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ECHOCARDIOGRAPHIC STUDY OF DIASTOLIC DYSFUNCTION IN NORMOTENSIVE ASYMPTOMATIC TYPE 2 DIABETIC PATIENTS

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Abstract

Background: Diastolic dysfunction is an important risk factor for development of heart failure and morbidity in diabetic patients. Early recognition and treatment can prevent its progress to heart failure. The aim of the study was to asses incidence of diastolic dysfunction in normotensive asymptomatic type 2 diabetic patients with the help of echocardiography and compare the results with those in healthy subjects. **Material and Methods:** Present study was prospective, observational case-control study, conducted in 18 to 65 years aged, type 2 diabetic patients, irrespective of duration of diabetes, may or may not be on antidiabetic treatment without cardiac symptoms or history of hypertension, were included as cases in the study Age and sex matched healthy subjects, willing to participate in study, were included as controls. **Results:** Prevalence of diastolic dysfunction in type 2 diabetic subjects was significantly higher compared to the control type group ($p<0.001$; odds ratio-5.35 and 95% confidence interval 2.14-12.46). Diastolic dysfunction was found to be significantly higher in those subjects with duration of diabetes >5 years ($p=0.001$). The mean BSL values were found to be significantly higher in cases ($p=0.0001$). DT values were significantly higher in cases as compared to controls ($p=0.0034$). E/A ratio in study group as compared to control group, was not statistically not significant ($p=0.06$). The mean DT in case group was significantly higher in study group as compared to control group ($p=0.003$). Diastolic dysfunction was seen significantly more in cases as compared to in controls. BMI and E/A were found to be significantly and positively correlated ($r=0.2$). **Conclusion:** It can be concluded from the study that incidence of pre-clinical diastolic dysfunction was higher in diabetes with longer duration of diabetes (>5 years), independent of coronary artery disease and hypertension.

Keywords: Diastolic Dysfunction, Diabetes, Echocardiographic, Normotensive.

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Introduction

The incidence of type 2 DM is increasing in Indian subcontinent with increasing urbanization and changes in lifestyle (lack of exercise, smoking, less fiber diet and increased stress).[1] The type 2 diabetic patients are at increased risk of developing cardiovascular diseases such as atherosclerosis, its complications and heart failure.[2] The Framingham Heart Study showed that the prevalence of HF was twice as high in diabetic men and five times as high in diabetic women aged between 45-74 years when compared to age matched controls; even after controlling other risk factors.[3] The type 2 diabetics are particularly susceptible to develop diastolic dysfunction owing to hyperglycemia associated ultrastructural and metabolic abnormalities in the myocardium that impair myocardial relaxation. Such diastolic filling abnormalities can be seen early in the course of diabetes even before onset of hypertension, renal disease and vasculopathy.[2] Diastolic dysfunction is an important risk factor for development of heart failure and morbidity in diabetic patients.[4,5] Early recognition and treatment can prevent its progress to heart failure. The aim of the study was to asses incidence of diastolic dysfunction in normotensive asymptomatic type 2 diabetic patients with the help of echocardiography and compare the results with those in healthy subjects.

Material and Methods

Present study was prospective, observational case-control study, conducted in department of general medicine, at Kamalnayan Bajaj Hospital Aurangabad., India. Study duration was of 1 year. Study was approved by institutional ethical committee.

Inclusion criteria

- 18 to 65 years aged, type 2 diabetic patients, irrespective of duration of diabetes, may or may not be on antidiabetic treatment without cardiac symptoms or history of hypertension, willing to participate in study, were included as cases in the study.
- Age and sex matched healthy subjects, willing to participate in study, were included as controls.

Exclusion criteria

- Age <18 years and >65 years.
- Subjects with evidence of coronary artery disease (excluded by history of angina, chest pain, ECG changes)
- Subjects with evidence of valvular disease
- Hypertensive patients, subjects receiving antihypertensive agents, E/O left ventricular hypertrophy on echocardiography.
- Subjects with arrhythmia or pericardial disease
- Subjects with systolic dysfunction (LVEF≤40%)
- Subjects not willing to participate in study,

Total 50 normotensive asymptomatic diabetic subjects were included in study group and 50 healthy individuals in control group. Data was collected by interviewing subjects, anthropometric measurements, laboratory investigation results and echocardiographic measurements. Mitral valve inflow velocities and deceleration time were measured with pulsed wave doppler in apical 4 chamber view. Parameters were measured during normal respiration as well as during Valsalva maneuver to unmask pseudo-normalization. Mitral

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valve inflow velocities (E and A) and deceleration time DT were measured with pulsed wave Doppler in apical 4 chamber view. Measurements with Valsalva maneuver were used to identify pseudonormalisation. Diastolic dysfunction was diagnosed if E/A <1 or>2 and/or DT <160msec or >240 msec. Pseudonormalisation was said to be present if AE/A>0.5. Obtained data was qualitative (presence or absence of diastolic dysfunction) as well as quantitative (age, Body Mass Index, duration of DM, E/A and Deceleration Time, DT). Qualitative data was analyzed using chi square test and Fischer's exact test and quantitative data was analyzed using unpaired test. Significance of association between two variables was assessed using correlation coefficient. GraphPad PRISM software was used for various statistical calculations.

Results

In the present study, 50 normotensive asymptomatic diabetic subjects and 50 healthy subjects were assessed. Out of 50 subjects in study group, 30(60%) had diastolic dysfunction. Impaired relaxation (Grade 1 diastolic dysfunction) was the prominent pattern of diastolic function seen in 26 subjects and pseudonormalisation was seen in 4 subjects. Amongst 50 subjects in control group, 11(22%) had diastolic dysfunction and all of them had impaired relaxation. It was found that Incidence of diastolic dysfunction was significantly higher in diabetics as compared to healthy controls ($p<0.001$). Prevalence of diastolic dysfunction in type 2 diabetic subjects was significantly higher compared to the control type group ($p<0.001$; odds ratio-5.35 and 95% confidence interval 2.14-12.46).

Table 1: Echocardiographic assessment of Diastolic Function

	Diastolic Dysfunction	**Normal Diastolic Function**	**Total**	**P value**
Echocardiographic assessment				<0.001
Study group	30	20	50	
Control group	11	39	50	

It was observed that out of 16 subjects with age ≥ 45 years 4 had diastolic dysfunction. This was found to be statistically not significant ($p=0.7$). These observations suggest that in 15 patients from study group with age ≥ 45 years and DM, diastolic dysfunction was possibly a result of DM & not of increased age. Similarly there was no significant difference in incidence of diastolic dysfunction with increase in age >45 years ($p=0.7$).

Table 2: Age wise diastolic function pattern in study

	Diastolic Dysfunction	**Normal Diastolic Function**	**Total**	**P value**
Study group				0.7
≥ 45	15	11	26	
< 45	15	9	24	
Control group				
≥ 45	4	12	16	
< 45	7	27	34	

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It was also observed that in the study group, among 30 subjects with diastolic dysfunction, 20 were with BMI ≥ 25 and 10 were with BMI < 25. In control group, it was observed that out of 22 subjects with BMI ≥ 25, 4 had diastolic dysfunction. This was not statistically significant (p=0.7). Above results suggests that in 20 patients with DM and BMI ≥ 25; who had diastolic dysfunction, occurrence of diastolic dysfunction was possibly a result of diabetes and not of increased BMI. In present study, there was no significant difference in incidence of diastolic dysfunction amongst obese and non-obese subjects (p=0.7).

Table 3: Diastolic function pattern in BMI classified groups in study group

	Diastolic Dysfunction	**Normal Diastolic Function**	**Total**	**P value**
Study group				0.7
BMI ≥ 25	20	9	29	
BMI < 25	10	11	21	
Control group				
BMI ≥ 25	4	18	22	
BMI < 25	7	21	28	

In study group, out of 32 subjects with duration of diabetes >5years, 25(78%) had diastolic dysfunction; 21(65%) with grade 1 diastolic dysfunction and 4(12.5%) with grade 2 diastolic dysfunction. Amongst 18 subjects with duration of diabetes <5 years; 5(27.77%) had grade 1 diastolic dysfunction. Diastolic dysfunction was found to be significantly higher in those subjects with duration of diabetes >5 years (p=0.001).

Table 4: Diastolic function pattern according to duration of diabetes:

Duration of diabetes (years)	**Diastolic Dysfunction**	**Normal Diastolic Function**	**Total**	**P value**
<5 years	25	7	32	0.001
>5 years	5	11	18	

Out of 50 subjects with type 2 DM, 28(56%) were male and 22 (44%) were female. Out of 30 subjects with diastolic dysfunction there were 17 males and 13 female. Total 32(64%) male and 18(36%) female were control healthy subjects.

The mean BSL values were found to be significantly higher in cases (p=0.0001). DT values were significantly higher in cases as compared to controls (p=0.0034). E/A ratio in study group as compared to control group, was not statistically not significant (p=0.06). The mean DT in case group was significantly higher in study group as compared to control group (p=0.003).

Diastolic dysfunction was seen significantly more in cases as compared to in controls. BMI and E/A were found to be significantly and positively correlated (r=0.2).

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Table 5: Mean and Standard deviation of numerical parameters of study population

Variables	Case Population		Control Population		p-Value
	Male (n=28)	Female (n=22)	Male (n=32)	Female (n=18)	
Age (years)	46.57+7.04	45.90 ± 9.53	40 ± 6.73	44.38 ± 8.03	NS
BMI (kg/m)	26.16+3.81	24.94 ± 5.01	26.12 ± 3.38	23.49 ± 4.28	0.95
Blood sugar level(mg/dl)	131.60 ± 39.0	145.86 ± 38.78	87.21+7.78	86.83+8.73	0.0001
E/A ratio (PW)	1.17±0.24	1.19 0.31	1.23±0.19	1.05+0.18	0.06
EA	0.169±0.1	0.20±0.1	0.17 ±0.1	0.16 0.1	0.96
EF (%)	65.92+5.49	66.72+5.33	67.90+6.03	66.83+3.66	0.19
DT (ms)	247.85 41.9	224.95+49.34	207.68+57.41	228.11:49.88	0.003
Diastolic dysfunction	17(60.71%)	13(59.09%)	6(18.75%)	5(27.77%)	<0.001

Discussion

Diastolic dysfunction is characterized by prolonged relaxation and increased filling pressure that lead to reduction in contraction velocity and reduction in cardiac output.[6] Decreased ventricular function in turn stimulate rennin angiotensin and sympathetic nervous system which further cause myocardial damage and if untreated results in myocardial remodeling. Arrhythmias, pump failure and death.[7,8] Thus, diastolic dysfunction should be recognized early and treated promptly to prevent associated morbidity and mortality. Heart failure (HF) is a complex syndrome in which both systolic and diastolic functional abnormalities can be identified. Primary abnormality in systolic dysfunction is reduction in contractile reserve with poor pumping function of the left ventricle whereas diastolic dysfunction is associated with impaired relaxation and inability of the ventricle to accept an adequate amount of blood.[7,8]

Diastolic function is affected by age (common in after 65 years of age) and various disease states such as dyssynchrony, increased mechanical loading, coronary artery disease, pericardial constrain, abnormalities of cardiomyocyte (excessive or abnormal collagen deposition, abnormal calcium homeostasis, defects in cytoskeletal proteins).[9] Diabetic cardiomyopathy, hypertensive heart disease and ischemic heart disease are important causes of diastolic dysfunction.[10]

Patil etal,[11] in their study of 127 asymptomatic, normotensive type 2 DM subjects found that 54.33% of asymptomatic type 2 DM patients had diastolic dysfunction. Shrestha etal,[12] noted that the prevalence of diastolic dysfunction in this group was 71% and amongst them impaired relaxation was detected in 8% and pseudo normal pattern of left ventricular filling was noted in 11% Similarly, in present study diastolic dysfunction was seen in 60% of type 2 DM subjects. Among them, 86.6% had impaired relaxation and 13.33% subjects showed pseudo normal pattern of LV filling.

Paul etal,[13] noted that LV diastolic dysfunction was much more common than previous studies (60% in their study). It was observed that 8% subjects of study group had pseudonormalisation. The use of pulmonary venous recordings in addition to Valsalva

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maneuver in their study might be responsible for a greater number of subjects with pseudonormalisation (28%) as compared to 8% subjects in our study.

Poulsen etal. Found that diastolic dysfunction was present in 40% subjects. They also noted close association between moderate to severe diastolic dysfunction and normal myocardial perfusion on myocardial perfusion scintigraphy. Boyer etal,[15] stated that the prevalence of LV diastolic dysfunction in asymptomatic normotensive subjects with type 2 DM to be in their study it was 75%.

From etal,[16] in their study of 484 subjects found that increase in the passive transmitral LV inflow velocity to tissue Doppler imaging velocity of medial mitral annulus during passive filling (E/e) ratio in diabetic patients is associated with subsequent development of HF and increased mortality.

In present study, duration of diabetes after which diastolic dysfunction was observed in significant number of subjects. Patil etal,[11] established that there is direct correlation between duration of DM and diastolic dysfunction ($p<0.02$); and that significant diastolic dysfunction occurs >5 years after the onset of DM. They also established that there is direct correlation between diastolic dysfunction and age of the patient and with obesity indices. In comparison, our study simulated the above study regarding effect of duration of diabetes >5 years being significant ($p=0.001$).

Masugata etal.,[17] in their case control study of 77 normotensive subjects found that, the cardiac diastolic dysfunction LV systolic dysfunction in patients with well controlled type 2 DM is related neither to hypertension nor to LV hypertrophy, but rather to aging and duration of type 2 DM. They observed linear relationship duration of diabetes and diastolic dysfunction ($r=0.6$). Similar findings were noted in present study.

Van Heerebeek etal,[18] in their study stated that, the cardiomyocyte resting tension is more important when LVEF is normal. Excessive diastolic left ventricular stiffness is an important contributor to heart failure in patients with DM. Diabetes is presumed to increase the stiffness through myocardial deposition of collagen and advanced glycation end products. In present study 60% of subjects from case group had diastolic dysfunction with normal LVEF. Diastolic dysfunction is observed in a patient with diabetes, it is earlier if diabetes is present for more than 5 years. It is advisable to echocardiographically screen all patients with Diabetes Mellites for presence or absence of diastolic dysfunction, preferably at the time of diagnosis. Further research work is needed to establish association between diastolic function and glycemic control and between diastolic function and various treatment modalities (lifestyle modification v/s OHA v/s insulin therapy) in diabetic patients.

Conclusion

It can be concluded from the study that incidence of pre-clinical diastolic dysfunction was higher in diabetes. We also observed there was high prevalence of pre-clinical diastolic dysfunction with longer duration of diabetes (>5 years), independent of coronary artery disease and hypertension. The study observed that Valsalva maneuver can be used as an effective and easy bedside maneuver to differentiate normal from pseudo normal pattern of LV filling.

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