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Original Research Article

Left Ventricular Diastolic Dysfunction in Patients with Type 2 Diabetes Mellitus

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Abstract:

Background and Aim: The prevalence of left ventricular diastolic dysfunction (LVDD) is significantly elevated in patients diagnosed with type 2 diabetes mellitus (T2DM). The determinants of LVDD in T2DM are not completely comprehended. The objective of this study was to establish the frequency of LVDD (left ventricular diastolic dysfunction) in Indian patients diagnosed with type 2 diabetes mellitus, who do not exhibit any obvious cardiac symptoms or signs. This was achieved by the use of colour flow Doppler study. Additionally, the study attempted to examine the relationship between LVDD and factors such as age, gender, duration of type 2 diabetes mellitus, and HbA1c levels.

Material and Methods: For a period of 2 years, a total of 100 normotensive patients with type 2 diabetes mellitus and no signs of cardiovascular disease were selected randomly in the Department of General Medicine at a prestigious teaching hospital in India. This study was conducted to examine the relationship between these variables. A semi-structured proforma was utilized to document the demographic profiles along with comprehensive medication history, as well as anthropometric measurements such as height, weight, and waist circumference. Blood pressure was assessed and blood samples were collected for a comprehensive blood count, liver function assessment, renal function evaluation, fasting and postprandial blood sugar analysis, HbA1c measurement, and lipid profile examination. Electrocardiographic and Echocardiographic examinations were conducted to evaluate Left Ventricular Diastolic Dysfunction (LVDD).

Results: The current investigation revealed that 56 out of 100 individuals with type 2 diabetes experienced diastolic dysfunction. Among these, 51 had grade I diastolic dysfunction, while five had grade II diastolic dysfunction. The E/A ratio showed a significant decrease in patients with diastolic dysfunction in comparison to patients with normal function.

Conclusion: LV diastolic anomalies are linked to factors such as age, gender, duration of diabetes, and HbA1c. The prevalence of diastolic dysfunction is much higher in individuals with asymptomatic type 2 diabetes mellitus compared to healthy individuals. Type 2 diabetes mellitus exhibited the most robust correlation with left ventricular diastolic dysfunction.

Keywords: Blood pressure, Left Ventricular Diastolic Dysfunction, Type 2 Diabetes Mellitus, Waist Circumference.

Introduction

Diabetes mellitus has become a significant concern in today's society, impacting public health on a large scale. In recent years, there has been a significant rise in the prevalence of diabetes mellitus. In recent years, researchers have put forward the idea that diabetic heart disease may be a unique clinical condition. Diabetes can have a significant impact on the heart, leading to both structural and functional changes, even in the absence of atherosclerotic disease. Left ventricular diastolic dysfunction (LVDD) is considered an early sign of diabetic cardiomyopathy, often appearing before systolic dysfunction and potentially leading to symptomatic cardiac failure. [1] The development of LVDD is linked to left ventricular hypertrophy, myocardial interstitial fibrosis, and impaired diastolic relaxation, resulting in myocardial stiffness. [2] Recognising the

significance of diastolic dysfunction and its potential progression to diastolic heart failure is crucial for early intervention. It has been widely reported that diabetic individuals have a high risk of developing heart failure, even if they do not have hypertension or coronary artery disease. There is a significant occurrence of diastolic dysfunction in individuals with type 2 DM, according to various studies. [3-6]

Research indicates that diastolic dysfunction tends to occur before systolic dysfunction in individuals with diabetes. The cause of this LVDD in individuals with diabetes remains unknown. [7] Diastolic dysfunction often manifests as an initial indication of diabetic heart muscle disease, occurring before any systolic damage occurs. A study found that diastolic dysfunction is linked to higher rates of all-cause mortality and cardiovascular mortality in a sample of middle-aged and elderly adults. [8]

Various mechanisms have been proposed to understand how diabetes mellitus impacts ventricular function. These include disruptions in energy phosphate metabolism, impaired calcium transport, the buildup of advanced glycation end products in the cardiac interstitium, imbalances in collagen synthesis and degradation, activation of the renin-angiotensin system, and impaired metabolism of glucose and free fatty acids. [9-12] Nevertheless, previous studies have not given equal importance to the function of the right ventricle, despite its significant contribution to overall myocardial contractility. Studies conducted in India have found a higher occurrence of left ventricle diastolic dysfunction among individuals with diabetes. However, there is a lack of research on right ventricle dysfunction in this population. [13,14]

Our study sought to investigate the frequency of LVDD in Indian patients with type 2 DM who do not exhibit obvious cardiac symptoms or signs. We utilised colour flow Doppler study to assess LVDD and examined its potential correlation with age, gender, duration of type 2 DM, and HbA1c levels.

Material and Methods

This study was conducted at a prestigious medical institution in India over a period of two years. The sample size was determined using G power statistics, taking into account the findings from a previous study.[15] A power of 90% and an alpha error of 5% were considered in the calculation.

Inclusion criteria:

Individuals diagnosed with type 2 diabetes mellitus

Exclusion criteria encompassed patients with pre-existing heart conditions such as coronary heart disease, congenital heart disease, valvular heart disease, cardiomyopathy, or other related conditions. If individuals had hypertension, a limited view on trans-thoracic echocardiography, Type 1 diabetes or underlying thyroid conditions, or consumed more than 14 units of alcohol per week, they were not included in the study. The study included a total of 100 patients.

The researchers utilized a semi-structured proforma to gather important information about the participants, including their demographic profiles, medication history, and various anthropometric measurements such as height, weight, and waist circumference. A variety of tests were conducted to assess different aspects of the individual's health, including blood pressure measurement and blood sampling for various blood tests such as complete blood count, liver function test, renal function test, fasting and postprandial blood sugar, HbA1c, and lipid profile. LVDD was evaluated through electrocardiographic and echocardiographic studies.

All study participants underwent an electrocardiogram (ECG) as part of the research. A transthoracic ECG was performed to evaluate the size of the ventricles, detect any abnormalities in the movement of the heart walls, and determine the left ventricular ejection fraction. Utilizing the parasternal long-axis and short-axis views. The ejection fraction was calculated using Simpson's method.

An apical four-chamber view was used to perform the Doppler ECG. The transmitral velocities were acquired by placing the sample volume at the level of the tips of the mitral leaflets. The early mitral inflow velocity (E) and late inflow velocity (A) were measured and used to calculate the E/A ratio. A E/A ratio below 1 was classified as grade 1 diastolic dysfunction. When the E/A ratio exceeded 1, other factors such as velocity propagation and E wave deceleration time were taken into account to distinguish grade II diastolic dysfunction from a normal pattern.

The assessment of mitral inflow involved using pulsed-wave Doppler with the transducer positioned in the apical four-chamber view. The Doppler beam was aligned perpendicular to the plane of the mitral annulus. Additionally, colour M-mode Doppler ECG was performed.

The measurement of mitral plane movement involved the use of tissue Doppler at the septal and lateral mitral annulus. The filling of the left ventricle was classified into four different patterns based on a combination of factors including the measurement of mitral inflow, tissue Doppler analysis of the movement of the mitral plane, and assessment of mitral inflow using colour M-mode.

The LA volume was estimated using the biplane area-length method, utilising measurements taken at the apical four and two-chamber views during end-systole, which represents the maximum size of the LA. The LA volume index is determined by dividing the LA volume by the body surface area. If the LA volume index reached 32 mL/m2, it was classified as moderate or severely increased.

Statistical analysis: The data was compiled and entered into a spreadsheet computer programme (Microsoft Excel 2007) and then exported to the data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were reported using measures such as means and standard deviations or median and interquartile range, depending on their distribution. The data for qualitative variables were displayed as counts and percentages. Confidence level and level of significance were set at 95% and 5% respectively for all tests.

Results

In this study, it was found that 56 out of 100 patients with type 2 diabetes experienced diastolic dysfunction. Among these patients, 51 had grade I diastolic dysfunction, while five had grade II diastolic dysfunction. No instances of grade III or grade IV diastolic dysfunction were identified in the current study. The E/A ratio had a mean value of 1.06±0.25. Patients with diastolic dysfunction had significantly lower E/A ratios compared to those with normal function.

The p-value obtained from the Chi-square test was less than 0.001, indicating a significant result.

Table 1: Demographic and anthropometric distribution

Variables	Number	Percentage (%)
Gender		
Male	55	55
Female	45	45
Age Groups (Years)		
31-40	25	25
41-50	24	24
51-60	30	30
61-70	21	21
Duration of diabetes (Years)		
0-4	39	39
5-9	33	33
10 and above	28	28
HbA1c values (in %)		
≤7	26	26
≥7	74	74

Table 2: Diastolic dysfunction and different variables

Age Groups (Years) N=100	No. of patients with diastolic dysfunction (n=56)				Percentage of patients with diastolic Grade I Grade II dysfunction
	Grade 1		Grade II		
31-40 (n=25)	6	10.71	-	-	10.71
41-50 (n=24)	13	23.21	-	-	23.21
51-60 (n=30)	18	32.14	2	3.57	35.71
61-70 (n=21)	14	25	3	5.35	30.35
Gender					
Male (n=55)	26	46.42	4	7.14	53.57
Female (n=45)	26	46.42	-	-	46.42
Duration of diabetes (Years)					
0-4	7	12.5	-	-	12.5
5-9	21	37.5	2	3.57	41.07
10 and above	24	42.85	2	3.57	46.42

Discussion

Several researchers have investigated the link between elevated blood sugar and various cardiovascular diseases. [16,17] Research has revealed that diabetes mellitus can lead to both structural and functional abnormalities in the cardiovascular system. These abnormalities have been found to be separate from the impact of atherosclerosis and play a significant role in the occurrence of negative cardiovascular events. Chronic hyperglycemia in DM demonstrates its harmful effects by causing non-enzymatic

glycation of tissue macromolecules, including proteins, lipids, and DNA, resulting in the formation of advanced glycated end products that are bound irreversibly.

These products have been discovered to build up in tissues, including the heart. [18,19] According to a recent study, 56% of patients with type 2 DM were found to have LVDD. A study conducted by Yadava SK et al. revealed that 47.8% of individuals with type 2 DM had diastolic dysfunction. [20] Sharavanan TKV et al. found that there was a high prevalence of diastolic dysfunction in individuals with diabetes, with a rate of 55.0%. [21] Nevertheless, the occurrence of this condition may differ among populations and study groups due to the varying parameters utilized in Doppler ECG for evaluating diastolic function.

While the E/A ratio are frequently used, relying solely on this parameter or specific manipulations may overlook more advanced cases of diastolic dysfunction. Based on this study, it has been found that as diabetics grow older, they become more susceptible to diastolic dysfunction, a potential health concern. It is evident that the prevalence of diastolic dysfunction increases with age, as nearly 66% of patients aged 50 years or older are affected by this condition. In a study conducted by Khalil SI et al., it was found that age plays a significant role in the development of diastolic dysfunction among individuals with type 2 diabetes. According to the study, the rate of diastolic dysfunction was significantly higher in the 41-50-year-old group (around 80%) compared to the 12-year-old group. Around 5% of individuals fall into the 21-30 age group. The average age of the study group was 40.79±7.65 years. [22]

In this study, it was found that there was a slightly higher prevalence of the condition in males (53.57%) compared to females (46.42%), although this difference was not found to be statistically significant. The study also explored the underlying causes and mechanisms that may contribute to these discrepancies. In a study conducted by Wachter R, it was found that the presence of diabetes has an impact on diastolic function in men. However, this effect was not observed to be different between women with diabetes and those without. Men who do not have diabetes generally experience fewer relaxation disorders than men who have diabetes.

The prevalence of diabetes has been steadily increasing over time. There was a strong statistical significance (p=0.001) found in the relationship between diabetes duration and diastolic dysfunction. According to a study conducted by Ashour K, it was found that patients who had been living with diabetes for six years or longer had a significantly higher occurrence of diastolic dysfunction compared to those with a shorter duration (83.67% versus 35.13%). [23] He also found that patients with an HBA1c level above 7.5% had a higher prevalence of diastolic dysfunction compared to those with an HBA1c level below 8%. David Suran and his colleagues [24] conducted a study using tissue Doppler imaging to evaluate the systolic and diastolic dysfunction of both ventricles in individuals with type 1 diabetes mellitus. Researchers discovered that the average E/E' value was considerably higher in individuals with type 1 diabetes compared to those without the condition. This finding indicates the presence of subclinical diastolic dysfunction in diabetic patients.

In a study conducted by Poulsen et al [25], it was discovered that there is a high prevalence of LVDD in individuals with T2DM. Furthermore, they also observed a notable correlation between the presence of LVDD and abnormal myocardial perfusion. They did, however, discover a less significant link between LVDD and vascular function. According to their findings, it was proposed that LVDD in T2DM could be linked to inherent LV dysfunction rather than being caused by vascular disease or arterial stiffening. These findings suggest a potential link between LVDD in T2DM and diabetic retinopathy, indicating that multiple factors, including intrinsic LV dysfunctions and arterial or vascular dysfunction, may contribute to this condition.

Not having a control group in the present study was a significant limitation in distinguishing diastolic abnormalities between diabetic and non-diabetic populations. The assessments were conducted only once for the patients; however, the evaluation of the results was done with precision. Assessing LA function using Two-dimensional Speckle Tracking ECG (2DSTE) is a quick and straightforward method. However, obtaining the Region Of Interest (ROI), especially in the auricle and outlet of pulmonary veins, can be challenging, resulting in inaccurate measurements.

Conclusion

LV diastolic abnormalities can be influenced by factors such as age, gender, duration of diabetes, and HbA1c levels. Individuals with asymptomatic type 2 DM showed a notably higher prevalence of diastolic dysfunction when compared to healthy subjects. Identifying Type 2 DM as the leading factor, there is a significant correlation with LVDD.

Timely detection and prompt initiation of treatment can effectively decrease morbidity rates, enhance outcomes, and ultimately prevent the development of heart failure in the future. In order to enhance the outlook for individuals with type 2 DM, it is crucial to optimise the treatment of diastolic heart

failure. It is important for individuals with type 2 diabetes to undergo ECG screening to detect any signs of subclinical diastolic dysfunction.

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