



LV Diastolic Dysfunction: An Earliest Marker of Diabetic Cardiomyopathy

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Abstract

Introduction: Diabetes mellitus (DM) has emerged as a modern epidemic and is at raising trend globally and will continue to be in future. Cardiovascular complications are major cause of death in patients with type II DM. Prior to the development of symptomatic diabetic cardiomyopathy, subclinical left ventricular diastolic dysfunction appears which can be detected by 2d-Echo, thus aiding clinician for taking early intervention .

Objective: To study the diastolic function of heart in normotensive asymptomatic Type 2 diabetes mellitus (T2DM) patients and its correlation with duration of diabetes ,age and glycosylated haemoglobin (HbA1c).

Material and Method: Prospective observational study was undertaken in Rohilkhand Medical College and Hospital, Bareilly including 50 normotensive diabetic patients admitted in the medical wards from 1st Jan 2018 to 31st Dec 2018. Detailed clinical examination was done; routine investigations including HbA1c, Blood sugar (fasting and post prandial) and 2D-ECHO were done. Data was collected, computed and analyzed statistically.

Results: Left ventricular diastolic dysfunction was present in 27 cases i.e 54%. Diastolic dysfunction was significantly associated with uncontrolled diabetes as assessed by HbA1c levels. Mean duration of diabetes was 8.07±7.77 years. In our study most of the subjects were having diabetes for 6-10 years and were between 56.38±12.2 years of age group. The mean E/A ratio was 0.73±0.13 among the patient who had diastolic dysfunction (E/A <1 considered as diastolic dysfunction) and 1.36±0.20 without diastolic dysfunction statistically it was significant.

Conclusion: This study concludes that myocardial damage in patients with diabetes affects diastolic function before systolic function. E/A ratio is significantly altered in diabetic patients with diastolic dysfunction. Duration of disease, glycemic levels and the type of treatments significantly alter the diastolic function in diabetic patients. 2-D ECHO is a simple non invasive and reproducible valuable tool in diagnosing diastolic dysfunction which helps in early detection of myocardial injury before actual clinical manifestation appears indicating early intervention/treatment and can retard the progression of further myocardial injury.

Introduction

Globally approximately 194 million adult cases of type 2 diabetes are prevalent and the expected number may increase to 333 million by 2025. In India, there are approximately 33 million diabetics and the number expected to reach 79.4 million in 2030.^[1] Asian Indians have a greater degree of insulin resistance compared to Caucasians which might be an important factor contributing to increased prevalence of type 2 diabetes.^[2-4] Asian Indians have higher insulin levels to a glucose load than Europeans was demonstrated by Mohan and team.^[4]

In the absence of coronary artery disease, hypertension or any known structural heart disease diabetic subject have been reported to develop congestive heart failure and other cardiac dysfunction.^[5] “Diabetic Cardiomyopathy” is the term which has been introduced for this condition. In 1974, Framingham study showed that heart failure was more common in diabetics due to diabetic cardiomyopathy.^[5] Various proposed mechanisms for diabetic cardiomyopathy are:

- Small and microvascular disease
- Autonomic dysfunction
- Metabolic derangements
- Glycosylation of myocardial proteins
- Interstitial fibrosis and the development of fibrosis possibly caused by the accumulation of a periodic acid-schiff-positive glycoprotein

All these leading to myocardial hypertrophy and diastolic dysfunction.^[7-10]

First stage of diabetic cardio-myopathy is left ventricular diastolic dysfunction followed by systolic dysfunction, hence early examination of ventricular function in every diabetic patient is important.^[11,12] This diastolic dysfunction can be very easily and early detected by echocardiography.

Thus, we took this study at RMCH Bareilly to detect left ventricular diastolic dysfunction in asymptomatic type 2 diabetes individuals and to use Echo-cardiographic assessment as an early detector of left diastolic dysfunction.

Material and Method

In this cross-sectional observational study 50 patients who visited to ROHILKHAND MEDICAL COLLEGE AND HOSPITAL between 1st Jan 2018 to 31st Dec 2018 were included.

Inclusion Criteria

All Type 2 diabetic patients

- Without any clinical symptoms of cardiovascular involvement
- Blood pressure <130/80mmHg
- Normal ECG were included in the study.

Exclusion Criteria

All Type 2 diabetes patients with other cardiac diseases like

- Valvular heart disease
- Ischemic and hypertensive heart disease
- Congestive heart failure
- Cardiomyopathy

The age and sex distribution of cases in given in following (Table 1). Out of 50 cases 20 were female and 30 were male.

Table 1: Age and sex wise distribution of cases (Nos= 50)

Age in years	Females	Males	Total
20-29	0	0	0
30-39	1	5	6
40-49	5	6	11
50-59	8	11	19
60-69	4	6	10
>70	2	2	4
Total	20	30	50

Detailed history and clinical examination was performed and laboratory investigations were done after explaining the nature of study and informed written consent taken from the cases. 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 (E/A ratio; left atrial size was assessed)

E/A <1 and increase in LA size were considered as the evidence of left ventricular diastolic dysfunction. Statistical analysis was done by estimating the prevalence rate of diastolic dysfunction and co-relating with the demographic variables like age and sex and its application to clinical practice. All data were analysed by using Statistical package for social sciences (SPSS) version 20 for windows .Chi-square and Fisher exact test was used to find the significance of proportion of diastolic dysfunction in the diabetic patients.

Result

50 cases were reported between 1st June to 31st May 2018 were reported. There was a linear increase in the prevalence of diastolic dysfunction with duration of diabetes. (Table 2).

Table 2 Duration of diabetes and its correlation with diastolic dysfunction

Duration in years	No. of cases	Dysfunction	
		Present	Absent
0-5	20	9	11
6-10	18	12	6
11-15	10	9	1
>15	2	2	0
Total	50	32	18(P=0.0337)

Prevalence of diastolic dysfunction increased gradually with the rise in HbA1c levels and it was statistically significant as shown in (Table 3).

Table 3 Correlation of diastolic dysfunction with HBA1C level

HBA1C level	6.4-7%	7.1-8%	8.1-10%	>10%
Diastolic dysfunction				
Present	3	6	16	6
Absent	12	3	3	1
No. of cases	15	9	19	7(P<0.001)

The patients in whom E/A ratio < 1 were considered to have diastolic dysfunction. The mean E/A ratio was 0.73±0.13 among the patient who had diastolic dysfunction and 1.36±0.20 without diastolic dysfunction statistically it was

significant.(Table 4) In this study left atrial size was compared in female and males which was significantly increased in both the sex who had diastolic dysfunction. HbA1c for patient with diastolic dysfunction was mean 8.89±1.56 (Table 4). And average age for patients with diastolic dysfunction was 56.38±12.2 with an average duration of 8.07±7.77years .(table 4)

Table 4 Comparison of study parameters among the prevalence of diastolic dysfunction

	Parameters	Present	Absent
1	Age(yrs)	56.38±12.2	47.2±10.1
2	Duration (yrs)	8.07±7.77	4.69±3.12
3	HBA1C	8.89±1.56	6.78±1.02
4	E(m/sec)	0.63±0.16	0.79±0.13
5	A(m/sec)	0.79±0.17	0.60±0.14
6	E/A	0.73±0.13	1.36±0.20

Discussion

Left ventricular diastolic dysfunction represents the first stage of diabetic cardio myopathy following systolic dysfunction ,thus it is the important for early examination of ventricular function in individuals with diabetes.^[11,12] Schannwell C M et al in 1999 was the first who found that diabetic patients with normal systolic ventricular function suffer a diastolic dysfunction which served as a early marker of a Diabetic cardiomyopathy.^[13] In 2001 Paul Poirier et al studied 40 diabetic patients without clinical evidence of cardiac disease by Doppler Echocardiography and concluded that diastolic function in diabetic patients were impaired even though found normal systolic function. Same findings were found in our study as above.

Several researchers have investigated, the role of elevated blood sugar in the causation of various cardiovascular diseases.^[14,15,16] These studies have shown that DM causes structural and functional abnormalities that are independent of the effect of atherosclerosis and these abnormalities contribute significantly to adverse cardiovascular events.^[23] Chronic hyperglycemia in DM expresses its toxicity by forming non-enzymatic glycation of tissue macromolecules, such as proteins, lipids,

and deoxyribonucleic acid (DNA) to form irreversibly bound advanced glycated end products.^[17] Such products have been found to accumulate in tissues such as the heart.^[18] This change in cardiac structure has been postulated to be due to deposition of glycoprotein and presence of microangiopathy.^[23,19] In diabetic heart, there is an increase in apoptosis leading to increased collagen deposition in a diffuse manner as a result of replacement fibrosis and connective tissue proliferation. Ultimately there is decreased ventricular compliance.^[20] Left ventricular diastolic dysfunction has been proposed to be the first stage of the putative “diabetic cardiomyopathy”.^[21] A reduced E/A ratio has been shown to be independently associated with increased all-cause mortality as well as cardiovascular mortality.^[22] These structural abnormalities may lead to increased wall stress, increased oxygen demand, ischemia, and the development of left ventricular diastolic dysfunction.^[23]

Left ventricular diastolic dysfunction was present in 27 cases i.e 54% which was almost comparable with other studies. (Table 5).

Table 5 Comparison of diastolic dysfunction with other studies

Studies	Percentage
Eichelberger et al	62
Poirier et al	60
Kurshid et al	60
TK Mishra, PK Path	60
Present study	54

Mean duration of diabetes was 8.07 ± 7.77 years. In our study most of the subjects were having diabetes of for 6-10 years and were between 56.38 ± 12.2 years of age group. This was because, as the duration of diabetes increased, other associated co-morbid diseases like Hypertension, IHD, were also present which were excluded in our study, so the patients with duration of diabetes more than 15 years and above age of 70 years were less. The mean E/A ratio was 0.73 ± 0.13 among the patient who had diastolic dysfunction (E/A <1 considered as diastolic dysfunction) and 1.36 ± 0.20 without diastolic dysfunction

statistically it was significant.(table 4) In this study, left atrial size which was significantly increased in cases who had diastolic dysfunction.

Conclusion

This study concludes that Myocardial damage in patients with diabetes affects diastolic function before systolic function. E/A ratio and Left atrial size are significantly altered in diabetic patients with diastolic dysfunction. Duration of diabetes, glycemic levels and the type of treatments significantly alter the diastolic dysfunction in diabetic patients. 2-D Echocardiography is a simple non invasive and reproducible valuable tool in diagnosing diastolic dysfunction which helps in early detection of myocardial injury before actual clinical manifestation appears indicating early intervention /treatment and can retard the progression of further myocardial injury.

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