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Original Article

Study of Left Ventricular Diastolic Dysfunction in Type 2 Diabetes Mellitus Patients

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Abstract

The aim of this study is to assess LV diastolic function in patients with diabetes with no overt cardiac symptoms or signs by color flow Doppler study with an intention to detect patients with LV dysfunction at an early stage. To correlate LV diastolic dysfunction (LVDD) with age, gender, duration of Type 2 diabetes, glycatedhemoglobin (HbA1c), and microvascular complications. **Mateials and Methods:** 50 patients of DM with no cardiac symptoms with minimum duration of 2 years are taken for this study. It is an observational type of study. The age group is between 40 years and above, who presented with either cellulitis or some general complaints like weakness of limbs or fever to the hospital with blood glucose being above normal. **Results and Conclusion:** Let ventricular diastolic is a common cardiac disorder (66%) in patients with type 2 DM without other associated risk factors. E/A ratio and other colorflow Doppler studies are equally good parameters for the assessment of LVDD.

Key words: Diabetes mellitus, Diastolic dysfunction, Echocardiography

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorder that shares phenotype of hyperglycemia. In India, the prevalence rates are estimated to be around 20% in cities, and recent figures showed surprising increasing rates in rural areas. To ascertain the true prevalence in any community, it is essential that there must be standardized methods for the diagnosis with proper acceptable criteria so that the results are comparable. Two broad categories of DM are Type 1 or Type 2. Type 1 is the result of complete or near total insulin deficiency. Type 2 DM is a heterogeneous disorder characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production.[1-10]

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This metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ system that leads to long-term chronic complications which account for much of the morbidity and mortality, attributed to the disease. An early diagnosis on that account can be of great help to prevent or delay the development of these complications. This underlines the necessity of early diagnosis.[11-18]

Since the advent of insulin, there has been a progressive decline in mortality from diabetes complications such as gangrene and infection but a progressive rise in the deaths from cardiovascular disease.

The association of coronary heart disease and DM is well known, but recent evidence suggests that diabetics may develop congestive heart failure in excess of the predicted prevalence of coronary heart disease.

Clinical and pathological studies have shown that abnormalities of left ventricular (LV) function, cardiomegaly and failure may occur with normal coronary arteries possibly due to microangiopathy of coronary circulation independent of large-vessel atherosclerosis.

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Congestive heart failure is a major public health problem in developed countries. Several epidemiological investigations have confirmed that up to half of patients in the community have heart failure due to diastolic dysfunction despite normal LV ejection fraction (EF). Some epidemiological and clinical arguments suggest that diastolic abnormalities may contribute to the high morbidity and mortality among patients with diabetes.

Indeed, in the community setting, data from the Framingham heart study have shown an increased incidence of congestive heart failure in patients with diabetes irrespective of coronary heart disease and hypertension. It was also observed in patients enrolled in clinical trials of myocardial infarction. Despite similar LV systolic function, patients with diabetes have more pronounced heart failure symptoms, use more diuretics, and have an adverse prognosis compared with those without diabetes. One putative explanation for this discrepancy is diastolic dysfunction of the left ventricle.[17,19-26]

Aims of the Study

The aims of this study are as follows:

1. To assess LV diastolic function in patients with diabetes with no overt cardiac symptoms or signs by color flow Doppler study with an intention to detect patients with LV dysfunction at an early stage.
2. To correlate LV diastolic dysfunction (LVDD) with age, gender, duration of Type 2 diabetes, glycated hemoglobin (HbA1c), and microvascular complications.

MATERIALS AND METHODS

Diagnostic Criteria

DM: If a patient is a known diabetic on treatment or with any fasting blood sugar level (F-BSL) ≥126 mg/dL.

Retinopathy

Microangiopathy was assessed by fundoscopy (direct ophthalmoscopy). The ophthalmologist doing fundoscopy was unaware of this study. The fundoscopic examination was done after dilating the pupil with tropicamide (1%). Retinopathy status was labeled as follow:

- No evidence of diabetic retinopathy;
- Background diabetic retinopathy defined as presence of one or more microaneurysms, punctate or striate intraretinal hemorrhages, and hard exudates;
- Pre-proliferative diabetic retinopathy defined as soft exudates, venous beading, and intraretinal microvascular abnormalities;
- Proliferative diabetic retinopathy characterized by neovascularization on or within one disk diameter of the disk in extent.

Autonomic Neuropathy

Autonomic function was evaluated by unmasking the sympathetic dysfunction by the blood pressure (BP) response to standing. A fall in systolic BP on erect position of >20 mmHg and diastolic BP >10 is considered as postural hypotension.

Diastolic Dysfunction

LVDD was considered to be present if any of the following findings were seen, as previously described as follows:

- E/A ratio <0.75 or >1.5,
- DT <150 or > 220 ms,

Selection of the Patients

1. The following patients are taken for the study. It is an observational type of study.
   a. Selection of patients is based on the history of DM, clinical examination, and laboratory parameters.
   b. Asymptomatic patients with minimum of 2-year duration of DM.
   c. Type 2 DM patients were taken for the study.
   d. Patients attending MGM Hospital as outpatients and inpatients from the year 2014 to 2016.
   e. Age range of the patients taken 40 years and above.
2. The following patients are excluded from the study.
   a. Myocardial infarction by history and resting electrocardiogram (ECG)
   b. Patients with angina pectoris
   c. Patients with hypertension
   d. Type 1 DM patients
   e. Significant alcoholic patients
   f. Patients with thyroid diseases
   g. Patients with renal failure
   h. Patients with other underlying heart diseases such as
      I. Congenital heart disease
      II. Valvular heart disease
      III. Pericardial disease – by history, chest X-ray (CXR) posteroanterior (PA) view, and echocardiography (Echo)
   i. Patients with regional wall motion abnormalities are excluded by Echo.

50 patients of DM with no cardiac symptoms with minimum duration of 2 years are taken for this study. It is an observational type of study. The age group is between 40 years and above, who presented with either cellulitis or some general complaints like weakness of limbs or fever to the hospital with blood glucose being above normal.

All patients are non-smokers, had no signs and symptoms of valvular heart disease, hypertension, angina pectoris, and myocardial infarction and did not have the history of alcoholism. All of them were asymptomatic for heart disease and those with symptoms of heart disease were excluded from the study. All the patients fulfilled the inclusion and exclusion criteria.

A thorough clinical examination is done with special emphasis on examination of retina, ankle jerks, and glove, and stocking type of sensory loss for the evidence of peripheral neuropathy, 24 h urinary protein for the presence nephropathy and supine, and standing BP is recorded for the evidence automatic neuropathy.

All of them are admitted to the hospital with ketoacidosis or cellulitis or had high blood sugar values when presenting to the outpatient department and are on treatment with insulin or oral hypoglycemic drugs as required. Routine urine examination, 24 h urinary proteins, fasting blood sugar, post-lunch blood sugar, blood urea, serum creatinine, serum cholesterol, chest X-ray PA view, ECG, M-mode 2D Echo, and color flow study performed.

Method of Echo Doppler Evaluation

M-mode, 2D Echo, and Pulsed wave Doppler are done with Hewlett Packard Echo machine. Doppler Echo was done in all patients with diabetes when their fasting blood sugar was below 140 mg% with treatment.

In the 2D Echo evaluation of patients with diabetes, a short axis and long axis view of the heart were obtained with the patient in left lateral recumbent position. An apical 4 chamber view of the heart was also seen. This is done to rule out any subclinical valvular heart disease and pericardial disease, especially constrictive pericarditis. In the short axis view with the cursor aligned just distal to the tips of mitral valve, an M-mode Echo is obtained to take the various dimensions such as LV dimensions in diastole and systole, septal, and posterior wall thickness.

Next, a color flow evaluation is performed to detect any subtle regurgitant lesion from an apical chamber view, and pulsed Doppler cursor is aligned parallel to the stream of inflow of blood from left atrium to left ventricle. A site is chosen along the cursor for sampling the mitral velocity profile such that the sample volume was taken just internal to the tips of mitral leaflets. A pulsed wave Doppler tracing is obtained, and the following parameters are measured.

1. Early diastolic flow velocity (E) cm/s
2. Late diastolic flow velocity (A) cm/s
3. E/A ratio
4. IVRT (ms)
5. Deceleration time (ms).

RESULTS

50 patients of Type 2 DM of minimum 2-year duration were included in the study group. These patients had no signs and symptoms of heart disease. They satisfied the inclusion and exclusion criteria and were taken up for the study.

The age of the patients is 40 years above, with a mean value of 53.72 years, of 50 patients studied, 15 patients are females, 35 are males. Heart rate was within normal range. Blood urea, serum creatinine, CUE, ECG, and CXR PA view were within normal limits.

Age Distribution

60% of total number of patients have diabetes with duration of 2-5 years. 40% of patients have diabetes with duration of 6-10 years.

63% of patients with diabetes of duration 2-5 years have diastolic dysfunction and 70% of patients with duration 6-10 years have diastolic dysfunction (Table 2).

Females shown more prevalence of diastolic dysfunction (80%) in comparison to the males (57%) (Table 3).

86% of the patients with HbA1c >7.5 have diastolic dysfunction (Tables 1-5).

Table 1: Age distribution

Age	No. of patients (%)	Patients with LVDD (%)	Patients without LVDD
40-45	5 (10)	2 (4)	3
46-50	16 (32)	10 (20)	6
51-55	12 (24)	8 (16)	4
56-60	6 (12)	5 (10)	1
61-70	11 (22)	8 (16)	3
Total	50	33	17

LVDD: Left ventricular diastolic dysfunction

Table 2: Correlation of diastolic dysfunction of diabetes mellitus with duration of diabetes

Duration of diabetes (years)	No. of patients with LVDD	No. of patients without LVDD
2-5 (30 patients)	19	11
6-10 (20 patients)	14	6

LVDD: Left ventricular diastolic dysfunction

Table 3: Correlation of chronic complications of diabetes mellitus with gender

Gender	No. of patients with LVDD	No. of patients without LVDD
Males (35 patients)	20	15
Females (15 patients)	13	2

LVDD: Left ventricular diastolic dysfunction

Table 4: Correlation of diastolic dysfunction with HbA1c

HbA1c	Total no. of patients	No. of patients with LVDD
>7.5	15	13
<7.5	35	20

LVDD: Left ventricular diastolic dysfunction, HbA1c: Glycated hemoglobin

Table 5: Correlation of chronic complications of diabetes mellitus with left ventricular dysfunction

Complication	Total no. of cases (%)	No. of cases with E/A<0.75 (%)	No. of cases with E/A>0.75
Autonomic neuropathy	13 (26)	10 (76)	3
Retinopathy	11 (22)	9 (81)	2
Albuminuria	15 (30)	11 (73)	4

Table 6: Total no. of patients with diastolic dysfunction

Total no. of patients	Patients with	Patients without LVDD
50	33	17

LVDD: Left ventricular diastolic dysfunction

Table 7: Echocardiographic evaluation

Parameter	Result (mean±SD)	Normal range
Ventricular septal wall thickness (cm)	0.843±0.11	0.6-1.1
LV posterior wall thickness (cm)	0.81±0.1	0.6-1.1
LV end-diastolic dimension (cm)	4.23±0.36	3.5-5.7
LV end-systolic dimension (cm)	2.80±0.30	2.7-3.7
Fractional shortening (%)	31.4±5.86	25-42
Ejection fraction (%)	57.98±2.1	55-60
Aorta root dimension (cm)	2.74±0.38	2.0-3.7
Left atrial dimensions (cm)	2.92±0.31	1.9-4.0

LV: Left ventricular, SD: Standard deviation

Table 8: Pulsed wave Doppler evaluation

Parameter	Result (Mean±SD)	Normal range
E wave (cm/s)	61.26±5.07	68±18
A wave (cm/s)	63.38±5	61±13
E/A ratio	0.83±0.15	1.17±0.35
IVRT (ms)	93.67±11.27	69±12
Deceleration time (m)	243.33±6.02	163.2±30.1

IVRT: Isovolumic relaxation time, SD: Standard deviation

56% of the patients with HbA1c <7.5 have diastolic dysfunction (Table 4).

Incidence of Diastolic Dysfunction (Tables 6-8)

DISCUSSION

Our finding demonstrates that pre-clinical diastolic dysfunction is common in patients with type 2 DM. Pre-clinical diastolic dysfunction is broadly defined as diastolic dysfunction with normal systolic function and no symptoms of heart failure.

Duration of diabetes of 6-10 years had more incidence of diastolic dysfunction.

Diastolic dysfunction was significantly high in patients age >45 years.

Diastolic dysfunction was present in majority of patients with autonomic neuropathy and retinopathy.

Boyer *et al*.[27] stated that prevalence of LVDD in asymptomatic normotensive patient with Type 2 DM is high.

Masugata *et al.*[28] in their study of 77 normotensive patients found that the cardiac diastolic dysfunction without LV systolic dysfunction in patients with well-controlled Type 2 DM is related neither to hypertension nor LV hypertrophy but rather to aging and duration of Type 2 DM.

Mishra *et al.*[29] in their case control study of 71 patients with Type 2 DM found that asymptomatic patients with diabetes have reduced diastolic function as compared with the patient without Type 2 DM. LV diastolic abnormalities correlated with the duration of diabetes.

Hameedullah *et al.* in their study population of 60 patients with type 2 DM found that there was a strong correlation between HbA1c level and diastolic indices. Diastolic dysfunction was more frequent in poorly controlled patients with diabetes, and its severity is correlated with glycemic control. Similarly, in our study, HbA1c >7.5% had a higher prevalence of diastolic dysfunction compared to HbA1c <7.5%.

Exiara *et al.*, in their study, stated that the prevalence of LVDD in normotensive, asymptomatic well-controlled type 2 diabetes patients is high and increases with age.

Sacre *et al.* found that there was an independent association between global cardiac autonomic neuropathy (CAN) and LVDD in patients with Type 2 DM.

Annonu *et al.* in their case control study of 66 patients found that there was an inverse correlation between the duration of diabetes and E/A ratio. E/A ratio <1 was associated with a higher prevalence of retinopathy (49% vs. 20%) and abnormal blood pressure response to standing (29% versus 4%) LV systolic and diastolic abnormalities are correlated with the duration of diabetes and with other diabetic microangiopathies, such as diabetic retinopathy and neuropathy. These results are comparable to our study,

where diastolic dysfunction was present in majority of the patients with autonomic neuropathy and retinopathy.

Poantal *et al.* in their study of 58 patients found that CAN was associated with LVDD in patients with Type 2 DM but without clinical manifestation of the heart disease. Similarly, Poirier *et al*. stated that diastolic dysfunction and CAN are associated in patients with otherwise uncomplicated well-controlled Type 2 DM.

The main finding of this study is that 66% of patients with Type 2 DM without evidence of structural heart disease or arterial hypertension demonstrate diastolic dysfunction of the left ventricle.

The systolic function was assessed by fractional shortening (FS) and EF. EF though it is reduced in diabetes patients, it is within normal limits with mean of 57.98 ± 2.1. Similar findings were noted by Verd *et al.*

FS is in the normal range with a mean of 32.9±4.8, similar findings were noted by Mittal *et al*.and Airaksinen *et al*. VSWT is within normal range.

LV diastolic function as measured by pulsed wave Doppler was found to be abnormal in 66% of patients (33 patients). In our study, a total of 33 out of 50 patients have diastolic dysfunction as defined by E/A <1, with mean E/A of 0.73 with standard deviation (SD) ± 0.01. Similar findings were noted by Bajraktari *et al*.[11]

All the patients with E/A ratio <0.75 equally shown evidence of LVDD in other color Doppler flow studies.

All these 33 patients had prolongation of DT >220 ms, with mean DT of 243.33 with SD ± 6.02.

Abnormal relaxation of the left ventricle is indicated by prolongation of isovolumetric relaxation time. In our study, the 33 patients had IVRT prolonged with a mean 102.77 and SD ± 2.93. Similar findings were noted in studies of Shappiro *et al.* Mittal *et al.* found in their study on diabetics the prolongation of IVRT with a mean value of 103.24 ± 3.46 ms.

Out of the 50 patients, 13 (25%) had postural hypotension and 10 out of these had diastolic dysfunction.

11 patients had retinopathy, out of which 9 had associated diastolic dysfunction.

15 patients had HbA1c >7.5, out of which 13 patients had associated diastolic dysfunction. Similar findings were noted in the study of Patil *et al*.[8]

Females shown more prevalence of diastolic dysfunction (80%) in comparison to the males (57%).

From the above discussion and comparison of present study findings with various studies, we found that there was a high prevalence of diastolic dysfunction in patients with asymptomatic Type 2 DM, and it was correlated with age, duration of diabetes, HbA1c, autonomic neuropathy, and retinopathy.

Our study demonstrates that the incidence of pre-clinical diastolic dysfunction is high in Type 2 DM patients. Furthermore, we found that there is a direct correlation between the duration of DM and diastolic dysfunction and that significant diastolic dysfunction occurs >5 years after the onset of DM independent of coronary disease or hypertension. Therefore, screening and aggressive management of patients with diabetes with pre-clinical diastolic dysfunction may delay the progression to heart failure.

CONCLUSION

1. Let ventricular diastolic is a common cardiac disorder (66%) in patients with type 2 DM without other associated risk factors.
2. E/A ratio and other color flow Doppler studies are equally good parameters for the assessment of LVDD.
3. Chronic complications of diabetes: Autonomic neuropathy, retinopathy, and nephropathy have correlation with LVDD.
4. Duration of DM, female gender, and HbA1c level are significant factors for the development of diastolic dysfunction.
5. Early diagnosis and institution of treatment with ACE inhibitors, angiotensin II receptor blockers, aldosterone antagonists, and diuretics will reduce the morbidity and improve the outcome of diastolic heart failure.
6. Patients with Type 2 DM should be screened for subclinical LVDD by echocardiography.

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