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Original Article

Internal Medicine Section

Left Ventricular Diastolic Dysfunction in Patients with Type 2 Diabetes Mellitus and its Association with Age, Gender, Duration and Glycosylated Haemoglobin: A Cross-sectional Study

SAWAN KUMAR SHUKLA[1], MAHENDRA TILKAR[2], KARAN SARAN KAPUR[3]

ABSTRACT

Introduction: Diabetes Mellitus (DM) is a group of metabolic disorders resulting in hyperglycaemia with disturbances in carbohydrate, fat, and protein metabolism. Hyperglycaemia when present for a long period of time leads to a host of metabolic abnormalities and also results in end organ damage. Diastolic dysfunction is an early sign of diabetic heart muscle disease preceding systolic and diastolic damage. Only a few studies have been conducted in central India to establish this prevalence and association in diabetic patients.

Aim: To assess Left Ventricular Diastolic Dysfunction (LVDD) in diabetic patients and its association with age, gender, duration, and glycosylated haemoglobin (HbA1c).

Materials and Methods: In this cross-sectional study, 150 normotensive patients with type 2 DM and no clinical evidence of cardiovascular disease were enrolled by simple random selection in the Department of General Medicine, Shyam Shah Medical College, Rewa, Madhya Pradesh, India. The sample size was calculated by standard formula with a confidence interval of 95% and an error margin of less than 5%. A semi-structured proforma was used to record the demographic profiles with full medication history, as well as, anthropometric measurements like height, weight, and waist circumference. Blood pressure was measured and blood was drawn for complete blood count, liver function test, renal function test, fasting and postprandial blood sugar, HbA1c, and lipid profile. Electrocardiographic and Echocardiographic studies were performed to assess LVDD. Data obtained by various methods was analysed statistically using Statistical Package for the Social Sciences (SPSS), version 20.0 and Chi-square test.

Results: The present study showed that 85 out of 150 type 2 diabetic patients had diastolic dysfunction, out of which 80 had grade I diastolic dysfunction and, five of them had grade II diastolic dysfunction. The prevalence of diastolic dysfunction was increased with age, duration, and HbA1c (≥7%) and was not affected by gender.

Conclusion: The study concluded that asymptomatic normotensive patients of type 2 DM have Heart Failure with preserved Ejection Fraction (HFpEF). LVDD were associated with age, gender, duration of diabetes, and HbA1c.

Keywords: Asympomatic, Echocardiography, Heart failure with a preserved ejection fraction

INTRODUCTION

The incidence of DM is increasing worldwide rapidly. Over the last decades, studies have proposed the presence of diabetic heart disease as a distinct clinical entity. Diastolic heart failure is also referred to as HFpEF. Many studies have reported that the incidence of heart failure (54.33%) in diabetic subjects is high even in the absence of hypertension and coronary artery disease [1-4]. Studies have reported a high prevalence of diastolic dysfunction among subjects with type 2 DM [5].

The evidence suggests that diastolic dysfunction precedes systolic dysfunction in diabetics. The pathogenesis of this LVDD in diabetics is not known [6]. Diastolic dysfunction is an early sign of diabetic heart muscle disease preceding systolic damage. Diastolic dysfunction is independently associated with increased all-cause mortality as well as cardiovascular mortality in a population-based sample of middle-aged and elderly adults [7].

The American College of Cardiology and the American Heart Association suggest that DM is considered one of the major risk factors for heart failure because it is of great importance to the advance of heart dysfunction [8]. One of the key markers of diastolic dysfunction severity is increased Left Atrial (LA) volume with or without Left Ventricular (LV) inflation pressure. Fibrosis and remodelling underlying LA dysfunction in HFpEF patients [9].

The present study aimed to determine the prevalence of LVDD in Indian patients with type 2 DM with no overt cardiac symptoms or signs by colour flow Doppler study and to associate LVDD with age, gender, duration of type 2 DM, and HbA1c. Previous studies suggested that LVDD is common in individuals with type 2 DM [10,11]. Hence, it is important that regular monitoring and screening for the progression of cardiac dysfunction is done along with appropriate therapeutic risk mitigation measures, given the long-term prognostic implications of LVDD.

MATERIALS AND METHODS

This cross-sectional study was conducted in Sanjay Gandhi Memorial hospital associated with Shyam Shah Medical College, Rewa, Madhya Pradesh, India, from April 2021 to March 2022 after clearance from Medical College Ethical Committee (IEC No. 430).

Inclusion criteria:

- Patients with type 2 DM [12]
- Patients attending SGMH Hospital as outpatients and inpatients from April 2021 to March 2022.

Newly diagnosed patients were also included in the study [12]. The age group of 30 to 70 years was used to avoid overlap of type 1 and other forms of DM.

Exclusion criteria:

- Myocardial infarction by history and resting Electrocardiogram (ECG)
- Patients with evidence of coronary artery disease-CAD {excluded by the history of angina, chest pain, ECG changes, and abnormal Treadmill Test (TMT) results}
- Patients with hypertension, thyroid disorder, respiratory or renal diseases
- Pregnant women
- Type 1 DM patients
- Significant alcoholic patient
- Patients with evidence of underlying heart diseases with normal systolic ejection fraction.

Sample size calculation: A total of 150 normotensive type 2 DM patients with no clinical evidence of cardiovascular disease were enrolled by simple random selection. The sample size was calculated by standard formula with a confidence interval of 95% and an error margin of less than 5%. The calculated sample size was 385. The study was designed during the Coronavirus Disease-2019 (COVID-19) pandemic, which resulted in a relatively small sample size. There could also be confounders posed by COVID-19 in the selection of the patients who were actively shielding not having visited the hospital. A total of 150 cases enrolled for the present study.

Study Procedure

A semi-structured proforma was used to record the demographic profiles with full medication history as well as anthropometric measurements like height, weight, and waist circumference. Blood pressure was measured and blood was drawn for complete blood count, liver function test, renal function test, fasting and postprandial blood sugar, HbA1c, and lipid profile. LVDD was assessed by electrocardiographic and echocardiographic studies.

Assessment of diastolic dysfunction: All the patients enrolled in the study underwent ECG. Transthoracic ECG was done to assess the ventricular dimensions, presence of regional wall motion abnormalities, and LV ejection fraction. The parasternal long-axis and short-axis views were utilised. The ejection fraction was obtained using Simpson's approach [13].

Doppler ECG was done using the apical four-chamber view. The transmitral velocities were obtained by positioning the sample volume at the level of the tips of mitral leaflets. The early mitral inflow velocity (E) and late inflow velocity (A) were obtained and the E/A ratio was calculated. The E/A ratio of less than 1 was considered grade 1 diastolic dysfunction. When the E/A ratio was more than 1, additional parameters like the velocity propagation and E wave deceleration time were considered to differentiate grade II diastolic dysfunction from a normal pattern [14].

Left Ventricular Diastolic Function (LVDD)

Mitral inflow was assessed with pulsed-wave Doppler done with the transducer in the apical four-chamber view with the Doppler beam aligned perpendicular to the plane of the mitral annulus along with colour M-mode Doppler ECG was done. Tissue doppler was used at the septal and lateral mitral annulus to measure the mitral plane movement. LV filling was divided into four distinct filling patterns, according to a combination of mitral inflow, tissue Doppler measurements of the mitral plane movement, and mitral inflow assessed with colour M-mode [15].

Left Atrial (LA) Volume Index

LA volume was approximated by the biplane area-length method, using measurements at the apical four and two-chamber views at end-systole (maximum LA size). LA volume index was calculated as LA volume divided by the body surface area. LA volume index was considered moderate or severely increased, if it was 32 mL/m^2 [15]. Diastolic dysfunction {in Echocardiography (ECG)} is presented in [Table/Fig-1] [16].

Grade of diastolic dysfunction	Pathological abnormality	Echocardiographic parameters
Grade I	Impaired relaxation	E/A ratio <1
Grade II	Impaired relaxation and compliance	E/A ratio >1 with increased left atrial pressures
Grade III	Restrictive filling (reversible)	E/A ratio >2.5 and elevated ventricular filling pressures
Grade IV	Restrictive filling (irreversible)	Same as grade III with irreversible changes

[Table/Fig-1]: Schematic diagram of diastolic dysfunction in ECG [16].

STATISTICAL ANALYSIS

Data were analysed for mean, percentage, standard deviation, chi-square test, multiple correlation, and multivariate analysis, by using SPSS-20.0 (SPSS) for Windows (SPSS, Chicago, IL). Variables that were not normally distributed were reciprocally transformed for analysis. The Chi-square test was applied to study quantitative and qualitative data with a p-value <0.05 considered statistically significant.

RESULTS

Prevalence of LVDD: The present study showed that 85 out of 150 types 2 diabetic patients had diastolic dysfunction, out of which 80 had grade I diastolic dysfunction and, five of them had grade II diastolic dysfunction. Grade III and grade IV diastolic dysfunction were not found in the present study [Table/Fig-2].

S. No.	Sex distribution	No. of cases	Percentage (%)
1	Male	85	56.67
2	Female	65	43.33
Total		150	100.00
Age distribution			
1	30 to ≤39 y	37	24.66
2	>39 to ≤49 y	36	24.0
3	>49 to ≤59 y	45	30.0
4	>59 to 70 y	32	21.34
Total		150	100.00
The mean age in the present study was 49.3±10.4 years			
Duration of diabetes			
1	0 to 4 y	58	38.67
2	5 to 9 y	50	33.33
3	10 years and above	42	28.0
Total		150	100.00
The mean duration of diabetes in the present study was 6.07±4.9 years			
HbA1c values (in %)			
1	≤7%	39	26
2	≥7%	111	74
Total		150	100.00
The mean HbA1c value was 9.184±2.83			

[Table/Fig-2]: Demographic and anthropometric distribution.

The mean E/A ratio was 1.047±0.356. The E/A ratio was much lower (0.7701±0.09) in patients with diastolic dysfunction, as compared to patients with normal function (1.326±0.24). The p-value was found less than 0.001 by the Chi-square test, which was significant.

DISCUSSION

As per the present study, the prevalence of LVDD was 56.66% in patients with type 2 DM. In a study done by Yadava SK et al., the prevalence of diastolic dysfunction in type 2 DM was 47.8% [17].

Sharavanan TKV et al., also showed a 55.0% prevalence of diastolic dysfunction in diabetic subjects [18].

However, the prevalence may vary between populations and study groups because of the different parameters used in Doppler ECG to assess diastolic function. Although E/A ratio is a commonly used parameter, using additional parameters or specific manipulations tends to miss advanced diastolic dysfunction [1]. According to this study, increasing age in diabetics is a risk factor for diastolic dysfunction. Considering nearly 66.66% of patients with diastolic dysfunction aged 50 years or older [Table/Fig-3], it is clear that age is directly proportional to the prevalence of diastolic dysfunction.

S. No.	Age group (in years) (n=150)	No. of patients with diastolic dysfunction (n=85)				Percentage of patients with diastolic dysfunction
		Grade I		Grade II		
1	30 to ≤39 y (n=37)	8	9.41	-	-	9.41
2	>39 to ≤49 y (n=36)	18	21.17	-	-	21.17
3	>49 to ≤59 y (n=45)	28	32.94	2	2.35	35.29
4	>59 to 70 y (n=32)	26	30.58	3	3.52	34.10
Total	150	80		5		
Diastolic dysfunction and sex distribution						
1	Male (n=85)	40	47.05	5	5.90	52.95
2	Female (n=65)	40	47.05	-	-	47.05
Total	150	80		5	-	
By Pearson Chi-square test, p-value=0.307, statistically not significant						
Diastolic dysfunction and duration of diabetes						
1	0 to 4 y (n=58)	12	14.11	-	-	14.11
2	5 to 9 y (n=50)	33	38.82	2	2.35	41.17
3	10 years and above (n=42)	35	41.17	3	3.52	44.69
Total	150	80		5	-	
By Chi-square test, p-value=0.001, significant						
Diastolic dysfunction and HbA1c						
1	≤7% (n=39)	25	29.41	-	-	29.41
2	≥7% (n=111)	55	64.70	5	5.88	70.59
Total	150	80		5	-	
By Chi-square test, p-value=0.001, significant						

[Table/Fig-3]: Diastolic dysfunction and age distribution.

However, in a study done by Hassan Ayman KM et al., diastolic dysfunction was not related to age (patients <30 and >60 years were excluded), but was related to the duration of DM [19]. Srivastava PM et al., confirmed that ageing is an independent predictor of cardiac and diastolic dysfunction in patients with type 2 diabetes. The mean age of patients in the present study was 60±1 years [20].

Khalil SI et al., also showed that age is an important risk factor for diastolic dysfunction in type 2 diabetes. In this study, the prevalence of diastolic dysfunction in the 41-50-year-old group was approximately 80% compared to the 12-year-old group. About 5% in the 21-30 age group. The mean age of the study group was 40.79±7.65 years [21].

The present study showed a higher prevalence (52.95%) in males whereas 47.05% in females but it was not statistically significant [Table/Fig-3], with underlying causes and mechanisms supporting discrepancies. Wachter R showed that the presence of diabetes affects diastolic function in men, but did not differ between diabetic and non diabetic populations in women. Men without diabetes had a lower prevalence of relaxation disorders (58.9%) compared with men with diabetes (69.7%). The presence of concomitant coronary artery disease did not change the outcome [22].

The present study showed that, if the duration of diabetes was more than 10 years, the prevalence was 90.47%. Diabetes prevalence steadily increased over time. A high level of statistical significance (p=0.001) was observed for the association between diabetes duration and diastolic dysfunction [Table/Fig-3]. In a study by Ashour K, it was concluded that patients with duration of diabetes of six years and more had a higher prevalence of diastolic dysfunction as compared with those patients with less duration (83.67% versus 35.13%) [23]. The prevalence was 70.59% while the HbA1c level of diabetes was ≥7%. Hassan Ayman KM et al., showed that LVDD was more prevalent in diabetic patients with HbA1c ≥8.1 (75%) [19].

Ashour K also demonstrated that patients with HBA1c >7.5% had more prevalence of diastolic dysfunction, than subjects with HBA1c <7.5% (75.43% vs 37.93% [23]. Freire CM et al., also confirmed the presence of diastolic dysfunction in patients with HbA1C >8% of his. For every 1% increase in HbA1C, there is an 8% increase in the risk of developing heart failure [24].

Thus, the data from the present study and the supporting data confirm the presence of diastolic dysfunction in normotensive diabetic patients without coronary artery disease. More importantly, diastolic dysfunction is an isolated entity with asymptomatic patients.

Limitation(s)

The lack of a control group in the present study was a major limitation to differentiate diastolic abnormalities between diabetic and non diabetic populations. In the current work, the authors tried to exclude ischaemia and coronary artery illness by non invasive symptom-limited routine implementation test and wall motion evaluation by transthoracic ECG. Despite normal treadmill exercise and wall motion test and resting ECG, the applied tools do not exclude the presence of atherosclerosis. The sample size of the present study was small. All the assessments were done only once for the patients though, the valuation of the results was estimated accurately. Assessment of LA function by Two-dimensional Speckle Tracking ECG (2DSTE) is rapid and easy, but difficulty to an obtaining Region Of Interest (ROI) particularly in the area of auricle and outlet of pulmonary veins leads to incorrect measurements.

CONCLUSION(S)

In the present study, the overall prevalence of diastolic dysfunction was 56.66% in asymptomatic normotensive type 2 diabetes patients. LV diastolic abnormalities are associated with age, gender, duration of diabetes, and HbA1c. Asymptomatic type 2 DM had a significantly high prevalence of diastolic dysfunction as compared to healthy subjects. Type 2 DM had the strongest association with LVDD. The study concluded that early diagnosis and Institution of treatment will reduce morbidity and improve the outcomes, and prevent future heart failure. To improve the current poor prognosis in patients with type 2 DM, the treatment of diastolic heart failure must be optimised. Patients with type 2 DM should be screened for subclinical diastolic dysfunction by ECG.

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PARTICULARS OF CONTRIBUTORS:
1. Postgraduate 3rd Year Resident, Department of General Medicine, Shyam Shah Medical College, Rewa, Madhya Pradesh, India.
2. Associate Professor, Department of General Medicine, Shyam Shah Medical College, Rewa, Madhya Pradesh, India.
3. Assistant Professor, Department of General Medicine, Shyam Shah Medical College, Rewa, Madhya Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Mahendra Tilkar,
Doctors Colony, Shyam Shah Medical College, Rewa-486001, Madhya Pradesh, India.
E-mail: tilkarmahendra@gmail.com

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