

Original Research Article

Left ventricular diastolic dysfunction in asymptomatic type 2 diabetes mellitus patients

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ABSTRACT

Background: Diastolic dysfunction has been described as an early sign of diabetic heart muscle disease preceding the systolic damage. The pathogenesis of ventricular dysfunction remains unknown and has been somewhat controversial. So far, very few population-based studies have been carried out in India, to demonstrate the prevalence of diastolic dysfunction in diabetic subjects. Hence the present study was done at our tertiary care centre to detect left diastolic dysfunction in asymptomatic type 2 diabetes individuals and to use echo-cardiologic assessment as an early detector of left diastolic dysfunction. The aim of this study was to detect left diastolic dysfunction in asymptomatic type 2 diabetes individuals and to use echocardiologic assessment as an early detector of left diastolic dysfunction.

Methods: A hospital based cross-sectional observational study was conducted with 50 patients for echocardiographic evaluation of diastolic dysfunction in asymptomatic Type 2 Diabetes Mellitus. E/A <1 and increase in LA size was considered as the evidence of left ventricular Diastolic Dysfunction.

Results: 15 (30%) patients were detected with Left Ventricular Diastolic Dysfunction (LVDD) among the 50 patients under study.

Conclusions: Diastolic dysfunction in patients with diabetes is present in 30% of patients even when diabetes is present at a younger age, and is of a shorter duration. This dysfunction is suggestive of pre-clinical diabetic cardiomyopathy. E/A, DT and peak A velocity are sensitive indices of diastolic LV dysfunction. Thus, diastolic dysfunction can be used as an early indicator, as it is a precursor to increased LV hypertrophy and clinical left ventricular dysfunction.

Keywords: Diabetes mellitus, Diastolic dysfunction, Echocardiography, E/A ratio, LA size

INTRODUCTION

Diabetes and cardiovascular diseases are rapidly gaining pandemic proportions in the South East Asian subcontinent, and India is leading the race of numbers.

Worldwide, there are approximately 194 million adult cases of type 2 diabetes and this number is expected to increase to 333 million by 2025. There are approximately 33 million diabetics in India presently and this number is expected to reach 79.4 million in 2030.¹

One of the important factors contributing to increased prevalence of type 2 diabetes in Asian Indians is the fact that they have a greater degree of insulin resistance compared to Caucasians.²⁻⁴ Mohan et al first demonstrated that Asian Indians have higher insulin levels to a glucose load than Europeans.⁴

The Framingham study pointed out a previously unknown factor in diabetic patients that causes much

higher incidence of cardiovascular complications.⁵ Diabetic individuals have higher serum concentrations of lipids and more hypertension, obesity, and thus the pathogenesis of advanced atherosclerosis. Type-2 diabetics are also prone to silent myocardial ischaemia even before the development of overt coronary artery disease.⁶ This is a reflection of accelerated coronary atherosclerosis, though autonomic neuropathy has also been implicated in its causation.⁷

Several mechanisms for diabetic cardiomyopathy have been proposed including small and microvascular disease, autonomic dysfunction, metabolic derangements, interstitial fibrosis and the development of fibrosis, possibly caused by the accumulation of a periodic acid-Schiff-positive glycoprotein, leading to myocardial hypertrophy and diastolic dysfunction.^{8, 9-11}

Diastolic dysfunction has been described as an early sign of this diabetic heart muscle disease preceding the systolic damage. The pathogenesis of this ventricular dysfunction remains unknown and has been somewhat controversial.¹²

Hence the present study was done at our tertiary care center to detect left diastolic dysfunction in asymptomatic type 2 diabetes individuals and to use echo-cardiologic assessment as an early detector of left diastolic dysfunction.

METHODS

A hospital based cross-sectional observational study was conducted with 50 patients for echocardiographic evaluation of diastolic dysfunction in asymptomatic Type 2 Diabetes Mellitus.

Study design

Cross-sectional observational study

Place of study

Dr. D.Y. Patil Medical College and Research Centre, Pimpri, Pune 411018

Period of study

July 2015 to September 2017

Sample size

50 cases

Inclusion criteria

All type 2 diabetic patients who clinically had no symptoms of cardiovascular involvement and blood

pressure <130/80mmHg, with normal ECG were included in the study.

Exclusion criteria

All patients with type 2 diabetes with other cardiac diseases like valvular heart disease, ischemic and hypertensive heart disease, congestive heart failure; cardiomyopathy was excluded from the study.

Methodology

50 patients thus taken were subjected to thorough clinical examination supported by relevant investigations. The following investigations were done:

- Blood glucose on admission: FBS, PPBS,
- Renal function tests, including electrolytes,
- Glycosylated hemoglobin (HbA1c),
- Fasting Lipid profile,
- Urine routine and microscopy,
- ECG,
- Fundoscopy,
- Chest x-ray,
- Echocardiography,

-Ejection fraction was calculated in all patients,
-E-peak velocity of early mitral flow,
-E-peak velocity of late mitral flow,
-E/A ratio,
-Left atrial size: Reduction in E-velocity increase in A-velocity.

Plasma glucose (fasting and post prandial) was measured by the glucose oxidase method and the urine sugar by Benedict's reagent. Biochemical investigations in the form of blood urea, serum creatinine and serum cholesterol were also carried out enzymatically. BMI (Body Mass Index) was calculated as $\text{weight (kgs.)} \div [\text{height (m)}]^2$.

From the transmitral recording, following measurements were carried out:

- Peak E velocity in m/sec-peak early transmitral filling velocity during early diastole (normal: 0.5-0.8),
- Peak A velocity in m/sec-peak transmitral atrial filling velocity during late diastole (normal: 0.3-0.5),
- Deceleration time (DT) in msec-time elapsed between peak E velocity and point where extrapolation of deceleration slope of E velocity crosses the zero baseline (normal: 150-220),
- Acceleration time (AT) in msec-time elapsed between point where extrapolation of acceleration slope of E velocity crosses zero baseline and peak E velocity. (normal: 60-100),

- Isovolumic relaxation time (IVRT) in msec-duration between aortic valve closure and mitral valve opening (normal: 60-100),
- Ratio of peak E to peak A (E/A) (normal: 1-2).

Conventional echocardiography. Standard and pulsed wave Doppler echocardiograms were obtained in all diabetic patients. All subjects were examined in the left lateral decubitus position, using a commercially available ultrasound system Phillips I/E 33 (Bothell, WA, USA) S5-1 phased-array transducer with M-mode, two-dimensional, pulsed and continuous wave, color-flow, and tissue Doppler capabilities.

Early (E) and late (A) diastolic myocardial velocities were obtained and their ratio was derived. E/A <1 and increase in LA size was considered as the evidence of left ventricular Diastolic Dysfunction.

Statistical analysis

Quantitative data was presented with the help of Mean and Standard deviation. Qualitative data was presented with the help of frequency and percentage table. Results were graphically represented where deemed necessary. Appropriate statistical software, including but not restricted to MS-Excel. SPSS version 20 was used for statistical analysis. Graphical representation was done in MS-Excel 2010.

RESULTS

A hospital based cross-sectional observational study was conducted with 50 patients for echocardiographic evaluation of diastolic dysfunction in asymptomatic Type 2 Diabetes Mellitus patients.

Distribution of patients according to BMI

35 (70%) patients were in the normal range while 10 (20%) and 5 (10%) patients were overweight and obese respectively. The mean BMI of patients was 24.69 kg/m².

Table 1: Distribution of patients according to BMI.

BMI	N	%
Normal	35	70
Overweight	10	20
Obese	5	10
Total	50	100
Mean ±SD	24.69±3.02	

Distribution of patients according to duration of diabetes

Most of the patients 28 (56%) had diabetes for <1year while 16 (32%) and 6 (12%) patients had diabetes for 1-3years and >3years respectively. The mean duration of diabetes was 16.48±13.37months.

Table 2: Distribution of patients according to duration of Diabetes.

Duration of diabetes	N	%
<12 months	28	56
12-36 months	16	32
>36 months	6	12
Total	50	100
Mean ±SD	16.48±13.37	

Blood glucose levels of patients

The mean FBS and PPBS values were 163.45±15.95 mmHg and 221.59±29.21 mg/dl respectively.

Table 3: Blood glucose levels of patients.

Blood glucose	Mean	± SD
FBS (mg/dl)	163.45	± 15.95
PPBS (mg/dl)	221.59	± 29.21

Biochemical parameters of patients

The biochemical parameters of patients are summarized in Table 4.

Table 4: Biochemical parameters of patients.

Parameters	Mean	±SD
Hba1c (%)	8.01	±1.23
Creatinine (mg/dl)	0.72	±0.19
Urea (mg/dl)	22.06	±3.84

Lipid Profile parameters of patients

The lipid profile parameters of patients are summarized in Table 5.

Table 5: Lipid Profile parameters of patients.

Parameters (mg/dl)	Mean	±SD
Cholesterol	189.94	±13.07
Triglyceride	184.54	±39.97
VLDL	33.58	±4.74
LDL	126.23	±30.04
HDL	44.16	±5.99

Liver function test parameters of patients

The liver function test parameters of patients are summarized in Table 6.

Distribution of patients according to left ventricular diastolic dysfunction (LVDD)

15 (30%) patients were detected with Left Ventricular Diastolic Dysfunction (LVDD) among the 50 patients under study.

Table 6: Liver Function Test parameters of patients.

Parameters (mg/dl)	Mean	± SD
Total bilirubin (mg/dl)	1.72	±2.67
SGOT (IU/l)	146.12	±427.83
SGPT (IU/l)	105.24	±291.14
Alkaline phosphatase (u/l)	110.02	±51.78
Total protein (g/dl)	7.05	±0.87
Serum albumin (mg/dl)	3.89	±0.98

Table 7: Distribution of patients according to left ventricular diastolic dysfunction (LVDD).

LVDD	N	%
Present	15	30
Absent	35	70
Total	50	100

Table 8: Echocardiography parameters of patients.

Parameters	patients without LVDD		Patients with LVDD		P value
	Mean	± SD	Mean	± SD	
LA volume index (ml/m ²)	26.26	± 2.75	26.78	± 0.66	>0.05
Relative wall thickness	0.34	± 0.05	0.39	± 0.12	<0.05
LV mass (g)	149.02	± 6.74	158.20	± 4.01	<0.05
LV mass index (g/m ²)	84.37	± 6.67	91.27	± 4.74	<0.05
LV hypertrophy (%)	13.1	± 2.33	18.8	± 1.36	<0.05
LV ejection fraction (%)	65.17	± 3.24	64.07	± 2.74	>0.05
E wave (cm/s)	0.69	± 0.18	0.56	± 0.12	<0.05
A wave (cm/s)	0.62	± 0.14	0.71	± 0.19	<0.05
E/A ratio	1.16	± 0.48	0.83	± 0.26	<0.05
DT (msec)	195.14	± 11.60	224.73	± 16.02	>0.05
AT (msec)	82.45	± 10.77	86.67	± 7.59	>0.05
IVRT (msec)	71.65	± 7.43	76.87	± 13.29	>0.05

Echocardiography parameters of patients

The echocardiography parameters of patients are summarized in Table 8.



Figure 1: Echocardiography showing E/A ratio <1.

DISCUSSION

A hospital based cross-sectional observational study was conducted with 50 patients for echocardiographic evaluation of diastolic dysfunction in asymptomatic Type 2 Diabetes Mellitus patients.

In our study, 35 (70%) patients were in the normal range while 10 (20%) and 5 (10%) patients were overweight and obese respectively. The mean BMI of patients was 24.69 kg/m². Sharavanan TKV et al reported among 66 diabetic patients with diastolic dysfunction, obesity was seen in 42 patients with a body mass index of more than 23 kg/m².¹³

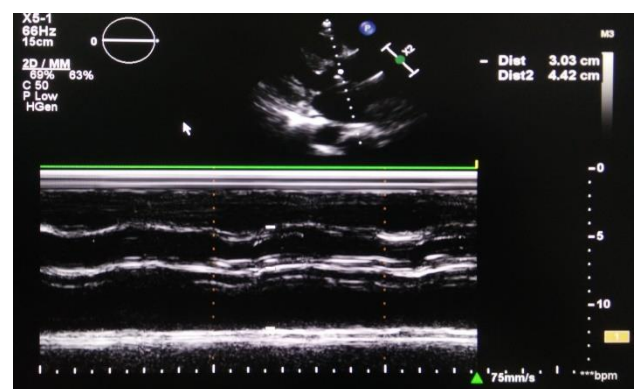


Figure 2: Echocardiography showing LA distention.

Russo C et al in a community-based study in an elderly cohort on effect of obesity and overweight on left ventricular diastolic function reported a strong association between obesity and left ventricular diastolic dysfunction.¹⁴

Dikshit NM et al found Mean BMI (kg/m^2) 24.06 ± 2.53 , 22.65 ± 1.92 , p value < 0.05 .¹⁵

It was observed in the present study that majority of the patients (56%) had diabetes for < 1 year while 16 (32%) and 6 (12%) patients had diabetes for 1-3 years and > 3 years respectively. The mean duration of diabetes was 16.48 ± 13.3 months.

Senthil N et al according to duration of diabetes 30 patients had Type I diabetes.¹⁶ 60 patients had a duration of diabetes less than 6 months (mean duration 3.2 months), 30 patients with duration 6 months-3 years (mean duration 1.33 years), and 10 patients had duration more than 3 years (mean duration 6.25 years).

In a study by Raev DC, diastolic dysfunction was present in patients of even 6 months duration of diabetes.¹⁷ Dikshit NM et al found, Total cholesterol (mg/dl) 206.2 ± 58.18 , Mean FBS (mg/dl) 180.8 ± 78.41 , Mean PPBS (mg/dl) 231.8 ± 86.95 in Diabetics and Total cholesterol (mg/dl) 189.2 ± 28.12 , Mean FBS (mg/dl) 86.44 ± 16.31 , Mean PPBS (mg/dl) 118.2 ± 14.2 in controls.¹⁵

In our study, mean \pm SD biochemical parameters of patients are summarized as: HbA1c (%) 8.01 ± 1.23 , Creatinine (mg/dl) 0.72 ± 0.19 and Urea (mg/dl) 22.06 ± 3.84 . Sharavanan TKV et al reported mean value of HbA1C of the subjects with diastolic dysfunction was 9.8515 ± 2.1399 and that of the patients with normal diastolic function was 9.1593 ± 1.5266 .¹³ Statistical significance was found between HbA1C and diastolic dysfunction in type 2 diabetic patients. The author's data implied a close relation of glycosylated hemoglobin and diastolic dysfunction.

In a study performed on Diastolic Dysfunction in Newly Diagnosed Type 2 Diabetes Mellitus and its Correlation with Glycosylated Haemoglobin (HbA1C) by Chaudhary AK et al, the observations of HbA1C were directly proportional to the incidence of diastolic dysfunction.¹⁸ Senthil N et al observed in their study 60 patients had HbA1c < 7 , 30 patients with 7-8 and 10 had > 8 .¹⁶

In our study the Mean \pm SD lipid profile parameters of patients are summarized as Total Cholesterol 189.94 ± 13.07 , Triglyceride 184.54 ± 39.97 , VLDL 33.58 ± 4.74 , LDL 126.23 ± 30.04 and HDL 44.16 ± 5.99 . Mean \pm SD liver function test parameters of patients are as follows: Total Bilirubin (mg/dl) 1.72 ± 2.67 , SGOT (IU/L) 146.12 ± 427.83 , SGPT (IU/L) 105.24 ± 291.14 , Alkaline phosphatase (U/L) 110.02 ± 51.78 , Total Protein (g/dl) 7.05 ± 0.87 and Serum albumin (mg/dl) 3.89 ± 0.98 .¹⁵ (30%) patients were detected with Left Ventricular Diastolic Dysfunction (LVDD) among the 50 patients under study.

Dikshit NM et al in a prospective study to assess normotensive diabetic patients by echocardiographic and

Doppler parameters found a total of 50 diabetics out of which 33 (66%) patients had diastolic dysfunction.¹⁵

Sharavanan TKV et al reported prevalence of diastolic dysfunction in diabetic patients was 66 (55.0%).¹³ Patil VC et al in their hospital based study done on Diastolic dysfunction in asymptomatic type 2 diabetes mellitus with normal systolic function demonstrated that the prevalence rate of diastolic dysfunction was 54.33%.¹⁹

Ashraf SM et al in their hospital based study on association of hypertension and diastolic dysfunction with type 2 diabetes mellitus on 212 diabetic patients found that 30.76% patients with Type II DM had diastolic dysfunction.²⁰

Patil MB et al in their cross-sectional hospital based study found that in 64% of patients with Type II diabetes mellitus, myocardial damage affects diastolic dysfunction before systolic dysfunction in diabetic individuals.²¹

Zarich SW et al reported that the prevalence of diastolic dysfunction was 30%.¹¹ Senthil N et al reported that among 60 patients with < 6 months duration of diabetes, LVDD was found in 18 patients.¹⁶ Out of 30 patients who had DM of 6 months-3 years duration LVDD was found in 9. Out of 10 patients who had DM more than 3 years duration, LVDD was found in 3 patients.

In the Framingham Heart study on the role of diabetes in congestive heart failure done by Kannel WB et al females were more than the males.²² Among 70 Type II DM patients, 21 had LVDD (30%) while among 30 Type I DM patients 9 had LVDD (30%).

In the present study, Mean \pm SD echocardiography parameters of patients without LVDD are summarized as follows: LA volume index (ml/m^2) 26.26 ± 2.75 , Relative wall thickness 0.34 ± 0.05 , LV mass (g) 149.02 ± 6.74 , LV mass index (g/m^2) 84.37 ± 6.67 , LV hypertrophy (%) 13.1 ± 2.33 , LV ejection fraction (%) 65.17 ± 3.24 , E wave (cm/s) 0.69 ± 0.18 , A wave (cm/s) 0.62 ± 0.14 , E/A ratio 1.16 ± 0.48 , DT (msec) 195.14 ± 11.60 , AT (msec) 82.45 ± 10.77 IVRT (msec) 71.65 ± 7.43 and Mean \pm SD echocardiography parameters of patients with LVDD are LA volume index (ml/m^2) 26.78 ± 0.66 , Relative wall thickness 0.39 ± 0.12 , LV mass (g) 158.20 ± 4.01 , LV mass index (g/m^2) 91.27 ± 4.74 , LV hypertrophy (%) 18.8 ± 1.36 , LV ejection fraction (%) 64.07 ± 2.74 , E wave (cm/s) 0.56 ± 0.12 , A wave (cm/s) 0.71 ± 0.19 , E/A ratio 0.83 ± 0.26 , DT (msec) 224.73 ± 16.02 , AT (msec) 86.67 ± 7.59 and IVRT (msec) 76.87 ± 13.29 .

Dikshit NM et al in a prospective study found that all subjects showed normal systolic function.¹⁵ Interventricular septum thickness, left ventricular dimensions (both end-systolic and end-diastolic) and left ventricular posterior wall thickness was greater in the diabetic group ($p < 0.01$). Left ventricular mass was increased by $\sim 20\%$ in the patient group (223.4 ± 54.44 vs

187±29.84, $p<0.01$). In regard to the pattern of left ventricular diastolic filling, diabetic patients showed a higher atrial peak filling velocity ($p<0.01$) and, consequently, a reduced E/A ratio ($p<0.01$). The diabetic patients also showed prolonged isovolumic relaxation and deceleration times ($p<0.01$).

In a study done by Senthil N et al LVDD was found in 30 (30%) patients.¹⁶ All patients had impaired relaxation by ECHO. None of the patients had pseudonormal pattern or restrictive pattern. Senthil N et al observed Echocardiography parameters of normal subjects as follows: IVRT (ms) 106±17, E wave (cm/s) 69±11, A wave (cm/s) 52±9, E/A 1.34±0.17, DT (ms) 189±42, A wave duration (ms) 129±16 and Impaired relaxation subjects found Number of IVRT (ms) 109±11, E wave (cm/s) 56±10, A wave (cm/s) 71±3, E/A 0.79±0.07, DT (ms) 224±51, A wave duration (ms) 128±25 respectively.¹⁶

Sharavanan TKV et al observed that echocardiography is of immense help to diagnose diastolic dysfunction in diabetic subjects who are normotensive and with no known cardiac disease.¹³ Schiller NB et al observed clinical use of 2D echo in detecting the cardiac derangements in type 2 diabetes mellitus has been justified.²³ Cosson S et al and Zarich SW et al suggested left ventricular diastolic dysfunction represents the earliest first stage indicator of diabetic cardiomyopathy and thus evaluation of cardiac status is mandatory in all diabetic patients.^{24,25}

CONCLUSION

Diabetes has been established as one of the major etiological factor in the development of cardiomyopathy and consequently heart failure. The results from this study reinforce the vital role of echocardiogram to evaluate the diastolic functional parameters. Early diagnosis and therapeutic interventions in diabetes mellitus before the deleterious cardiac sequelae become established, modulate the cardiac metabolism and prevent congestive cardiac failure.

Diastolic dysfunction in patients with diabetes is present in 30% of patients even when diabetes is present at a younger age, and is of a shorter duration. This dysfunction is suggestive of pre-clinical diabetic cardiomyopathy. E/A, DT and peak A velocity are sensitive indices of diastolic LV dysfunction. It is suggested that all patients of diabetes should be routinely and repeatedly subjected to 2-D color Doppler echocardiographic assessment of cardiac functions in the long-term management of this metabolic disease.

This has important therapeutic implications and helps physicians planning early intervention strategies. Thus, diastolic dysfunction can be used as an early indicator, as it is a precursor to increased LV hypertrophy and clinical.

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