Aziz et al. (10) evaluated the cardiac functions in children with diabetes and concluded that the diameter of aorta, left LA, IVSS, LVPW, LVDD and LVDs were higher, while FS was lower. They also demonstrated that the patients had lower E and A wave velocity in right and left. All these results confirmed the findings of the present study.

Our findings also manifested that the diabetic children with an increase in Hb A1c had higher levels in LVMI and left deceleration time but none of their lipids profiles changed. In the same line, M Abd-El Aziz et al. (10) categorized diabetic patients based on HbA1c status (good and poor control) and concluded that all conventional parameters were similar. Mehravar et al. (17) also confirmed the correlation between HbA1c and cholesterol, TC, LDL and HDL ratio. In a study by Mostofizadeh et al. (18), dyslipidemia was presented as high as 74.8% among Iranian children with diabetes. The most common lipids profile abnormality in their study was hypercholesterolemia followed by high LDL. Furthermore, the patients with poorly controlled glucose had a significantly higher LDL in comparison to the well-controlled patients. The inconsistency of their results with that of the present study might be due to age of the patients. In addition, it may be partly explained by the fact that a single HbA1c may not reflect the overall control of diabetes and might cause insufficient and deceptive information about long-term glycemic control. So, the mean HbA1c value averaged from several time measures instead of a single instantaneous value can provide more accurate information about glycemic control. Rexhepi et al. (19) grouped the diabetic patients in controlled and uncontrolled diabetic dyslipidemia.

After comparing some cardiac findings between these two groups, they found no differences between the groups in relation of left ventricular dimensions, the thickness of left ventricular septum and posterior wall, EF, FS, and LVM. The present study revealed that children with longer periods of diabetes had lower LAs / Aos, LVMI, IVSD, PWD and right E/A and had a higher right acceleration time. Moreover, any of the lipids profiles did not change in duration; though the level of HbA1c was higher in patients with longer durations. In the study by Aderibigbe et al. (21), inconsistent with our findings, a marked decrease was found in the percentage of subjects showing high levels of CHOL, LDL and triglyceride after receiving treatment for 7 years when compared to those who had received treatment for less than 7 years. The dissimilarity might be due to the difference in the time duration considered for the groupings. In this regard, Abd-El Aziz et al. (10) found no significant correlation between the duration of diabetes and the conventional echocardiography findings. However, we found significant changes in some of the parameters including LA diameter in systole / aortic diameter in systole, LVMI, IVSD, PWD, right E/A, and right acceleration. Abd-El Aziz et al. (10) compared the conventional echocardiography findings between the patients with and without dyslipidemia. They revealed that all the conventional findings were similar except for the left peak a velocity. We, recently, conducted a similar study on Doppler tissue imaging findings (1) and found that the left ICT' and right S' were higher in the abnormal status of HBA1c. All TDI findings were similar in patients with short and long duration. Patients with higher TG had lower values of left A/A'. The patients with abnormal cholesterol had higher right S', right E' and right A' but had lower right E/E'. Right S' was higher in DMT1 children with abnormal LDLs while their

right E/E' was lower. Any of the DTI findings did not change in line with the HDL changes. Dyslipidemia can serve as an early biomarker for cardiovascular dysfunction in children with TDM1.

4.1- Study limitation

The main limitation of the study was the lack of proper cooperation on the part of the participants, especially the controls.

5- CONCLUSION

In general, the findings demonstrated that the type I diabetes mellitus children with uncontrolled Hb A1c had higher levels in LVMI and left deceleration; furthermore the LA / Ao diameter in systole were lower in and LVMI, IVSD, PWD and right E/A and right acceleration time were higher when the duration of diabetes increased.   The present study revealed that the damage of heart function in systole and diastole such as MPI, ejection fraction and fractional shortening changed by lipids profiles of cholesterol, low-density lipoprotein and high-density lipoprotein when triglyceride changes did not affect the cardiac functions. Therefore, in children with DMT1, the lipid profile have different effects on the conventional echocardiography finding, especially in respect to the systolic and diastolic parameters.

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7- CONFLICT OF INTEREST

The authors would like to declare for no conflict of interest.

8- ABBREVIATIONS

AT: Acceleration Time, DT: Deceleration Time, Aod: Diameter of Aorta in Diastole, LAd: Diameter of LA in Diastole, Aos: Diameter of Aorta in Systole, LAs: Diameter of LA in Systole, ET: Ejection Time, IVSD: Interventricular Septal Dimension in Diastole, LVDD: Left Ventricular end-Diastolic Dimension, PWD: Posterior Wall Dimension in diastole, IVSS: Interventricular Septal dimension   in   Systole,   LVDS: Left Ventricular end-Systolic Dimension, PWS: Posterior Wall dimension in Systole, EF: Ejection Fraction (calculated in the apical two   and   four   chamber   views   with Simpson's apical biplane method), FS: Fractional Shortening, RWT: Relative Wall Thickness, E: peak E velocity, A: peak   A   velocity,   MPI: Myocardial Performance   Index,   LVMI: Left Ventricular   Mass   Index,   TG: Triglycerides   , CHO: Cholesterol, LDL: Low-Density Lipoprotein   , HDL: High-Density Lipoprotein.

9- AUTHORS' CONTRIBUTION

Noori designed the study; Teimouri analyzed the data; Noori, Nakhaee and Teimouri wrote the primary version of the manuscript. All Authors agree for the publication of the present manuscript.

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