Diastolic Dysfunction In Asymptomatic Type 2 Diabetes Mellitus Evaluated By Echocardiography

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Abstract: Introduction: As per the latest edition of International Diabetes Federation (IDF) Diabetes Atlas, diabetes mellitus now affects almost 371 million people worldwide, and majorities (90%-95%) have type 2 DM, which is measured metabolic cum vascular disease. There is marked increase in incidence of congestive heart failure, coronary artery disease in diabetic patients. Despite similar left ventricular systolic dysfunction, patients with diabetes have more pronounced heart failure symptoms and adverse prognosis compared with non-diabetic; one putative explanation for these discrepancies is LVDD in DM. The diastolic abnormalities are present in diabetic patients without overt diabetic complications of cardiovascular system, reinforcing the importance of early examination of ventricular function. Methods: This was a simple randomized study, conducted from August 2012 to October 2014. 50 patients with type 2 DM who had no symptoms of cardiovascular disease with normal BP and normal ECG were enrolled. Informed consent was obtained from the patients and they underwent a thorough physical examination, supported by laboratory investigations. A Doppler 2D echo was done in each patient and a calculation of LV ejection fraction, LA dimension; E velocity, A velocity and E/A ratio, IVRT and DT of E were done. Results: Our study consisted of 50 patients with type 2 DM, 27(54%) were males and 23 (46%) females. Majority of patients were in the age group of 50–70 years. Diastolic dysfunction was present in 26 (52%) patients out of whom 16 were males and 12 females. There was a linear increase in prevalence of diastolic dysfunction with increasing age, increased duration of diabetes mellitus and increasing HbA1c levels. Moreover statistically significant are Ejection Fraction, E/A Ratio, IVRT (msec), DT of E such as echocardiographic measurement with different studies. Conclusion: LV diastolic dysfunction is an early manifestation of diabetic cardiomyopathy. Its prevalence correlates with duration of diabetes, HbA1c values. LVDD contributes significantly to morbidity of CHF in diabetic patients. LVDD may be the 1st stage of Diabetic cardiomyopathy and should be screened for LVDD.[Satyam P NJIRM 2017; 8(6):66-70]

Key Words: Type 2 diabetes mellitus, LV diastolic dysfunction, Echocardiography.

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Introduction: A chronic illness such as Diabetes mellitus requires continuing medical care and ongoing patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications. Diabetes care is complex and requires multifactorial risk reduction strategies beyond glycemic control. Its incidence is increasing rapidly, and by 2030, this number is estimated to almost double in both developed and developing countries.[1,2]

India is diabetic capital of the world, according to the International Diabetes Foundation. The disease affects more than 50 million Indians - 7.1% of the nation's adults - and kills about 1 million Indians a year. The average age on onset is 42.5 years.[3]

Diabetes and Heart: The existence of a diabetic cardiomyopathy was first proposed by Rubler et al[4]in 1972 on the basis of postmortem findings. In 1974, in the Framingham study it was found that the heart failure was more common due to diabetic cardiomyopathy which involved 5209 patients followed up for 18 years and demonstrated that patients with diabetes had a greater probability of developing clinical heart failure. The study also exposed increase in congestive heart failure, coronary artery disease and myocardial infarction in diabetic patients.[4]

Patients with signs and symptoms of heart failure with preserved left ventricular systolic function i.e., ejection fraction of 60 % are said to have diastolic heart failure (DHF). One of the major risk factor such as Diabetes Mellitus is responsible for DHF. The mortality rate among the patients with diastolic heart failure is lower in ranges (5-8%) compare to (10-15%) systolic heart failure patients. According to Framingham heart study, the data suggests that hyperglycemia as such is an independent risk factor.[4, 5] The leading cause of LV systolic dysfunction and congestive heart failure in developed countries is coronary heart disease (CHD), with a prevalence of 66% in the recent multicenter heart failure trials.

Thus, ischemic heart disease often contributes to the appearance of heart failure, and the development of heart failure in many cases may be a reflection of progression of CHD. This indicates that the prevention and treatment of heart failure in many patients should include use of established primary and secondary prevention guidelines, including control of blood pressure, use of statins and aspirin, smoking cessation, and implementation of ACEI therapy in persons with diabetes and cardiovascular riskfactors.[6]

Although similar LV systolic dysfunction, patients with diabetes have more distinct heart failure symptoms, use more diuretics, and have an contrary prognosis compared with those without diabetes; one putative explanation for these discrepancies is diastolic dysfunction of the left ventricle in diabetes mellitus.[7] It also represent the first stage of diabetic cardiomyopathy earlier changes in systolic function, supporting the importance of early examination of ventricular function in individuals with diabetes.[8, 9] The diastolic abnormalities are present in diabetic patients without evident diabetic complications of cardiovascular system,[10] it is the earliest and specific functional abnormality in diabetic cardiomyopathy and can affect patients who are free of macrovascular complications, even newly diagnosed diabetes mellitus patients and less than 1 year duration.[11]

Diastole includes the time period during which the myocardium loses its ability to generate force and shorten and returns to an unstressed length and force.[12]By delay of diastolic dysfunction arises when these processes are lengthy, slowed, or incomplete. Moreover, if diastolic function is truly normal, it must remain normal both at rest and during the stress of a variable blood pressure, heart rate, stroke volume and end-diastolic volume.

Diastolic dysfunction denotes to a condition in which abnormalities in mechanical function during diastole. It may be sectioned into a decrease in passive myocardial diastolic compliance, and impairment in active LV relaxation. It may also occur in the presence or absence of a clinical syndrome of heart failure and with normal or abnormal systolic function. Therefore, whereas diastolic dysfunction defines as abnormal mechanical property, diastolic heart failure describes a clinical syndrome[8]

Methods: This was a simple randomized study conducted at Smtshardaben general hospital and vadilal sarabhai hospital, Ahmedabad, over a period of two years between August 2012 to October 2014.

Inclusion criteria: The study included a total of 50 cases type 2 diabetes mellitus, which clinically had no symptoms of cardiovascular disease and normal blood pressure of < 130/80 mmHg, with normal ECG.

Exclusion criteria: All patients with type 2 diabetes mellitus with overt cardiac diseases like Ischemic and hypertensive heart disease congestive heart failure, valvular heart disease, and cardiomyopathy were excluded from the study.

Informed consent was obtained from the subjects. Patients underwent thorough clinical examination supported by relevant investigations. The patients underwent the investigations like ECG, FBS, PPBS, Urea, creatinine, Glycosylated haemoglobin (HbA1c), Urine albumin, Fasting Lipid profile, Fundus examination, Echocardiography. Doppler Echo was done in each patient and 3-4 cardiac cycles were analysed to get best phase for better outcome of results. Ejection fraction was calculated in all patients. In Doppler study, values like E-peak velocity of early mitral flow, A- peak velocity of late mitral flow, E/A ratio, IVRT time, DT of E time are evaluated. Reduction in E velocity increase over A velocity with E/A ratio of <1 and increase in left atrial (LA) size were considered as the evidence of left ventricular diastolic dysfunction (DD).

Statistical analysis was done by estimating the prevalence rate of diastolic dysfunction and co-relating with the glycemic control.

Results: Our study consisted of 50 patients with type 2 DM, among whom 27 (54%) were males and 23 (46%) females. Diastolic dysfunction was present in 26 (52%) of the cases among them, 16 (32%) were males, 10 (20%) were females. Though statistically not significant, diastolic dysfunction was more prevalent in females.(Figure-1)

Out of 26(52%) patients, maximum prevalence of diastolic dysfunction was found in 50-59 years age group (n=16,61.5%), (Figure-2). prevalence of diastolic dysfunction increases with longer duration of diabetes. (Table-1).

Table 1: Prevalence of Diastolic Dysfunction Increases With Longer Duration of Diabetes

Duration in year	No of Patient	Diastolic dysfunction
0-5	16 (32%)	2 (7.7%)
6-10	30 (60%)	21 (80.7%)
≥ 10	4 (08%)	3 (11.5%)
Total	50 (100%)	26 (100%)

Out of 14 patients having retinopathy, 8 patients (30.7%) had LVDD.(Table 2)

Table 2: Correlation Between Diabetic Retinopathy And Diastolic Dysfunction Change%

Retinopathy	No of Patients	LVDD	P value
Yes	14 (28%)	8 (30.7%)	0.8008
No	36 (72%)	18 (69.3%)	0.8008
Total	50 (100%)	26 (100%)	

LVDD: Left ventricular Diastolic Dysfunction

Biochemical tests such as Fasting Blood Sugar (142 ± 9.94 mg/dl), PPBS (226 ± 18.61 mg/dl), Blood Urea (31 ± 5.08 mg/dl), Serum Creatinine (0.88 ± 0.14 mg/dl), Total Cholesterol (192.30 ± 15.41 mg/dl), Triglycerides (122.04 ± 15.79 mg/dl), HDL (38.98 ± 3.20 mg/dl).

Out of 26 patients having Diastolic dysfunction, 6 (23.1%) had HbA1c 5.7 – 6.4 and 20 (76.9%) had HbA1c >6.5 (Table-3), suggesting that Prevalence of diastolic dysfunction is increased gradually with the rise in HbA1c levels, indicating association between uncontrolled DM and LVDD.

Table 3: Correlation between HbA1C level and Diastolic Dysfunction

HbA1C level	Total	Diastolic Dysfunction		P value
		Present	Absent	
<5.6	2	0	2	0.149
5.7 – 6.4	14	6	8	0.545
> 6.5	34	20	14	0.537
Total	50	26	24	

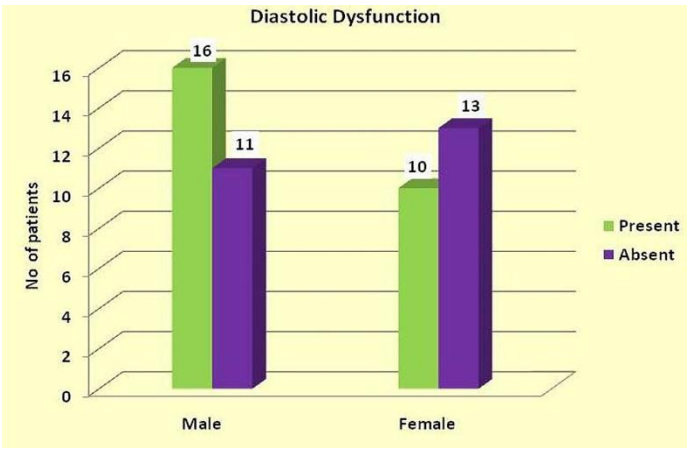
HbA1C: Glycated Haemoglobin

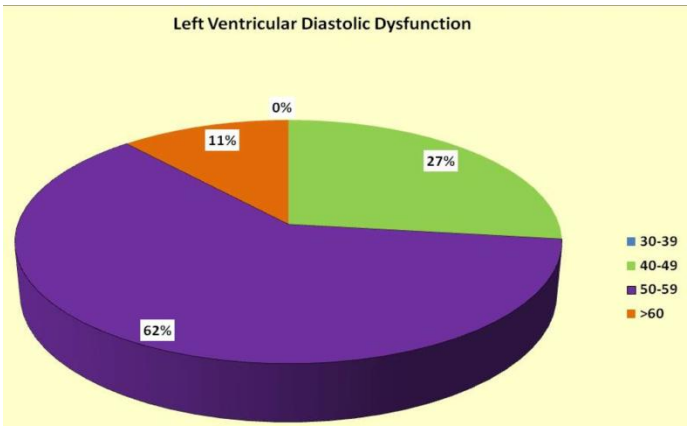
LVDD present in 46.15% patients receiving OHA, 50 % Patients receiving Insulin and 75% patients receiving both OHA and insulin. Suggest in higher incidence of LVDD in patients on both OHA and insulin. Prolongation of DT of E more than 200 msec is a significant indicator of early LV diastolic dysfunction. In the present study, DT of E was > 200 msec in 23 (46%) patients. All these patients had E/A < 1 and IVRT > 100 msec suggestive of early diastolic dysfunction. 25 patients (50%) had DT of E between 150 msec to 200 msec. (Table- 4)

Table 4: Echocardiographic Measurement

Echocardiographic Measurement	Mean in present study	Abdul Khaliq et al[24]	John Boyer et al [25]	P value
Systolic Parameters				
Ejection Fraction	63.12 ± 6.19	58 ± 11	64 ± 7	0.009
Fractional Shortening	35.42 ± 5.03	32.7 ± 5.32	29.06 ± 5.03	0.089
Diastolic Parameters				
Mitral E	67.32 ± 6.22	55 ± 10.6	79 ± 10.07	0.008
Mitral A	70.72 ± 7.42	59 ± 9.5	62 ± 10.2	0.048
E/A Ratio	0.95 ± 0.10	0.9 ± 0.2	0.95 ± 0.29	0.4485
IVRT (msec)	87.94 ± 20.36	109 ± 11	79 ± 14	<0.0001
DT of E	180.68 ± 34.64	208 ± 44	173 ± 34	<0.0001

E: Peak Velocity Flow In Early Diastole; A: Atrial Contraction; IVRT: Isovolumic Relaxation Time; DT: Deceleration Time





Discussion: Several studies have exposed that impairment of the LV diastolic function may be

spotted in patients with diabetes. Diastolic LV abnormalities have been originally revealed by cardiac catheterization. Regan et al[13] demonstrated in normotensive, diabetic patients without coronary artery disease and without clinical evidence of heart failure, increased left-ventricular end-diastolic pressure, a decreased left-ventricular end-diastolic volume with a normal ejection fraction. Paul Poirier et al[14] in 2001 assessed 40 diabetic patients without clinical indication of cardiac disease by Doppler Echocardiography and came to conclusion that diastolic function in diabetic patients was reduced even in patients with normal systolic function.

Numerous studies in humans have discovered the association of diabetes with histopathological abnormalities of myocardium. Alterations in intramyocardial coronary arteries, similar to those seen in other organs of diabetic patients have been described. Endothelial proliferation and subendothelial hyaline thickening with PAS-positive material in the vessel wall have been described in some but not all patients with or without overt congestive heart failure Capillary basement membrane thickening and capillary microaneurysms have also been observed in hearts of diabetics.[15-17]Zoneraich et al[18] who conducted their study in young normotensive type 1 diabetics, found small vessel disease in 72% of diabetic patients, while it was present in only 12% of non-diabetic subjects.

Interstitial accumulations of advanced-glycated end products (AGEs), which include collagen, elastin and other connective tissue proteins, as well as fibrosis in the myocardium, have been reported in biopsy or post-mortem studies of human diabetic hearts.[13,19] The mechanism of collagen accumulation in the diabetic myocardium seems to be due to impaired degradation rather than enhanced synthesis.[20] The interstitial abnormalities could explain an increase in end-diastolic stiffness as well as LV mass and contribute to the diastolic dysfunction.[13] In the less advanced forms of tissue abnormality, the interstitial changes seem to predominate for some time and are associated with preserved cell morphology that is consistent with normal systolic function. As a potential diagnostic tool, it has been suggested that collagen accumulation in the extracellular matrix of the heart is responsible for abnormal acoustic properties of the myocardium in diabetic patients.

In our study most of the patients are with duration of diabetes less than 10 years.As the duration of diabetes increased, other associated co-morbid diseases like hypertension, IHD, would also appear and hence could not be included in our study. So the patients with duration of diabetes more than 15 years and above age of 70 years were less. When the treatment profile was evaluated most of the patients were on OHA / OHA with insulin, most of the subjects had poor glycemic control.Reasons are multifactorial Viz., poor compliance of the patient with reference to treatment, lifestyle modifications, inadequate doses, poor regular checkup.

Left ventricular diastolic dysfunction (LVDD) was found in 26(52%) of our patients. This prevalence of diastolic dysfunction was almost comparable with other studies such as Paul Poirier et al[14] has 60%,Abdul Khaliq et al[24] has 48% and John Boyer et al[25] has 56%.Gender wise comparison of LVDD showed 54% male subjects had diastolic dysfunction compared to 46% of females. This could be due to hormonal changes.Results are comparable to other studies[24,25] The prevalence of diastolic dysfunction increased with duration of diabetes. The previous studies also confirmed the above findings[14,24,25].

Patients with retinopathy, HbA1c level have high prevalence of diastolic dysfunction. Moreover statistically significant are Ejection Fraction, E/A Ratio, IVRT (msec), DT of E such as echocardiographic measurement with different studies.[21-25]

Conclusion: The prevalence of left ventricular diastolic dysfunction in asymptomatic, normotensive patients with type 2 DM without significant coronary artery disease is much higher than previously suspected as evidenced by the results of this study and also of similar other studies. Significant differences in the parameters of left ventricular diastolic dysfunction were found. These results contribute to better understanding of pathological process resulting in cardiac failure in diabetic patients and support the optimum therapeutic strategies. Left ventricular dysfunction may be the 1st stage of Diabetic cardiomyopathy and should be screened for left ventricular diastolic dysfunction.

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