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Original Research Article

Prevalence of left ventricular diastolic dysfunction among patients with type 2 diabetes mellitus in a tertiary care centre

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Abstract

Introduction: Type II DM is characterized by insulin resistance and hyperglycaemia, which increase the chances of dyslipidemia, obesity and hypertension, thereby increasing the risk of cardiovascular disease. Left ventricular diastolic dysfunction (LVDD) is the first stage of dilated cardiomyopathy and an important predictor of heart failure in patients with T2DM.

Materials and Methods: Demographic details were taken from all cases and controls. Height and weight were taken and Body mass index was calculated. After overnight fasting, blood analysis for Blood glucose levels, both fasting and post parandial, lipid profile and renal profile. Velocities of Transmitral early diastolic filling (E-wave), atrial contraction late filling (A wave) were measured using 2D doppler, isovolumteric relaxation time and deceleration time were also measured for all the case and control subjects.

Results: The fasting blood sugar among the male was 147.2 ± 22.1mg/dL and post parandial it was 269.8 ± 15.2mg/dL, while among the females it was 142.9 ± 18.5mg/dL and 273.1 ± 13.9dL respectively in the cases, while the same was in the normal range in the controls. The lipid profile was also significantly higher in the cases and normal in the controls. The E/A ratio among the patients was 0.72 ± 0.2 in males and 0.77 ± 0.1 in females and in controls the same was 1.23 ± 0.4 and 1.11 ± 0.2 respectively, showing a significance difference. The E/e ratio was 19.1 ± 4.6 and 19.2 ± 5.1 in males and females respectively in patients and 8.4 ± 1.3 and 8.9 ± 2.1 in males and females of the controls respectively. The IVRT also was significantly different with 78 ± 3.1 in males and 79.2 ± 4.4 of the females and 96.4 ± 3.7 in males and 97.2 ± 2.9 in females of the controls. Diastolic dysfunction was present in 38 (60%) of the males and 23 (62.2%) of the females among the patients and in 4 (6.3%) of the males and 3(8.1%) of the females among the controls.

Conclusion: Early detection of Diastolic dysfunction in patients with Type II diabetes mellitus will help in taking corrective on time and prevent mortality at a later stage.

Keywords: Diastolic dysfunction, diabetes mellitus, heart failure

Introduction

Diabetes mellitus is one of the chronic health problems worldwide having high rate of morbisity and mortality with number of complications. It has been estimated that around 9.9% of the total world population will be affected by Diabetes mellitus by the year 2045 [1]. Type II Diabetes mellitus is diagnosed on about 90% of the diabetic positive cases and this is attributed to the sedentary lifestyle and obesity [1]. India is said to have the highest number of diabetic patients in the world with over 33 million people affected. This is estimated to rise to nearly 70 million cases by the year 2030 [2, 3].

Type II DM is characterized by insulin resistance and hyperglycaemia, which increase the chances of dyslipidemia, obesity and hypertension, thereby increasing the risk of

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cardiovascular disease. Abnormal levels of inflammatory mediators and presence of cytokines, renal and vascular complications also are other risk factors for cardiovascular disease in DM patients [4-7].

Rubler in 1972 first described diabetic cardiomyopathy in a study involving 4 diabetic patients with heart failure, with normal coronary arteries and having no etiology for heart failure [8]. Many other studies have also proved that DM increases the risk of heart failure [9, 10, 11] to 8 fold [13].

Left ventricular diastolic dysfunction (LVDD) is the first stage of dilated cardiomyopathy and an important predictor of heart failure in patients with T2DM [12].

The pathogenesis of LVDD is not clear, however, metabolic disturbances such as increased fatty acids, changes in calcium homeostasis, carnitine deficiency, inflammatory cytokines, IGF-I, angiotensin II, micro-angiography, endothelial dysfunction etc. seem to play a role [7, 14].

Pre-clinical and sub clinical LVDD in diabetic patients may be present for many years before leading to a heart failure. Therefore, an early detection of this condition may help in prevention of heart failure. LVDD can be detected with no invasive procedures using Doppler echocardiography. Thus, this study was conducted to determine the association of T2DM with LVDD in asymptomatic patients and the relation to patient's age, duration of Diabetes, HbA1c, levels, Body mass index and biochemical profile.

Materials and Methods

This study was done at TRR institute of medical sciences by the Department of General medicine during the period December 2020 to January 2022. A total of 200 adult patients between 30 to 70 years of age were enrolled in this case-controlled study, where 100 patients were normotensive cases with Diabetes mellitus type 2 for more than 5 years and on whom, no cardiac disease evidence was studied. 100 healthy persons without diabetes were age and weight matched with the cases.

This study was carried out after the clearance from the Institutional Ethical Committee. Patients with previous evidence of coronary artery disease such as angina, chest pain, ECG changes were excluded from the study. Patients with vulvular disease, hypertensive patients on antihypertensive drugs, ACE inhibitors and patients with poor transthoracic echo window were also excluded from the study.

The nature of the study was thoroughly explained to the patients and informed consent was taken from them. Demographic details were taken from all of them. Height and weight were taken and Body mass index was calculated. Hip circumference, waist circumference were also measured. After overnight fasting, blood analysis for plasma glucose, HbA1c, Total cholesterol (TC), Low density cholesterol (LDL), very low density cholesterol (VLDL), High density cholesterol (HDL) and triglyceride levels was done.

Transthoracic 2_dimensional echocardiogram with pulsed Doppler for transmitral inflow and Tissue Doppler Imaging with 2-D Echo was dine for assessing diastolic Dysfunction. Velocities of Transmitral early diastolic filling (E-wave), atrial contraction late filling (A wave) were measured, E/A ratio was calculated, isovolumteric relaxation time and deceleration time were also measured for all the case and control subjects. Left ventricular ejection fraction (systolic function) was also calculated using modified Simpson's method.

Fundoscopy was done to assess microangiopathy after dilating the pupil with 1% tropicamide. Postural autonomic neuropathy was done by taking the blood pressure in an erect position after taking it in the seated position. A fall of >30mmHg was considered to be abnormal. Diastolic dysfunction was considered to be present if the patient had E/A ratio <1 or >2, deceleration time of <150 or >220ms, isovolumetric relaxation time was <60 or >100ms or E/e ratio was >15.

Statistical analysis was done on Excel using mean and percentages. Chi square test and student t test were done for comparisons. p-value of <0.05 was considered to be significant.

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Results

Out of the total 100 patients with T2DM, 63% were males and 37% were females. Among the controls also 58% were males and 37% were females. The mean age of the males among the cases was 53.4 ± 6.3yrs and among the females it was 47.1 ± 7.8yrs. The age was approximately similar among the controls as they were all matched for age. The duration of diabetes mellitus among the males was 13.5 ± 3.8 yrs and among the females the same was 14.2 ± 7.2 yrs. The fasting blood sugar among the male was 147.2 ± 22.1mg/dL and post parandial it was 269.8 ± 15.2mg/dL, while among the females it was 142.9 ± 18.5mg/dL and 273.1 ± 13.9dL respectively. The total cholesterol also was significantly raised among the cases with 219.6 ± 11.4mg/dL in males and 231.5 ± 9.9 mg/dL in females, while in controls the same was 139.7 ± 8.2mg/dL in males and 143.6 ± 9.4mg/dL in females. The other lipid parameters such as LDL, HDL and TG were also significantly raised among the patients in comparison to the controls. However, there were so significant difference among the renal parameters such as urea and creatinine between the cases and controls (table: 1).

Table 1: Biochemical parameters among the cases and controls

Variables	Cases		Controls		p value
	Males n=63	Females n=37	Males n=63	Females n=37	
Age (in years)	53.4 ± 6.3	47.1 ± 7.8	52.8 ± 8.6	47.7 ± 5.7	NS
Diabetes duration (in years)	13.5 ± 3.8	14.2 ± 7.2	NA	NA	-
Fasting Blood sugar (mg/dL)	147.2 ± 22.1	142.9 ± 18.5	82.7 ± 5.7	85.6 ± 4.1	<0.001
Post parandial Blood Sugar (mg/dL)	269.8 ± 15.2	273.1 ± 13.9	129.4 ± 9.4	131.7 ± 11.4	<0.001
Total cholesterol (mg/dL)	219.6 ± 11.4	231.5 ± 9.9	139.7 ± 8.2	143.6 ± 9.4	<0.001
LDL (mg/dL)	139.4 ± 6.3	149.4 ± 3.1	89.5 ± 6.4	95.7 ± 8.5	<0.001
HDL (mg/dL)	37.6 ± 4.1	34.7 ± 5.6	47.5 ± 7.5	44.6 ± 7.2	<0.001
Triglycerides (mg/dL)	211.4 ± 4.8	215.3 ± 9.5	131.4 ± 8.6	134.8 ± 7.3	<0.001
Urea (mmol/L)	6.1 ± 1.8	6.4 ± 1.3	5.1 ± 3	4.8 ± 4.2	NS
Creatinine (umol/L)	1.19 ± 0.4	1.24 ± 0.7	1.04 ± 0.6	1.07 ± 0.8	NS
eGFR (mL/min/1.73m2)	97.4 ± 9.3	95.1 ± 11.5	116.6 ± 9.1	113.4 ± 9.5	NS
HbA1c (%)	8.6 ± 1.1	8.9 ± 1.8			

The waist to hip ratio among the diabetic cases was 0.89 ± 0.31 in males and 0.83 ± 0.14 in females while in controls, 0.72 ± 0.21 in males and 0.71 ± 0.18 in females was the hip ratio showing a significant difference in both the groups. The BMI was normal in 12 (19.1%), 23 (36.5%) were overweight and 28 (44.4%) were obese among the male cases and 7 (18.9%) among the females of the same group had normal BMI, 14 (37.9%) were overweight and 16 (43.2%) were obese. Among the controls, 46 (73%) of the males had BMI in the normal range and 17 (27%) were overweight while among the females, 29(78.4%) were in the normal range, 6 (16.2%) were overweight and 2 (5.4%) were obese (Table: 2).

Table 2: Obesity parameters

Variables	Cases		Controls		Significance
	Males (no: 63)	Females (no: 37)	Males (no: 63)	Females (no: 37)	
Waist to hip ratio	0.89 ± 0.31	0.83 ± 0.14	0.72 ± 0.21	0.71 ± 0.18	<0.001
BMI					
Normal	12 (19.1%)	7 (18.9%)	46 (73%)	29(78.4%)	
Overweight	23 (36.5%)	14 (37.9%)	17 (27%)	6 (16.2%)	<0.001
Obese	28 (44.4%)	16 (43.2%)	0	2 (5.4%)	

The E/A ratio among the patients was 0.72 ± 0.2 in males and 0.77 ± 0.1 in females and in controls the same was 1.23 ± 0.4 and 1.11 ± 0.2 respectively, showing a significance difference. The E/e ratio was 19.1 ± 4.6 and 19.2 ± 5.1 in males and females respectively in

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patients and 8.4 ± 1.3 and 8.9 ± 2.1 in males and females of the controls respectively. The IVRT also was significantly different with 78 ± 3.1 in males and 79.2 ± 4.4 of the females and 96.4 ± 3.7 in males and 97.2 ± 2.9 in females of the controls. Diastolic dysfunction was present in 38 (60%) of the males and 23 (62.2%) of the females among the patients and in 4 (6.3%) of the males and 3(8.1%) of the females among the controls (table: 3).

Table 3: 2D echo findings

Variables	Cases		Controls		P value
	Males (no: 63)	Females (no: 37)	Males (no: 63)	Females (no: 37)	
E/A ratio	0.72 ± 0.2	0.77 ± 0.1	1.23 ± 0.4	1.11 ± 0.2	<0.001
E/e ratio	19.1 ± 4.6	19.2 ± 5.1	8.4 ± 1.3	8.9 ± 2.1	<0.001
IVRT (ms)	78 ± 3.1	79.2 ± 4.4	96.4 ± 3.7	97.2 ± 2.9	<0.001
DT (ms)	171.3 ± 12.4	172.7 ± 9.2	143.3 ± 10.3	140.7 ± 7.5	<0.001
EF (%)	53.1 ± 4.4	56.2 ± 8.3	51.4 ± 3.7	52.2 ± 5.6	NS
Diastolic dysfunction Present Absent	 38 (60.3%) 25 (39.7%)	 23 (62.2%) 14 (37.8%)	 4 (6.3%) 59 (93.7%)	 3(8.1%) 34(91.9%)	<0.001

Out of the total 61 patients with diastolic dysfunction, 11 (18%) of them were below 40 years of age, with 47 (77%) of them with HbA1c ≥ 7.5%. 39 (63.9%) lived with diabetes for more than 10 years, with 162.4 ± 17.3 while patients who lived with diabetes for more than 10 years were 25 (64.1%). The fasting blood sugar in the patients with DD was significantly higher with 162.4 ± 17.3 mg/dL while in the patients without DD it was 138.5 ± 9.6 mg/dl. 23 (37.7%) patients with DD had retinopathy and 12 (19.7%) had autonomic neuropathy, while the same was seen in 2 (5.1%) and 1 (2.6%) patients without DD (Table 4).

Table 4: Association of Dependent variables in patients with T2DM with diastolic dysfunction cases

Variables	Diastolic dysfunction		Total (n:100)
	Presence (n:61)	Absence (n:39)	
Age: <40 yrs ≥ 40 yrs	 11 (18%) 50 (82%)	 8 (20.5%) 31 (79.5%)	 19 (19%) 81 (81%)
HbA1c (%) <7.5 ≥ 7.5	 14 (23%) 47 (77%)	 17 (45.5%) 22 (56.5%)	 31 (31%) 69 (69%)
Duration of DM <10 yrs ≥ 10yrs	 22 (36.1%) 39 (63.9%)	 14 (35.9%) 25 (64.1%)	
Fasting Blood Sugar (mean)	162.4 ± 17.3	138.5 ± 9.6	
Post Parandial Sugar	272.3 ± 18.5	205.4 ± 20.5	
Retinopathy	23 (37.7%)	2 (5.1%)	25 (25%)
Autonomic neuropathy	12 (19.7%)	1 (2.6%)	13 (13%)

Discussion

Dilated cardiomyopathy is associated with Diabetes mellitus and can lead to the development of heart failure. Diastolic dysfunction is one of the early marker cardiomyopathy and this is seen much before the development of systolic dysfunction. This reduction in the ventricular compliance is due to the deposition and cross linking of collagen fibres [16].

This study shows that the left ventricular diastolic dysfunction was seen early in the patients with diabetes mellitus. In the present study, the number of males were more than the females and the mean age of the males among the cases was 53.4 ± 6.3yrs and among the females it was 47.1 ± 7.8yrs. A study by Poirier *et al*. reported the patients with asymptomatic LVDD to

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be between 38-67 years of age [15]. However there was no significant difference in the ages between the diabetic patients who had diastolic dysfunction with those who did not. Surest *et al*. also found no difference in the ages between these two groups of patients [16].

Most of the patients in our study were obese and the rest were overweight. Only 19% of them had normal BMI. In a study by Sharavanan, most of the patients were obese corroborating our study [18]. Similar results were reported by a study by Russo *et al*. [19]. In contrast, Jain *et al*. reported diastolic dysfunction in 70% of patients with diabetes had normal BMI [20].

There was significant reduction in the DD parameters in cases in comparison to the controls with the E/A ratio being 0.72 ± 0.2 in males and 0.77 ± 0.1 in females among the cases and 1.23 ± 0.4 in males and 1.11 ± 0.2 in females. Similarly, the E/e ratio was 19.1 ± 4.6 in males, 19.2± 5.1 in females in cases and 8.4 ± 1.3 in males and 8.9 ± 2.1 in females among controls. The worsening of the DD parameters was also observed in a study by Fontes-Carvalho *et al*. [25]. In another study by Dinh *et al*., insulin resistance was found to be independently associated with LVDD [26]. Increased E/e ratio and lowered E velocity was observed in the study by Fontes-Carvalho *et al*., thus corroborating our study [25].

In the present study, 61% of patients with diabetes had diastolic dysfunction while 39% did not. The fasting blood sugar among these patients was 162.4 ± 17.3 mg/dL, which was significantly higher to the patients who did not have diastolic dysfunction (138.5 ± 9.6). The post parandial blood sugar in these 61 patients was 272.3 ± 18.5mg/dL and 47 (77%) of them had HbA1c levels greater than 7.5%. Among the patients who did not have DD, the post parandial sugar levels was 205.4 ± 20.5 mg/dL and 22 (56.5%) had a HbA1c levels more than 7.5%. A similar result was observed by Ayman *et al*., where a high prevalence of DD was seen among the patients with no diabetic control [17]. 54.33% prevalence of DD was observed in diabetic patients by Patil *et al*., while 66.5% was reported by Cioffi *et al*. and 66% by Dikshit *et al*. [21-23]. A lower incidence was observed in a study by Zarich *et al*. [24].

Retinopathy was seen in 23 (37.7%) patients with DD, while autonomic neuropathy was seen in nearly 19%. Sacre *et al*. also reported an independent association of autonomic neuropathy and DD in patients with diabetes, Van Heerebeek *et al*. stated that in cases where LVEF is normal, cardiomyocyte resting tension is important [27, 28].

Conclusion

Subclinical and asymptomatic left ventricular diastolic dysfunction is an important predictor of cardiovascular disease and heart failure. Therefore early detection of the same can prevent long term mortality by taking proper corrective action at the earliest.

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