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ORIGINAL ARTICLE

Visfatin Levels and Cardiovascular Parameters among Children and Adolescents with Type 1 Diabetes Mellitus

Ghada Mohammed Abdellatif[1], Sahar Sharawy[1], Moustafa Sobhy Shokr[2], Weaam Ibrahim Ismail[3], Maha Metwally[4], Doaa M. Abdelrahman[1], Mona Mohammed Elsharkawy[1]
[1] Pediatrics Department, Faculty of Medicine, Zagazig University, Egypt
[2] Pediatrics Resident, Al Ahrar Teaching Hospital, Egypt
[3] Clinical Pathology Department, Faculty of Medicine, Zagazig University, Egypt
[4] Radiodiagnosis Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author:
Moustafa Sobhy Shokr

Email:
mostafasobhy7793@gmail.com

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ABSTRACT

Background: The risk of cardiovascular problems such as heart failure is higher in those with type 1 diabetes mellitus (T1DM). In cardiovascular-metabolic illnesses, potential diagnostic applications for the novel adipokine visfatin have been discovered. This study aimed to demonstrate the association between visfatin and cardiovascular parameters in children and adolescents who had T1DM.

Methods: We performed this case-control study on 60 children distributed into 2 groups; 30 patients of T1DM subdivided into poor control group (n=16), good control group (n=14) according to hemoglobin A1C (HbA1C), and 30 well age and sex matched as a control group. They were subjected to the determination of serum visfatin level, echocardiography, and Doppler study to detect carotid intima-media thickness (CIMT).

Results: Serum visfatin differed significantly between the studied groups (p=0.001). Serum visfatin was negatively correlated with serum triglycerides, HbA1C, and random blood sugar levels. Serum visfatin was positively correlated with posterior wall diameter at diastole (PWD-D) and high-density lipoprotein cholesterol among cases with poor glycemic control. The optimal serum visfatin cutoff point for identifying poorly managed diabetes is 2.3975, with a corresponding area under the curve of 0.865, specificity of 81.8%, sensitivity of 87.5%, negative predictive value of 94.76%, positive predictive value of 63.6%, with overall accuracy of 83.3%.

Conclusion: There is a correlation between serum visfatin levels and some of the evaluated cardiovascular parameters, demonstrating the significance of visfatin in the development of cardiovascular complications in type 1 diabetic patients, visfatin can serve as a reliable marker of CIMT.

Key Words: Visfatin, Cardiovascular Parameters, Type 1 Diabetes Mellitus.

INTRODUCTION

Insulin-secreting β cells in the pancreas are destroyed in people with type 1 diabetes mellitus (T1DM), making it difficult for the body to produce insulin (insulitis). An elevated hemoglobin A1C (HbA1C) is another hallmark of type 1 diabetes triggered by the dysfunction of the pancreatic β cells [1].

Wang et al. [2] showed that diabetes mellitus (DM), particularly T1DM, is related to a substantial increase in the danger of developing coronary heart disease as well as heart failure. Additionally, Rawshani et al. [3] confirmed that females

experience a greater reduction in life expectancy (3.5 years) when T1DM is diagnosed before the age of 10 compared to males.

Vascular stiffness and impaired vascular compliance are caused by cardiovascular risk factors including type 1 diabetes. The risk of cardiovascular death and disease has been shown to rise in tandem with vascular stiffness. Even before vascular problems develop, patients with T1DM often experience significant arterial stiffness. As a result, there is a lot of focus on figuring out what causes diabetes to hasten atherosclerosis in the diabetic population [4].

Echocardiography and ultrasonography are non-invasive alternatives to invasive imaging techniques like coronary angiography for assessing patients with type 1 diabetes. Studies have proven that these examinations are safe, economically affordable, and well-accepted, particularly among younger age groups [5].

Intima-media thickness (IMT) is a widely used indicator of atherosclerosis severity in adults and a reliable predictor of future progression to more severe forms of the disease. Current advances in imaging technology have allowed for its detection at an earlier stage via a noninvasive ultrasound [6].

Bayir et al. [7] ascertained that, young children who had T1DM also had thicker carotid intima-media. Young children with T1DM and healthy control participants were compared using artery wall IMT in the common carotid arteries to determine the influence of vascular risk factors. That work hypothesized that kids with T1DM had higher IMT and stiffness in their arteries. Due to the high prevalence of cardiovascular morbidity in the diabetic population, noninvasive approaches for monitoring vascular alterations may find application in clinical practice.

The novel adipokine known as visfatin was first revealed to be produced primarily by visceral adipose tissue. Measured using computed tomography, visceral fat is strongly associated with visfatin levels. Therapeutic targeting of this adipokine in cardiovascular-metabolic diseases has been proposed [8].

We aimed in this work to demonstrate the association between visfatin serum level and cardiovascular parameters among children and adolescents with T1DM.

METHODS

The study participants were recruited from the Zagazig University Pediatric Hospital, Department of Pediatrics and Diabetes Outpatient as part of a case-control research that covered sixty subjects.

The approval for the study was obtained from the Pediatrics Department of Zagazig University Hospitals after obtaining approval from the Institutional Review Board (#9156/8-12-2021) and the research was conducted in accordance with the Helsinki Declaration. Written informed consent was obtained from all participants' relatives.

A) Control group: Thirty children without diabetes were chosen as a control group. They were all between the ages of 7 and 14, with an equal number of boys and girls.

B) Patient group: Thirty children diagnosed with T1DM aged from 6 to 15 years subdivided into a poor control group (n=16) and a good control group (n=14) according to HbA1C. Males were 56.7% while females were 43.3%. Inclusion and exclusion criteria were used to select the patients for this investigation.

Inclusion criteria:

Young people between the ages of 6 and 15 years including male and female patients meet the American Diabetes Association (ADA) diagnostic criteria for T1DM [9,10]. Human insulin therapy had been administered routinely to all patients.

Exclusion criteria:

Type 2 diabetes mellitus, and kids who had obesity or either renal or liver disorders were excluded. Patients were screened out of the research if they had preexisting cardiovascular disease or other metabolic disorders, or if parents did not give informed consent. Children and adolescents with T1DM had their medical records searched for information. Standard clinical signs of DM were used to make the diagnosis, including polyuria and polydipsia; requiring insulin from the onset of disease while not being obese and showing no signs of insulin resistance, and may be presenting with diabetic ketoacidosis. Levels of glucose in the blood that are either randomly above 200 mg/dl or during fasting above 126 mg/dl are determinants of diabetes [10].

All diabetic individuals were classified as either having good or poor glycemic control. According to the ADA, the target age-specific Age-related thresholds for HbA1C are as follows: When less than 6 years to be from 7.5 to 8.5 percent; 6 to 12 years, to be ≤8 percent; from 13 to 18 years, to be ≤7.5 percent. Patients whose HbA1C levels were higher than the ADA's target range for their age were classified as having poor glycemic control.

All subjects undergone the following:

Complete history taking (T1DM, and onset of disease), and complete physical examinations were done. Echocardiography: After giving each child a

50 mg/kg dose of oral syrup containing the hypnotic medication chloral hydrate, we performed a transthoracic echocardiographic examination utilizing GE Vivid 7 equipment fitted with a 7s MHz transducer. Patients were scanned while lying flat on their backs or their sides in the lateral decubitus positions. M-mode echo in our present investigation, is a common technique for evaluating left ventricular function when segmental wall motion anomalies are absent, and then M-mode, pulsed, continuous wave Doppler and color flow mapping as well as 2-dimensional Echocardiography, were taken of each patient using the conventional angles for detecting congenital heart defects, including the parasternal long axis, short axis, apical four, and five chamber views and all of the left ventricular dimensions, Left ventricular systolic functions, Left ventricular mass (LVM gm), left ventricular mass index (LVMI gm/m2), as well as Relative wall thickness (RWT), were assessed.

Carotid intima-media thickness (CIMT):

The Polish Ultrasonography Society suggested using B-mode sonography with an X5-1MHZ matrix linear transducer to examine both carotid arteries. The CIMT was calculated by measuring the lateral separation of the adventitia's first echogenic line and second hypoechoic line. As a rule of thumb, we choose a range of 0.25 mm to 0.1 mm. When the IMT of the carotid artery is more than 1 mm [11].

Routine laboratory testing included: Complete blood count (CBC), blood glucose level, and lipid profile estimation including total cholesterol, low-density lipoprotein, high-density lipoprotein cholesterol, triglycerides, and glycosylated HbA1C.

Determination of serum visfatin level using ELISA kit:

Each individual had one milliliter of blood drawn from a vein using a sterile plastic syringe and placed on a plain tube for serum separation. After 20 minutes, when coagulation had occurred, after centrifuging the tube at 3000 rpm for 20 minutes, the serum was refrigerated at -20°C until further analysis could be performed. The Chinese company Shanghai Sunred Biological Technology Co., Ltd., supplied the kit (Catalog No. 201-12-0026). Each specimen's serum visfatin concentration is determined using a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA) with this kit. Following the producer's recommendations, we determined serum visfatin levels using a standard curve after an ELISA assay.

Statistical analysis

Data was collected, tabulated, and analyzed using IBM Corp. Released in 2015. IBM SPSS Statistics 23 for Windows Edition. New York State, Armonk; IBM Corp. Quantitative data was characterized by means, standard deviations, and medians (ranges), whereas qualitative data was characterized by numbers and adjectives (percentage). Quantitative data were compared using the Kruskal-Wallis test (for non-normally distributed data) or the one-way analysis of variance (ANOVA) test (for normally distributed data); when there was a statistically significant difference, pairwise comparisons, and Tukey HSD comparisons were used to further examine the data and identify any remaining differences. A test for the correlation coefficient was used to compare several variables in a linear correlation that was either positive or negative. The ROC curve with the determination of the area under the curve (AUC) was also applied.

RESULTS

Family history of DM differed significantly between study groups ($p<0.001$) (all those within the control group had negative family history) with non-significant difference between groups as regards gender or age (Table 1).

In terms of left ventricular internal systolic diameter (LVISD), LVM, posterior wall diameter at diastole (PWD-D), and posterior wall diameter at systole (PWD-S), the groups differ significantly from one another with (p values=0.011, <0.001, 0.013, 0.003 respectively). There is a large disparity between the poor glycemic control group and the healthy control group ($p=0.004$). The ejection fraction percentage was much greater in the control group, and this difference was statistically significant. In terms of LVMI, there is a statistically significant difference among the groups that were analyzed ($p<0.001$) (Table 2).

There is a statistically significant difference between the studied groups regarding CIMT on the right, left, and mean carotid artery as assessed by carotid Doppler ($p=0.01$, 0.014, 0.004 respectively). On pairwise comparison, the difference is significant between poor glycemic control and healthy control groups ($p=0.003$) (Table 3).

Serum visfatin levels vary significantly amongst the groups that were compared ($p=0.001$). Poor glycemic control stands out from the other groups when compared pairwise (Table 4).

CIMT was significantly positively correlated with all LDL cholesterol, triglycerides, and total cholesterol and significantly negatively correlated with all

LVESD (left ventricular end-systolic diameter), RWT (relative wall thickness), and EF (ejection fraction) (Table 5).

Serum visfatin was significantly positively correlated with all HDL cholesterol, FS percentage, and PWD-S. There was a non-significant correlation between visfatin and any of the other studied parameters on poor glycemic control patients. Mean CIMT was significantly negatively correlated with both LDL cholesterol and LVESD (Table 6).

The optimal serum visfatin cutoff point for identifying poorly managed diabetes is 2.3975, with a corresponding AUC of 0.865, specificity of 81.8%, sensitivity of 87.5%, negative predictive value of 94.76%, positive predictive value of 63.6%, and overall accuracy of 83.3% (Figure 1).

The best cutoff of serum visfatin in the diagnosis of abnormal mean CIMT is 1.368 ng/ml with AUC of 0.975, sensitivity of 100%, specificity of 93.2%, positive predictive value of 20%, negative predictive value of 100% and overall accuracy of 93.3% (Figure S1).

Table 1: Comparison between the studied groups regarding demographic data

	Good glycemic control group (n=14)	Poor glycemic control group (n=16)	Healthy Control group (n=30)	p
Gender:				
Female	6 (42.9%)	7 (43.8%)	15 (50%)	0.874
Male	8 (57.1%)	9 (56.3%)	15 (50%)	
Family history:				
Negative	6 (42.9%)	8 (50%)	30 (100%)	<0.001**
Positive	8 (57.1%)	8 (50%)	0 (0%)	
Age (year):				
Mean ± SD	10.64 ± 2.13	10.75 ± 3.19	9.73 ± 2.16	0.322

Table 2: Comparing the studied groups as regards echocardiographic data

	Groups			Test	
	Good glycemic control group (n=14)	Poor glycemic control group (n=16)	Healthy Control group(n=30)	KW	p
	Median (IQR)	Median (IQR)	Median (IQR)		
LVEDD (cm)	3.55(2.6 – 3.95)	3.84 (3.52 – 4.23)	2.46 (1.58 – 3.69)	9.843	0.007*
Pairwise	P_1>0.999	P_2 0.009*	P_3 0.15		
LVISD (cm)	0.74 (0.65 – 0.89)	0.88 (0.77 – 1)	0.674 (0.61 – 0.816)	8.965	0.011*
Pairwise	$P_1$0.17	P_2 0.009*	P_3>0.999		
RWT (cm)	0.43 (0.36 – 0.55)	0.5 (0.4 – 0.57)	0.445 (0.368 – 0.93)	1.133	0.568
LVMI (g/m^2)	66.5 (44.75-73.5)	92 (72.75 – 131.25)	44 (16 – 76)	14.802	0.001**
Pairwise	$P_1$0.048*	P_2<0.001**	P_3>0.999		
LVM (g)	67.5 (52.25 – 93)	100 (84 – 144.5)	45 (15 – 73)	19.663	<0.001**
Pairwise	$P_1$0.08	P_2<0.001**	P_3 0.252		
	Mean ± SD	Mean ± SD	Mean ± SD	F	p
FS (%)	41.25 ± 6.87	41.44 ± 12.98	43.48 ± 12.16	0.261	0.771
EF (%)	68.71 ± 6.63	71.21 ± 9.95	75.68 ± 11.72	2.468	0.094
PWD-D(cm)	0.77 ± 0.2	0.93 ± 0.23	0.7 ± 0.253	4.727	0.013*
HSD	$P_1$0.19	P_2 0.009*	$P_3$0.617		
PWD-S(cm)	1.11 ± 0.25	1.17 ± 0.39	0.91 ± 0.13	6.475	0.003*
HSD	$P_1$0.762	P_2 0.004*	$P_3$0.052		

F One way ANOVA test, IQR interquartile range, KW Kruskal Wallis test, p_1 difference between poor glycemic control and good glycemic control groups, p_2 difference between poor glycemic control and healthy control group, p_3 difference between good glycemic control and healthy control groups.

LVISD: left ventricular internal systolic diameter, LVM: left ventricular mass, LVMI: Left ventricular mass index, PWD-D: posterior wall diameter at diastole, PWD-S: posterior wall diameter at systole, LVEDD: Left ventricular

end-diastolic diameter, LVISD: left ventricular end-systolic internal diameter, RWT: Relative wall thickness, EF%: Ejection fraction, FS%: Fractional shortening

Table 3: Comparing the studied groups as regards Carotid intimal thickness

	Groups			Test	
	Good glycemic control group (n=14)	Poor glycemic control group (n=16)	Healthy Control group (n=30)	KW	p
	Median (IQR)	Median (IQR)	Median (IQR)		
Right (cm)	0.05 (0.04 – 0.063)	0.06 (0.05 – 0.07)	0.045(0.02 – 0.05)	9.172	0.01*
Pairwise	$P_1$0.442	P_2 0.008*	P_3 0.636		
Left (cm)	0.05 (0.04 – 0.07)	0.06 (0.05 -0.07)	0.045 (0.03 – 0.06)	8.511	0.014*
Pairwise	P_1>0.999	P_2 0.015*	P_3 0.288		
Mean (cm)	0.06(0.05 – 0.07)	0.05(0.04 – 0.06)	0.045(0.025 –0.055)	11.572	0.003*
Pairwise	$P_1$0.643	P_2 0.003*	P_3 0.226		

IQR interquartile range, KW Kruskal Wallis test, p_1 difference between poor and good glycemic control groups, p_2 difference between poor and healthy glycemic control groups, p_3 difference between good glycemic control and healthy control groups.

Table 4: Comparison between the studied groups regarding serum visfatin

	Groups			Test	
	Good glycemic control group (n=14)	Poor glycemic control group (n=16)	Healthy control group (n=30)	KW	p
	Median (IQR)	Median (IQR)	Median (IQR)		
Serum visfatin (ng/ml)	3.55(2.38 – 8.22)	1.76 (1.47 – 2.19)	4.13 (2.788 – 9.074)	18.778	0.001**
Pairwise	P_1 <0.001**	$P_2$0.006*	P_3 >0.999		

IQR interquartile range, KW Kruskal Wallis test, p_1 difference between poor and good glycemic control groups, p_2 difference between poor and healthy glycemic control groups, p_3 difference between good glycemic control and healthy control groups.

Table 5: Correlation between both serum Visfatin, mean CIMT and the studied clinical and laboratory parameters in patients with good glycemic control

	Serum Visfatin (ng/ml)		Mean CIMT (cm)	
	r	p	r	p
Age (year)	0.233	0.367	-0.367	0.147
BMI	-0.114	0.663	-0.095	0.718
Weight (kg)	0.121	0.624	-0.207	0.406
Height (cm)	0.255	0.323	-0.205	0.43
SBP (mmHg)	0.359	0.158	-0.184	0.479
DBP (mmHg)	0.329	0.198	0.201	0.438
Hemoglobin (g/dl)	0.044	0.868	-0.056	0.83
Platelet (10^3/mm^3)	0.264	0.306	0.06	0.82
WBCs (10^3/mm^3)	0.404	0.108	0.338	0.184
HDL cholesterol (mg/dl)	0.409	0.103	0.022	0.932
LDL cholesterol (mg/dl)	0.18	0.49	0.708	<0.001**
Total cholesterol(mg/dl)	0.188	0.471	0.546	0.023*
Triglycerides (mg/dl)	0.126	0.629	0.513	0.035*
HbA1C (%)	-0.22	0.397	-0.27	0.295

RBS (mg/dl)	-0.017	0.948	0.218	0.401
Disease duration (year)	-0.285	0.267	-0.367	0.148
LVIDD (cm)	-0.42	0.093	0.43	0.085
LVESD (cm)	0.132	0.613	-0.638	0.006*
RWT (cm)	-0.411	0.101	-0.64	0.006*
LVMI (g/m^2)	-0.211	0.416	-0.128	0.624
LVM (g)	-0.107	0.683	-0.152	0.56
FS (%)	0.038	0.886	-0.039	0.883
EF (%)	-0.193	0.458	-0.536	0.027*
PWD-D (cm)	-0.403	0.109	-0.306	0.232
PWD-S (cm)	-0.078	0.765	0.283	0.272
Mean CIMT (cm)	0.204	0.432		

r Spearman rank correlation coefficient *p < 0.05 is statistically significant ** p ≤ 0.001 is statistically highly significant. BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, WBCS: white blood cells, HDL: high density lipoprotein, LDL: low density lipoprotein, RBS: random blood sugar, LVISD: left ventricular internal systolic diameter, LVM: left ventricular mass, LVMI: Left ventricular mass index, PWD-D: posterior wall diameter at diastole, PWD-S: posterior wall diameter at systole, LVEDD: Left ventricular end-diastolic diameter, LVIDD: left ventricular internal end diastolic, LVESD: left ventricular end-systolic diameter, LVISD: left ventricular end-systolic internal diameter, RWT: Relative wall thickness, EF%: Ejection fraction, FS%: Fractional shortening, CIMT: Carotid Intima-Media Thickness Test

Table 6: Correlation between both serum Visfatin, mean CIMT and the studied clinical and laboratory parameters in patients with poor glycemic control

	Serum Visfatin (ng/ml)		**Mean CIMT (cm)**	
	r	**p**	**r**	**p**
Age (year)	0.034	0.912	-0.108	0.725
BMI	0.30	0.316	-0.234	0.442
Weight (kg)	0.44	0.133	-0.207	0.406
Height (cm)	0.177	0.563	-0.07	0.821
SBP (mmHg)	-0.149	0.628	0.233	0.266
DBP (mmHg)	0.531	0.062	-0.364	0.224
Hemoglobin (g/dl)	0.283	0.348	-0.225	0.459
Platelet (10^3/mm^3)	0.407	0.168	-0.227	0.457
WBCs (10^3/mm^3)	0.126	0.681	0.334	0.264
HDL cholesterol (mg/dl)	0.791	<0.001**	-0.252	0.409
LDL cholesterol (mg/dl)	-0.258	0.394	0.608	0.028*
Total cholesterol(mg/dl)	0.066	0.861	0.348	0.24
Triglycerides (mg/dl)	0.05	0.872	0.061	0.834
HbA1c (%)	-0.55	0.051	0.275	0.363
RBS (mg/dl)	0.193	0.528	-0.206	0.499
Disease duration(year)	-0.285	0.267	-0.367	0.148
LVIDD (cm)	-0.42	0.093	0.43	0.085
LVESD (cm)	0.132	0.613	-0.638	0.006*
RWT (cm)	0	>0.999	0.008	0.979
LVMI (g/m^2)	-0.424	0.149	0.168	0.586
LVM (g)	-0.354	0.236	0.156	0.612
FS (%)	0.693	0.009*	-0.21	0.429
EF (%)	-0.312	0.3	-0.011	0.971
PWD-D (cm)	-0.088	0.774	0.067	0.829
PWD-S (cm)	**0.591**	**0.033***	-0.026	0.934
Mean CIMT (cm)	-0.395	0.182		

r Spearman rank correlation coefficient *p < 0.05 is statistically significant ** p ≤ 0.001 is statistically highly significant. BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure, WBCS: white blood cells, HDL: high density lipoprotein, LDL: low density lipoprotein, RBS: random blood sugar, LVISD: left ventricular internal systolic diameter, LVM: left ventricular mass, LVMI: Left ventricular mass index, PWD-D: posterior wall diameter at diastole, PWD-S: posterior wall diameter at systole, LVEDD: Left ventricular end-diastolic diameter, LVIDD: left ventricular internal end diastolic, LVESD: left ventricular end-systolic diameter, LVISD: left ventricular end-systolic internal diameter, RWT: Relative wall thickness, EF%: Ejection fraction, FS%: Fractional shortening, CIMT: Carotid Intima-Media Thickness Test

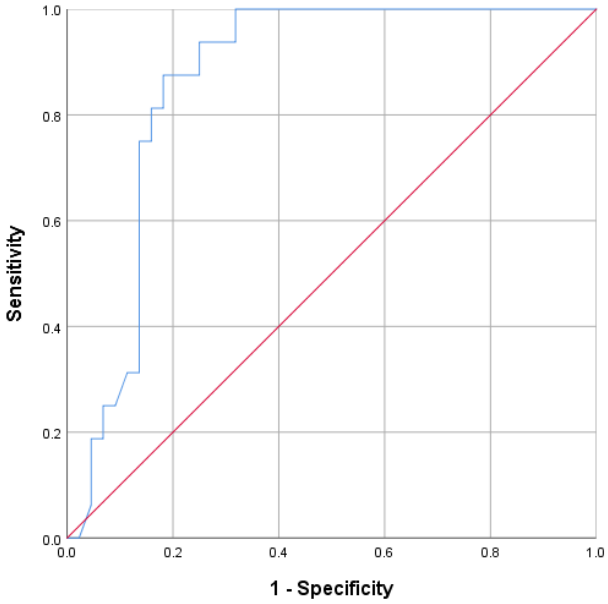

Figure 1: ROC curve showing Performance of serum visfatin in diagnosis of poor controlled type 1 diabetes among the studied patients

DISCUSSION

Macrophages in visceral adipose tissue, and not adipocytes, are responsible for the release of adipokine visfatin. In response to inflammatory signals, macrophages migrate into adipose tissue where they express visfatin. It has been proposed that this adipokine be used as a therapeutic target in the treatment of cardiometabolic disorders [8].

On one hand, patients with simple type 2 diabetes mellitus were the first to be documented to have increased plasma visfatin levels. On the other hand, women with gestational DM have been shown to have lower plasma visfatin levels. Obesity, insulin resistance, and albuminuria in people with type 2 diabetes were all linked to visfatin expression and plasma levels [12].

This study aimed to examine the potential value of visfatin as a marker of early development of atherosclerosis or heart failure and to demonstrate the connection between visfatin and cardiovascular parameters in children and adolescents with T1DM.

This is one of the few studies looking at visfatin's potential use in preventing cardiovascular problems in T1DM children and adolescents at an early age.

In our study, the mean age of the patient group was 10.7 years and about 57% of patients were males. Differences in gender or age between the case and control groups were not statistically significant. Also, Łukawska et al. [13] examined the correlation between visfatin levels and cardiovascular parameters. They found no significant correlation in age and sex between asymptomatic women with T1DM and control in their study. In our results, no significant differences were found between studied diabetic patients and the control group regarding height, weight, and BMI, this goes in agreement with Bayir et al. [7]

In contrast with our findings, Rad et al. [5] found a significant difference between the mean body mass index (BMI) in diabetic patients and the control group and El Samahi et al. [14] found a significant increase in BMI and waist/height.

Regarding echocardiographic data, there were significantly increased values of echocardiography

of LVISD, LVIDD, PWD-D, and PWD-S. Comparing bad control to good control groups, the differences were significant between poor glycemic control and healthy control groups. Łukawska et al. [13] found significantly higher IVRT in females who had T1DM when compared to the control group.

Weber et al. [15] observed comparable results to ours, with a marked rise in LVIDs in diabetes patients compared to the control group. According to research by Rakha and Aboelenin [16]**,** the prevalence of PWD was much higher in diabetes patients compared to the control group**.** T1DM patients had thicker LVPWs than controls, according to research by Jędrzejewska et al. [17]

In disagreement with our study, Rakha and Aboelenin [16] discovered no differences in LVPW thickness among children with a mean duration of diabetes of 42 months. Probable causes of this variation include differences in illness course.

Our T1DM subjects had larger cardiac dimensions in the poor control group compared to the good control group, but this difference was not statistically significant. A study using data from the Swedish National Diabetes Register found that people with T1DM have a mortality risk from cardiovascular causes that is still double that of the general population and that this risk increases by several folds among patients with higher HbA1C percentages. The association between HbA1C and fatal cardiovascular disease events may be stronger than its association with nonfatal events. [18].

In our study, there were lower EF and FS in diabetic cases compared to the control group, but without significant differences. Rakha and Aboelenin [16] found that EF and FS showed no statistically significant variation across groups. Łukawska et al. [13] noted that; by comparing the T1DM group to the control group, the EF was considerably lower in the T1DM group.

In addition to the early vascular endothelial dysfunction caused by T1DM, reports of abnormalities in myocardial function have also been made. Further evidence that diabetic microangiopathy and macroangiopathy are connected in type 1 diabetic patients comes from a paper linking early atherosclerotic alterations in teenagers with diabetic nephropathy [19].

Atherosclerosis and cardiovascular disease are more likely to occur in cases who had type 1 diabetes, and this is linked to increased ultrasonographic markers of carotid artery stiffness and intima-media thickness. In the preclinical stages of atherosclerotic disease, endothelial dysfunction and intima-media thickness rise most noticeably [20].

Our findings corroborated these findings, showing that there was a statistically significant difference between the groups assessed with regards to CIMT on the right, left, and mean carotid artery as determined by carotid Doppler. On pairwise comparison, CIMT was significantly increased in poor glycemic control than in healthy control groups. Poor glycemic control was associated with higher CIMT in the right and left carotid arteries compared to adequate glycemic control, although this difference was not statistically significant. Łukawska et al. [13] found that T1DM patients showed noticeably thicker CIMT than the control group. Rad et al. [5] reported that patients with type 1 diabetes had considerably higher CIMT than the control group.

In our research, we found that serum visfatin levels varied significantly between the study groups. The serum visfatin levels of the poor glycemic group were found to be lower than those of the other groups. Previous research indicated that individuals with type 1 diabetes have lower levels of circulating visfatin than healthy controls [14]. Previous research by Toruner et al. [21] indicated that individuals with T1DM had lower levels of circulating plasma visfatin. Fasting visfatin levels were also observed to be lower in patients with type 1 diabetes compared to healthy people in a study conducted on adult patients by Alexiadou et al. [22]

It is unclear why there is conflicting evidence about visfatin levels in type 1 diabetes. Some of the discrepancies may be explained by the fact that our diabetic patients were younger, had shorter periods of diabetes, and had higher HbA1C levels than the other study groups. It is possible that the increased exogenous insulin dose in this patient group is responsible for the decreased plasma and adipose tissue visfatin expression [23].

In our study, positive significant correlations were found between serum visfatin and both cholesterol HDL and total cholesterol. While Toruner et al. [21] observed no association between visfatin levels and any of the assessed lipid parameters or diabetes duration. Dogru et al. [24] similarly observed no correlation between visfatin levels and lipid markers in T2DM patients. López et al. [25]; Haider et al. [26] and Alexiadous et al. [22] found no correlation between visfatin and disease duration in adults with type 1 diabetes.

Hassan and Arshad [27] found that visfatin is positively correlated with total cholesterol, VLDL-C,

and triglycerides in both sexes and cleared that visfatin is negatively correlated with HDL-C, both in men and women. According to El Samahi et al. [14], visfatin levels were shown to be inversely related to age, height, weight, and body mass index.

Our study had several limitations. Our follow-up time was not long enough, and the study was a single-center study so we cannot do generalization to the data. To generalize the results, we suggest doing longer-term, multi-center research.

Conclusion

Type 1 diabetics may be at a higher risk for developing diabetic cardiomyopathy due to modest differences in echocardiographic characteristics associated with increased heart dimensions compared to control subjects. Children and adolescents with type 1 diabetes have thicker carotid intima-media compared to healthy controls. This noninvasive test has the potential to aid in the early detection of type 1 diabetic children at risk for cardiovascular disease. Based on our findings, our study concluded that there is an association between visfatin levels and cardiovascular parameters in children and adolescents with T1DM, revealing a key role of visfatin in the pathogenesis of type 1 diabetics. Visfatin is a good marker of CIMT in type 1 diabetic children.

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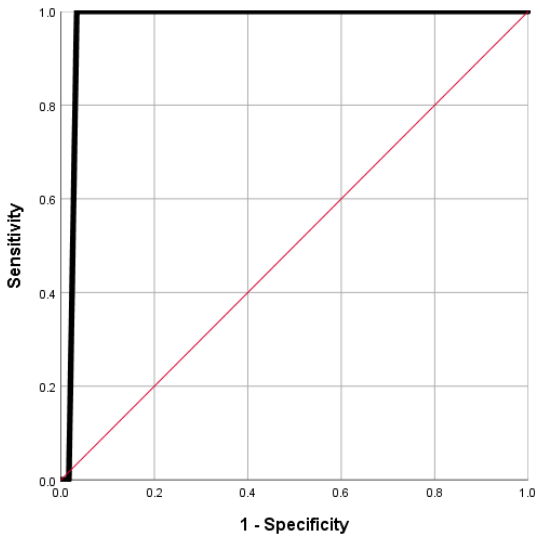

Figure S1: ROC curve showing Performance of serum visfatin in diagnosis of abnormal mean CIMT among the studied patients

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