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Echocardiographic Evaluation of Diastolic Dysfunction in Asymptomatic Patients with Type 2 Diabetes Mellitus and Its Relation with HbA1c Levels

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Abstract

***Background:** Cardiovascular complications contribute as a major cause of morbidity and mortality in diabetic patients. Diastolic dysfunction (DD) is considered as an early sign of diabetic cardiomyopathy and linked to factors like duration of diabetes, insulin resistance and HbA1c levels. Diastolic dysfunction is a predictor of heart failure, making early detection and management crucial.*

***Material and Methods:** The study was conducted in the Departments of General Medicine and Cardiology at School of Medical Sciences and Research, Sharda Hospital, Greater Noida, Uttar Pradesh. 70 patients diagnosed with type 2 diabetes mellitus (DM) fulfilling the inclusion criteria were selected for the study. FBS, PPBS, HbA1c levels and other relevant parameters were studied and DD was assessed using 2-D Echocardiography.*

***Result:** The mean age of patients was 54.8 ± 11.6 years. The mean FBS, PPBS, and HbA1c were 164.4 ± 16.2 mg/dL, 223.3 ± 29.1 mg/dL, and 8.1 ± 1.6%, respectively. Out of 70 patients enrolled in the study, 36 (51.4%) had diastolic dysfunction. Patients with DD had a considerably lower E/A ratio (0.68) than patients without DD (1.04), which was statistically significant. According to the study, the longer the duration of DM, the higher was the risk of DD ($p < 0.05$).*

***Conclusion:** DD is highly prevalent in asymptomatic diabetic patients and is positively correlated with HbA1c level, obesity and the duration of diabetes. In order to delay the progression of cardiac complications, all diabetic patients should undergo regular echocardiographic evaluations for early detection of diastolic dysfunction, and necessary interventions be implemented to reduce the cardiovascular burden.*

Introduction

Diabetes Mellitus, a chronic disease is characterised by hyperglycaemia either due to relative insulin deficiency or insulin resistance. The prevalence of diabetes is rising globally, reaching epidemic proportions. 11.4% of the Indian population is estimated to have diabetes.

DM causes micro and macrovascular complications that impact almost every organ system in the body, including the heart, which contribute to its morbidity and mortality. Patients with diabetes have a much higher incidence of coronary artery disease and congestive heart failure. Compared to people without diabetes, diabetic men and women have a 3.8 and 5.5 times the relative risk of heart failure, respectively. Cardiovascular problems linked to diabetes include left ventricular dysfunction, increased left ventricular mass, increased left ventricular wall thickness, and certain diabetic cardiomyopathies[1]. Left ventricular diastolic dysfunction has been demonstrated in diabetic patients who are normotensive and have no symptoms of cardiac disease[2,3]. Increased mortality among type 2 diabetic patients with heart failure with normal ejection fraction also suggests a role for diastolic heart failure[4].

Diastolic dysfunction refers to a condition in which impairments in mechanical function are present during diastole. Both normal and impaired systolic function and the presence or absence of a clinical heart failure syndrome can cause abnormalities in diastolic function. Therefore, whereas diastolic dysfunction characterizes an aberrant mechanical property, diastolic heart failure describes the clinical condition. Numerous epidemiological, clinical, and autopsy research conducted during the past three decades have suggested that diabetic heart disease exists as a separate clinical entity. Diastolic heart failure (DHF) is also referred to as HF with retained left ventricular systolic function. Numerous investigations have shown that even in the absence of hypertension and coronary artery disease, diabetic people have a significant prevalence of heart failure. Pre-clinical diastolic dysfunction is also very common in DM subjects, according to studies[5].

Early assessment of ventricular function in diabetics is crucial because left ventricular diastolic dysfunction (LVDD) is the initial stage of diabetic cardiomyopathy that

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occurs before alterations in the systolic function[6,7]. The diastolic abnormalities are seen in diabetic patients in the absence of diabetic consequences of cardiovascular system[8,9].

Patients with diabetes have worse heart failure symptoms, take more diuretics, and have worse prognosis than people without diabetes, even though their left ventricular systolic dysfunction is similar. Diastolic dysfunction of the left ventricle in diabetes mellitus is one possible explanation for these differences. Left ventricular diastolic failure thus indicates the first stage of diabetic cardiomyopathy preceding alterations in systolic function.

An early diagnosis can be of considerable help to prevent or delay the onset of these consequences. The mortality rate from diabetes complications like infection and gangrene has gradually decreased since the invention of insulin, but the mortality rate from cardiovascular disease has gradually increased. Echocardiography offers considerable information about diastolic dysfunction and dimensions, compared to that provided by clinical evaluation. Studies support the use of echocardiography to improve patient diagnosis and management after history and physical examination[10]. The following variables are frequently measured: velocity at the mitral annulus level during early ventricular filling (e'); late ventricular filling wave (A) and ratio between the peak velocities of the early (E) and late (A) diastolic filling waves at the mitral valve (E/A ratio), isovolumetric relaxation time (IVRT), and deceleration time (DT)[11]. Accordingly, it is highly recommended to perform early detection and management of myocardial dysfunction in the diabetic population before the development of overt heart failure.

The objective of our study was to assess diastolic dysfunction in asymptomatic patients with type 2 diabetes mellitus and to find its relationship with HbA1c levels.

Material and Methods

This was a cross-sectional prevalence, analytical study conducted over a period of 18 months in a tertiary care teaching hospital in North India. Informed consent was taken from each patient. 70 patients of type 2 DM treated with oral hypoglycaemics agents and/or insulin without history suggestive of coronary heart diseases and/or congestive heart failure, attending the diabetic clinic in the department of medicine were included. Complete history and physical examination of all the patients was done and the findings were recorded. Patients with history of hypertension, thyroid disorder, chronic liver and kidney disease were excluded from the study.

Blood samples were collected to estimate FBS, PPBS, HbA1c levels, renal function tests, liver function tests and lipid profile. Cardiac evaluation was done by ECG and 2D echocardiography. Methods used to assess diastolic dysfunction were E/A ratio, left atrial size and iso-volumetric relaxation time (IVRT) on 2D echo.

The data obtained was analysed using SPSS software version 23. For each assessment point, data was statistically analysed using one way ANOVA, 't'-test and chi-square test. The level of significance was set at $p < 0.05$. Pearson correlation test was used to analyse correlation between the two variables.

Results

70 patients were enrolled in which 43 (61.4%) were males and 27 (38.6%) were females. Mean age was 54.9 years in males and 56.1 years females. Overall mean age was 54.9 ± 11.6 years. Mean body mass index (BMI) among the patients was 24.8 ± 2.9 kg/m^2, in which 18 subjects (25.7%) were overweight and 6 subjects (8.5%) were obese. Mean duration of diabetes was 7.7 ± 3.4 years. 38.6% of the subjects had diabetes duration <5 years, 44.3% had diabetes for 5 - 10 years and 17.1% had diabetes for >10 years. Mean FBS, PPBS and HbA1c among the study subjects was 164.4 ± 16.2 mg/dL, 223.3 ± 29.1 mg/dL and 8.1 ± 1.6%, respectively (Fig. 1).

36 (51.4%) patients were detected with diastolic dysfunction (DD) among the 70 patients under study. Mild diastolic dysfunction was found in 29 patients, moderate in 6 patients while 1 patient had severe dysfunction on 2D echo (Table I).

Table I: Distribution of patients according to diastolic dysfunction (DD)

Diastolic Dysfunction	Mitral E/A Ratio	Deceleration Time (m sec)	N = 70	%
Normal Function	0.75 <E/A <1.5	<220	34	48.6
Mild Dysfunction	EA ≤0.75	>220	29	41.4
Moderate Dysfunction	0.75 <E/A <1.5	150 - 200	6	8.6
Severe Dysfunction	E/A ≥1.5	<150	1	1.4

Table II shows that chances of development of diastolic dysfunction increases with the duration of diabetes ($p < 0.05$). Mean HbA1c in patients without and with DD was 6.97 ± 1.3% and 9.04 ± 1.2% respectively. Hence, HbA1c was found to be higher in subjects with DD, as compared to without DD.

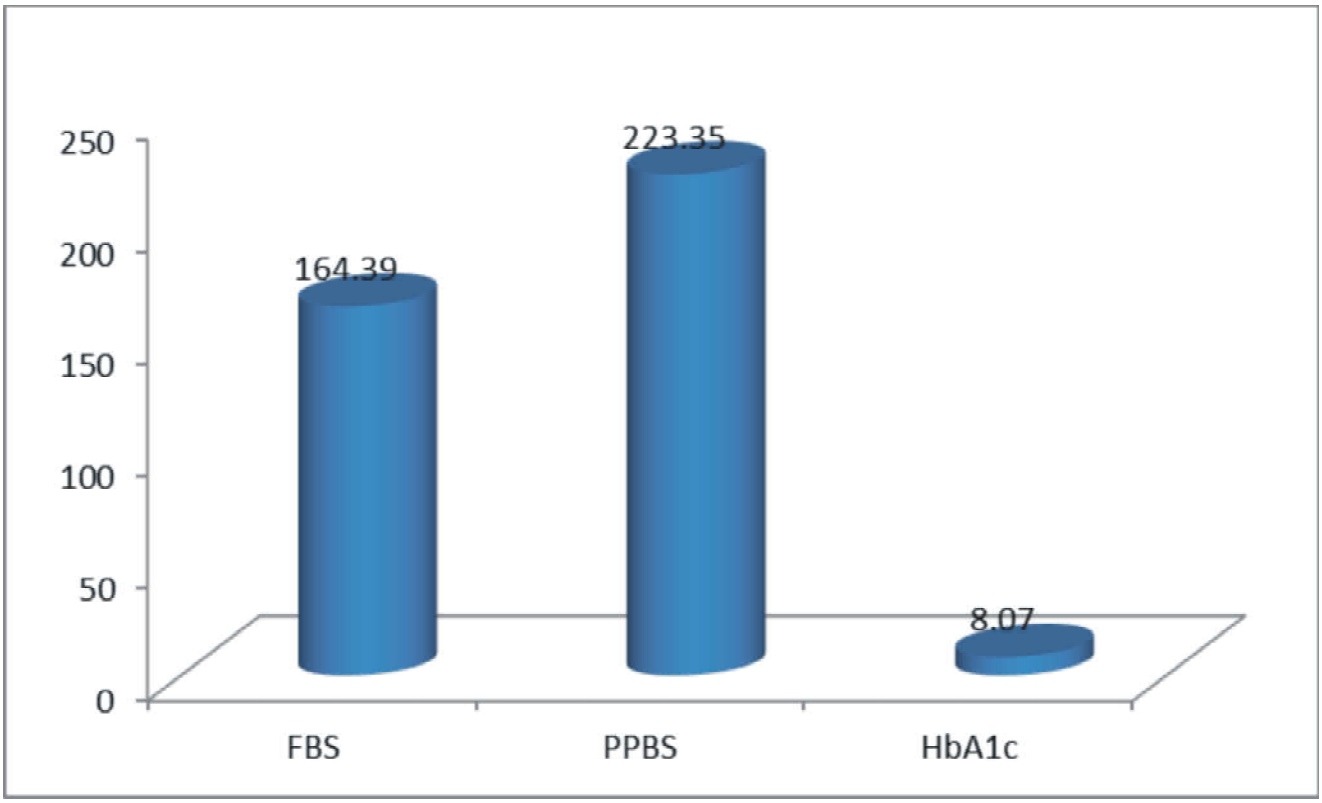

Fig. 1: *Blood glucose levels and HbA1c of patients.*

Table II: Correlation of diastolic dysfunction with duration of diabetes and HbA1c

Duration of Diabetes (in years)	Patients without DD (N = 34)		Patients with DD (N = 36)		p value
	N	%	N	%	
<5	16	47.06	8	22.22	0.005*
5 - 10	14	41.18	11	30.56	
>10	4	11.76	17	47.22	
	Mean	SD	Mean	SD	
HbA1c	6.97	1.30	9.04	1.23	0.001*

**Statistically significant.*

In our study, severity of diastolic dysfunction increased significantly with increase in HbA1c ($p < 0.05$) (Table III).

Table III: Comparison of HbA1c according to severity of diastolic dysfunction (DD)

Diastolic Dysfunction	Mean HbA1c	SD	p value
Normal Function	6.2	0.91	<0.01*
Mild Dysfunction	6.9	1.07	
Moderate Dysfunction	8.0	1.53	
Severe Dysfunction	9.0	1.67	

**Statistically significant.*

Discussion

Numerous experts have looked into how hyperglycaemia contributes to the development of diabetic cardiomyopathy. Diabetes mellitus greatly increases the risk of unfavourable cardiovascular events by causing structural and functional abnormalities that are unrelated to the effects of atherosclerosis. The toxicity of chronic hyperglycaemia in diabetes mellitus is manifested through the formation of irreversibly bound advanced glycated end products through the non-enzymatic glycation of tissue macromolecules, including proteins, lipids, and deoxyribonucleic acid (DNA). It has been discovered that these substances build up in organs like the heart. Increased apoptosis in the diabetic heart causes replacement fibrosis and connective tissue proliferation, which in turn causes increased collagen deposition in a diffused way resulting in the reduction of ventricular compliance. It has been suggested that the initial stage of the alleged "diabetic cardiomyopathy" is left ventricular diastolic dysfunction. It has been demonstrated that a lower E/A ratio is independently linked to higher cardiovascular and all-cause mortality[12,13].

In our study, 61.4% of patients were male and 38.57% were females. The average age of patients was 54.9 ± 11.6 years. In a research by Sai Vittal *et al*[14], the average age of the 50 patients was 54.1 ± 10.99 years. Sarkar *et al*[15] also found

that the majority of patients with diastolic dysfunction (80 individuals) were between the ages of 50 and 59.

65.7% of patients had normal BMI whereas 25.7% were overweight, and 8.6% were obese. The mean BMI was 24.8 ± 2.6 kg/m^2. Only 20% and 10% of the patients in a research by Jain *et al*[16] were overweight and obese, respectively, with the majority of the patients falling within the normal range. A study by Sharavanan *et al*[17], however, found that a higher percentage of patients with diastolic dysfunction were obese. According to a research by Russo *et al*, obesity and diastolic dysfunction are strongly correlated[18].

In our study out of 70 patients, 36 (51.4%) had diastolic dysfunction (DD). 41.4% had mild, 8.6% had moderate, and 1.4% had severe DD. Guria *et al*[19] studied 100 asymptomatic diabetic patients and found diastolic dysfunction in 54 (54%) patients. 4 patients had grade 3, 26 patients had grade 2, and 15 patients had grade 1 diastolic dysfunction in their study. Vittal *et al*[14] found that 66% of the patients, whereas Sharavanan *et al*[17] found that 55% of the patients had diastolic dysfunction. Diastolic dysfunction was seen in 54.33% patients with asymptomatic type 2 diabetes mellitus in a study by Patil *et al*[20]. These results were similar to that found in our study.

According to our study, the likelihood of diastolic dysfunction increases as duration of diabetes mellitus increases ($p < 0.05$). These results are in line with those of other studies. Aaron *et al* discovered a strong correlation between the duration of diabetes and the ratio of early mitral velocity E to medial mitral annulus velocity (e')[22]. Additionally, they discovered that LV diastolic dysfunction (E/e'>15) was independently linked to diabetes duration greater than 4 years. Additionally, VC Patil discovered that diastolic dysfunction was more common in patients with diabetes mellitus who had the disease for 11 - 15 years ($p < 0.05$)[20]. In another study by Bonito *et al*[23], diastolic dysfunction was found in patients with diabetes duration of less than four years and occasionally less than one year. Sarkar *et al*[15] discovered that a higher prevalence of diastolic dysfunction was linked to a longer duration of DM. Guria *et al*[19] likewise found a position correlation between DD and the duration of diabetes.

Patients with and without DD had mean HbA1c values of 9.04 ± 1.2% and 6.8 ± 1.3%, respectively. HbA1c was therefore higher in DD subjects than without it, with a statistically significant difference ($p < 0.05$). Our study found that a higher HbA1c significantly increased the degree of diastolic dysfunction ($p < 0.05$). These results are in line with a study by Hameedullah *et al*[24] who discovered a substantial association between DD and HbA1C levels. According to Guria *et al*[19], the population with LVDD had a mean HbA1c of 11.07 ± 3.66%, which was statistically significant ($p = 0.004$), compared to the population without LVDD were mean HbA1c was 9.11 ± 2.95%. This means that a patient with diabetes who has a higher HbA1c is more likely to have a higher probability of LVDD.

Similarly, the mean HbA1c of individuals with LVDD was 7.95 ± 1.09%, while that of individuals without LVDD was 7.21 ± 1.22%, according to a study of 100 cases of newly diagnosed diabetes mellitus by Srinivasa *et al*. Because the mean HbA1c of the LVDD population was greater than that of the normal LVDD population, this study also found a positive correlation between the higher HbA1c levels and the incidence of LVDD in the diabetic cohort[25]. According to a previously published study, diastolic dysfunction was observed in 9.09% of diabetic patients with an HbA1c range of 6 - 7%; 33.33% of cases with an HbA1c range of 7.1 - 8%; and 100% of cases with an HbA1c of ≥8.1%[26].

The majority of patients were on OHA or OHA with insulin when the treatment profile was assessed, and the majority of subjects had poor glycaemic control for a variety of reasons including inadequate drug dosages, poor lifestyle, poor treatment compliance, and irregular checkups. Insulin, OHA, and a combination of the two were used to treat 38.89%, 33.33%, and 27.78% of the participants with DD in this study, respectively. Insulin, OHA, and a combination of the two were administered to 32.35%, 47.06%, and 20.59% of participants without DD, respectively. In their investigation, Khade *et al*[27] found no correlation between the prevalence of diastolic dysfunction and the kind of treatment ($p = 0.27$). Compared to 23.5% of individuals on insulin and 50% of those on both insulin and OHAs, diastolic dysfunction was observed in 55.2% of patients receiving OHAs. Our findings were similar to those of Madhumathi *et al*[28], who discovered that the incidence of diastolic dysfunction was similar across different treatment groups.

This study highlights the need of early diastolic dysfunction identification as part of preventive management strategy for our diabetic patients. The higher rate of heart disease-related morbidity and mortality among diabetics necessitates the adoption of screening tests, such as echocardiograms, which are easily accessible and affordable.

Limitations of the study

1. Subclinical coronary disease was not ruled out by stress electrocardiography, stress echocardiography, myocardial perfusion imaging, or coronary angiography; and
2. Smaller sample size was studied.

Conclusion

It is clear from the discussion above that diastolic dysfunction is strongly correlated with both the duration of the diabetes mellitus and the HbA1c levels. In order to evaluate heart function for long-term therapy, it is recommended that all diabetic patients must have routine and repeated echocardiographic evaluations. Diastolic dysfunction and diabetes together can have a double-edged effect. Patients who are not diagnosed in a timely manner suffer from higher rates of morbidity and mortality. Our research highlights the necessity of using a Doppler echocardiogram to assess diabetic individuals who are frequently asymptomatic for diastolic insufficiency in order to make prompt intervention. This early diagnosis will definitely help in lowering the disease burden, as well as preventing cardiac complications.

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