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Original research article

To study Left Ventricular Diastolic Dysfunction in Non hypertensive Asymptomatic Patient with Type 2 Diabetes Mellitus

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Abstract

Background: Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency in insulin secretion and/or insulin action. Diabetic subjects have been reported to develop congestive heart failure in the absence of coronary heart diseases, hypertension or any known structural heart disease.

Aims: (1) To study the echocardiographic findings in T2DM patients who are non-hypertensive; (2) To assess the diastolic functions and its association with various factors.

Methods: This was a cross sectional study conducted at Medicine OPD over the duration of one year. A total of 100 participants were enrolled. All cases of type 2 diabetes mellitus (DM) reporting at OPD of Medicine with blood pressure <130/80 were included in the study. Data was collected on a predesigned semi-structured questionnaire.

Results: 68% cases had diastolic dysfunction of which 54% cases had impaired relaxation 9% cases had pseudonormal and 5% cases restricted filling. 56% were males and 44% were females. Association of diastolic dysfunction with age, duration of diabetes, HbA1c levels, presence of retinopathy was found to be statistically significant ($p<0.05$). Out of echocardiographic observations, association with diastolic dysfunction was found to be significant ($p<0.05$) among E/A, IVRT m-s, Deceleration time and E/e'.

Conclusion: The incidence of left ventricular diastolic dysfunction is higher in type II diabetes mellitus patients who are free of clinically detectable heart disease.

Keywords: Diabetes mellitus, cross sectional study, predesigned semi-structured questionnaire, diastolic dysfunction.

Introduction

Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency in insulin secretion and/or insulin action. Various genetic and environmental factors influence the etiology and prognosis of diabetes. Diabetes mellitus was formerly considered a disease of affluent. It has now become apparent that increase in Diabetes mellitus is due to demographic changes, cultural transition and population ageing, urbanization, increased consumption of refined foods, westernization, sedentary habits and over nutrition.[1,2]

The World Health Organization estimates that India will have the largest number of diabetic subjects in the world by 2025 and one out of 5 diabetic subject in the world will be an Indian. India is going to be the "Diabetic capital of the world".[1,2] WHO has estimated that the number is likely to be 5.72 crore by 2025. The rapid increase in population, increased longevity and high ethnic susceptibility to diabetes, coupled with rapid urbanization and changes from traditional lifestyles will most likely trigger a Diabetes mellitus epidemic.[1,2]

Diabetes mellitus has become a leading cause of premature death, disability and high health care costs. It is a silent killer disease. Diabetic subjects have been reported to develop congestive heart failure in the absence of coronary heart diseases, hypertension or any known structural heart disease.[3]

The term 'diabetic cardiomyopathy' has been introduced for this condition. It has been suggested that microangiopathic lesions of the myocardium, altered composition and fibrosis of myocardial interstitium and accumulation of lipids in myocardial cells are involved in pathogenesis of diabetic cardiomyopathy.[4,5] Studies using Doppler echocardiography have confirmed the findings of abnormal diastolic function as an early indicator of cardiac involvement in asymptomatic patients with Type 1 or Type 2 diabetes mellitus.[6]
One reason for the poor prognosis in patients with both diabetes and ischemic heart disease seems to be an enhanced myocardial dysfunction leading to accelerated heart failure (diabetic cardiomyopathy). The diastolic dysfunction can be very easily and early detected by echocardiography by using variables (E/A, IVRT, DT, E/e') which are used for measuring diastolic functions of heart.

Improved glycemic control, better control of hypertension, and prevention of atherosclerosis with cholesterol-lowering therapy may prevent or mitigate diabetic cardiomyopathy. An early clinical trial suggested that sulfonylureas used for control of hyperglycemia are cardiotoxic and may exacerbate diabetic cardiomyopathy. This side effect, however, was not confirmed in a recent large clinical trial.[7] However, the existence of a primary myocardial disease, "diabetic cardiomyopathy", has been proposed as evidence has accumulated for the presence of myocardial dysfunction in diabetic patients in the absence of ischemic, valvular or hypertensive heart disease.[8]Thus, the research was conducted to study the echocardiographic findings in T2DM patients who are non-hypertensive; and to assess the diastolic functions and its association with various factors.

Material and Method:

The present study was conducted as an observational Cross sectional study on adult patients with type 2 diabetes mellitus (DM) reporting at Medicine OPD over the duration of one year. A total of 100 participants were enrolled in the study. Informed consent was obtained from all the study participants after explaining them nature and purpose of study. Participants were

enrolled on the basis of inclusion and exclusion criterias. Data was collected on a predesigned semi-structured questionnaire which included information on baseline characteristics of participants and a detailed clinical examination was conducted. Biochemical investigations and ECG was also done.

Inclusion criteria: All cases of type 2 DM diagnosed by WHO criteria; aged 25-60 years; Blood pressure <130/80 (at least 3 recordings with the highest recording taken into consideration). Exclusion criteria: Past history acute coronary syndrome; patients with Rheumatic heart disease; documented overt renal disease like CRF; diabetic patient more than 10 years duration; cardiac signs and symptoms, exertional dyspnoea, chest pain; and past history of hypertension

Statistical analysis: Data was compiled using MS Excel and analyzed. Categorical variables were expressed in frequency and percentages. Chi-Square test was used to test difference in proportions. P value <0.05 was considered to be statistically significant.

Results:

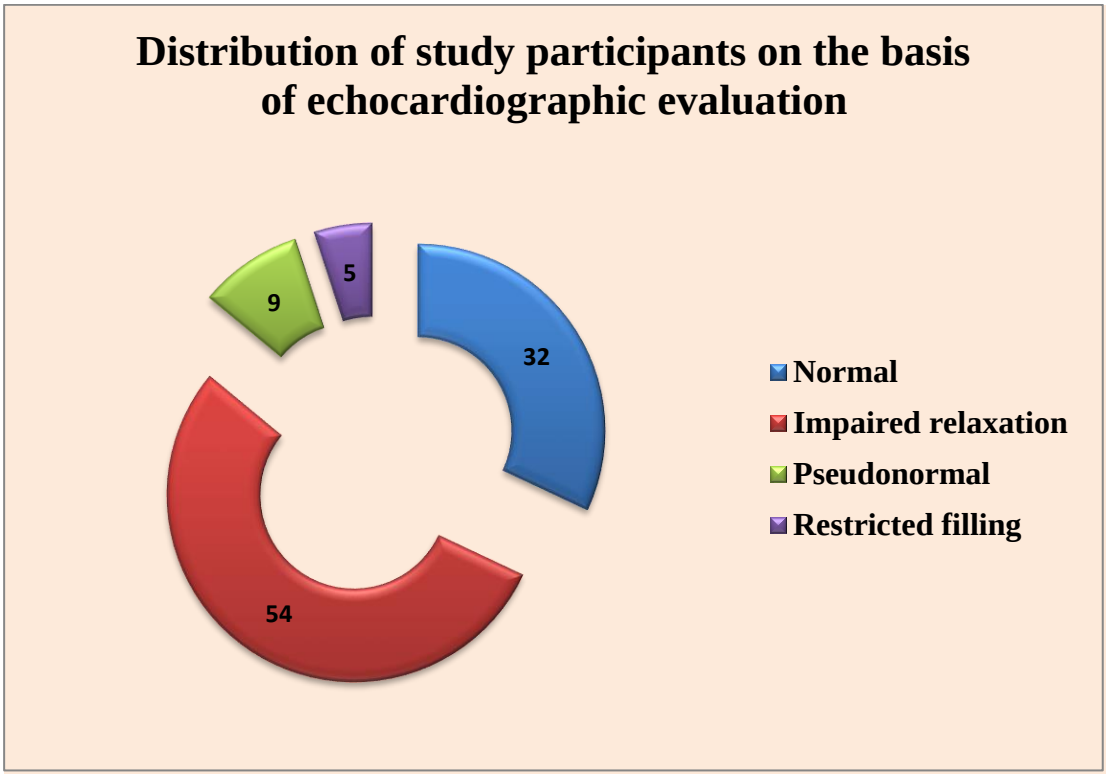

Figure 1: Distribution of study participants on the basis of echocardiographic evaluation

Table 1: Association of diastolic dysfunction with baseline characteristics of study participants

Variable	Category	No. of cases (%)	Diastolic dysfunction		Chi square, p value
			Present (%)	Absent (%)	
Sex	Male	56(56%)	37(66.1%)	19(33.9%)	0.218, 0.640
	Female	44(44%)	31(70.4%)	13(29.5%)	
Age (years)	25-39	22(22%)	10(45.4%)	12(55.54%)	12.18, 0.002
	40-49	32(32%)	19(59.3%)	13(40.6%)	
	50-60	46(46%)	39(84.7%)	7(15.2%)	
Cholesterol (mg/dl)	<200	81 (81%)	56(69.1%)	25(30.86%)	0.273, 0.872
	200-239	16 (16%)	10 (62.5%)	6(37.5%)	
	≥240	3 (3%)	2 (66.66%)	1 (33.33%)	
BMI (Kg/m^2)	19-24.9	50 (50%)	37(74%)	13(26%)	1.81.2, 0.404
	25-25.9	38(38%)	23(60.5%)	15(39.4%)	
	30-39.9	12(12%)	8(66.6%)	4(33.3%)	

Table 2: Association of diastolic dysfunction with clinical profile of study participants

Variable	Category	No. of cases (%)	Diastolic dysfunction		Chi square, p value
			Present (%)	Absent (%)	
Duration of diabetes	<2 years	36(36%)	18(50%)	18(50%)	12.005, 0.0024
	2-5 years	39(39%)	27(69.2%)	12(30.7%)	
	> 5 years	25(25%)	23(92%)	2(8%)	
HbA1c (in %)	<7.5	27(27%)	13(48.14%)	14(51.85%)	6.69, 0.009
	>7.5	73(73%)	55 (75.34%)	18 (24.65%)	
Nephropathy	Present	32 (32%)	22(68.75%)	10(31.25%)	0.012, 0.912
	Absent	68 (68%)	46 (67.64%)	22 (32.36%)	
Retinopathy	Present	29 (29%)	27(93.01%)	02(6.8%)	11.8, 0.0005
	Absent	71 (71%)	41 (57.77%)	30(42.2%)	

Table 3: Association of diastolic dysfunction with Echocardiographic observations of study participants

Variable	Category	No. of cases (%)	Diastolic dysfunction		Chi square, p value
			Present (%)	Absent (%)	
E/A	<1	54 (54%)	54(100%)	0(0%)	67.719, <0.001
	01-Feb	41 (41%)	9 (21.95%)	32(78.05%)	
	>2	5 (5%)	5 (100%)	0 (0%)	
IVRT m-s	<60	3 (3%)	3(100%)	0(0%)	27.552, 0.000001
	60-100	57 (57%)	27(47.36%)	30(52.63%)	
	>100	40 (40%)	38 (95%)	2(5%)	
Deceleration Time m-s	<160	07 (7%)	06(85.71%)	1(14.28%)	12.48, 0.001
	160-220	75(75%)	44(57.14%)	31(41.33%)	
	>220	18 (18%)	18(100%)	0 (0%)	
E/e’	<8	9(9%)	2(22.2%)	7(77.7 %)	15.26, 0.0004
	8 to 12	77(77%)	52(67.53%)	25(32.4%)	
	>12	14(14%)	14(100%)	0(0%)	

Figure 1 displays distribution of study participants on the basis of echocardiographic evaluation. Out of the 100 cases, 68 cases (68%) had diastolic dysfunction of which 54 cases (54%) had impaired relaxation 9 cases had pseudonormal and 5 cases (5%) restricted filling.
Association of diastolic dysfunction with baseline characteristics of study participants have been displayed in **table 1**. 56% of the study participants were males & 44% were females the diastolic dysfunction was seen to be higher among the females (70.4%) compare to males (66.1%) but this observation was statistically insignificant. 22% of cases are in age group 25-39 and 32% cases are in the age group 40-49 and 46% of the cases are in the age group 50-60. The incidence of diastolic dysfunction is highest in the age group 50-60 years. P<0.05 indicate that the association between age and diastolic dysfunction is statistically significant. Maximum number of the patient 81 cases (81%) had serum cholesterol level <200 followed by 12 (12%) cases had serum cholesterol level 200-239 and 3 (3%) cases had serum cholesterol level 240mg/dl and above. The maximum incidence of diastolic dysfunction 69.1% was seen in those with serum cholesterol <200mg/dl followed by 66.66% in those with serum cholesterol level 240 and above followed by 62.5% cases in those with serum cholesterol 200-239 mg/dl. Diastolic dysfunction was found to have no relation with increasing level of serum cholesterol and data was statistically insignificant (p =0.872).50% of cases had a BMI between 19-24.9 kg/m^2, 38% of patient had BMI of 25-25.9 and 12% of the cases had a BMI 30-39.9. The incidence of diastolic dysfunction was highest 74% in BMI 19-24.9 followed by 66.6% in BMI of 30-39.9 while lowest 60.5% in BMI 25-25.9 This finding is statistically in significant (p= 0.404).

Table 2 depicts association of diastolic dysfunction with clinical profile of study participants. 36% of the study population had diabetic duration < 2 years 39% had a diabetic duration of 2-5 years and 25% had a diabetic duration > 5 years. Maximum prevalence of diastolic dysfunction had seen in diabetic duration of more than 5 years which was statistically significant (p value 0.0024).73% of the patient had HbA1C levels greater than 7.5 of which 75.34 % of the cases developed diastolic dysfunction rest 27 % of the cases have their HbA1c <7.5 % of which 48.14 % developed diastolic dysfunction. The findings were statistically significant (p= 0.009). 32% of the patient had nephropathy of which 22 patients (68.75%) shown diastolic dysfunction and 68% of the patients who does not have nephropathy of which 46 patients (67.64%) shows diastolic dysfunction. The data is statistically insignificant (p 0.912).29% of the patient had retinopathy of which 27 patients (93.01%) shown diastolic dysfunction and 71% of the patients who does not have retinopathy of which 41 patients (57.77%) shows diastolic dysfunction. The data is statistically significant (p 0.0005).

Association of diastolic dysfunction with Echocardiographic observations of study participants have been displayed in **table 3**. Maximum number of the cases 54% have E/A values <1 and 100% of these cases have diastolic dysfunction followed by 41% of the cases have E/A value between 1-2 of which 9 cases (21.95%) have diastolic dysfunction followed by 5% of the cases have E/A value >2 and all the 5 cases (100%) have diastolic dysfunction and the data is statistically significant (p<0.001). A total of 57 cases (57%) have IVRT between 60-100 of which 27 cases (47.36%) have diastolic dysfunction followed by 40 % of the cases having IVRT>100 of which 38 cases (95%) followed by 3% of the cases have IVRT <60 of which all the 3 cases(100%) have diastolic dysfunction. The data is highly significant (p <0.001). Maximum number of the cases 75 cases (75%) have DT between 160-220 of which 44 cases (57.14%) have diastolic dysfunction followed by 18 % of the cases having DT >220 of which all cases developed diastolic dysfunction followed by 7 cases have their DT < 160 of 6 cases developed diastolic dysfunction. The data is statistically significant (p<0.001). Out of 100 cases, 77(77%) have E/e' 8-12 of which only 52 cases (67.53%) developed diastolic

dysfunction followed by 14 cases have their E/e' >12 of which all 14 cases (100 %) developed diastolic dysfunction. The data is statistically significant (p= 0.0004).

Discussion:

In this study Echocardiography was done in 100 type 2 diabetes mellitus patients with normal resting ECG to detect the prevalence of left ventricular diastolic dysfunction.

In present study 68 cases (68%) had diastolic dysfunction of which 54 cases(54%) had impaired relaxation 9 cases had pseudonormal and 5 cases (5%) restricted filling. Similar results were observed by the study of Mamatha B Patil et al [9], Paul poinier et al[10], S. Cosson et al[11], Patil et al [12], Gani et al [13] and Rajput et al [14] which reported diastolic dysfunction in 64 %, 60 %, 69 %, 54.33 %, 65.8% and in >60 % of the patients respectively.

In the present study among the patients with the diastolic dysfunction 56% of the participants were males & 4% were females the diastolic dysfunction was seen to be higher among the females (70.4%) compare to males (66.1%) but this observation was statistically insignificance (p= 0.640). The result was similar to study by Sohail Ashraf et al[15] where diastolic dysfunction was more common among males (17.5%) than females (12.2%). Although this may vary, as in study by Rajput et al[14] with equal incidence in male and female and Mamatha B Patil et al [9]with female incidence more than male incidence.

In the present study a total of 100 type 2 diabetic patients were included with an age range of 25 to 60 years. 22% of cases were in age group 25-39 years, 32% cases in the age group 40-49 years and 46% of the cases in the age group of 50-60 years. The incidence of diastolic dysfunction was highest in the age group 50-60 years. This finding was statistically significant (p = 0.002). Similar results were found in study by Patilet al[12] where diastolic dysfunction was significantly higher in age >45 years compared to age <45 years (p < 0.05). Mamatha B patilet al[9] reported linear increase in the prevalence of diastolic dysfunction with increasing age group. Also, as per Ganiet al[13] the age of patients had significant correlation with E/A ratio of trans mitral doppler flow (p<0.01).

In the present study 50% of cases had a BMI between 19-24.9 kg/m^2, 38% of patient had BMI of 25-25.9 kg/m^2 and 12% of the cases had a BMI 30-39.9 kg/m^2. The incidence of diastolic dysfunction was highest 74% in BMI 19-24.9 followed by 66.6% in BMI of 30-39.9 kg/m^2 while lowest 60.5% in BMI 25-25.9 kg/m^2. This finding is statistically insignificant (p= 0.404). Virendra et al[12], 33.33% of male and 24.41% of female patients had high BMI and the association between BMI with diastolic dysfunction was found to be statistically significant. Another similar study by C Halley et al[16], 460 (26.5%) and 407 (23.5%) were overweight and obese, respectively, and had higher prevalence of diastolic dysfunction (*P*<0.001). Using multivariable logistic regression, BMI remained significant in both ordinal (all stages of diastolic function) and binary (normal versus abnormal). In contrast to this, study by Gani et al[13] observed that BMI and waist/hip ratio did not have significant correlation with EF and with E/A ratio.

In the present study 36% of the population had diabetic duration < 2 years,39% had a diabetic duration of 2-5 years and 25% had a diabetic duration >5 years. Maximum prevalence of diastolic dysfunction had seen in diabetic duration of more than 5 years which was statistically significant (p= 0.0024). Gani et al[13] found that the duration of diabetes was independently associated with diastolic dysfunction. The duration of diabetes had significant correlation with EF (r = -0.26, p<0.01) and with E/A ratio (r= -0.295, p<0.01). Virendra c Patil et al[12] in their study, out of 78 (61.41%) subjects with duration of diabetes between 6-10 years, 32 (41.02%)

had diastolic dysfunction. Out of 49 (38.58%) subjects with duration of diabetes between 11-15 years, 37 (75.51%) had diastolic dysfunction. Comparing duration of diabetes of 6 to 10 years and 11 to 15 years with diastolic dysfunction, patients with 11 to 15 years duration of diabetes had more prevalence of diastolic dysfunction ('P' < 0.02). Di Bonito et al[17]found that IVRT and atrial peak filling velocity was greater in diabetic patients where as the early to late atrial filling velocity was significantly reduced. This demonstrates that an impairment of ventricular diastolic function occurs early in the natural history of NIDDM. Another study by Madhumathi R et al [18] observed that on comparing duration of diabetes with diastolic dysfunction, 21 (42%) patients had duration of diabetes less than 5 years and 20 (40%) patients had duration of diabetes 5-10 years. Statistically it was significant as we had higher percentage of patients with diastolic dysfunction as duration of diabetes increased. The results were similar to our study observations.

As per recent study 73% of the patient had HbA1C levels greater than 7.5 of which 75.34 % of the cases developed diastolic dysfunction rest 27 % of the cases have their HbA1c <7.5 % of which 48.14 % developed diastolic dysfunction .The findings were statistically significant (p 0.009).The results were similar to that of study by Virendra C Patil et al[104] where out of 89 subjects with HbA1c < 7.5%, 39 (42.82%) had diastolic dysfunction; and, out of 38 subjects with HbA1c > 7.5%, 31 (81.57%) had diastolic dysfunction. Subjects with HBA1c > 7.5% had more prevalence of diastolic dysfunction, than subjects with HBA1c < 7.5% ('P' < 0.02). Mamatha B Patil et al[9], the prevalence of diastolic dysfunction increased gradually with the rise in HbA1C levels. Madhumathi R et al[18], 25(50%) subjects had HbA1c >8% which indicated poor glycemic control. Prevalence of diastolic dysfunction increased gradually with the rise in HbA1c levels and it was statistically significant.

Current study found that 32% of the patient had nephropathy of which 22 patients (68.75%) shown diastolic dysfunction and 68% of the patients who does not have nephropathy of which 46 patients (67.64%) shows diastolic dysfunction. The data is statistically insignificant (p= 0.912). Sampson et al[19], found a gradual decrease in E/A ratio in type 1 diabetic patients according to the presence of microalbuminuria and proteinuria. A significantly higher proportion of abnormal diastolic function (E/A < 1) was observed in the group of diabetics with proteinuria. However, the possible influence of arterial blood pressure on the appearance of diastolic dysfunction in the early stages of diabetic nephropathy was postulated as a significantly higher blood pressure was observed in the subgroup of diabetics with proteinuria. In the study population 29% of the patient had retinopathy of which 27 patients (93.01%) shown diastolic dysfunction and 71% of the patients who does not have retinopathy of which 41 patients (57.77%) shows diastolic dysfunction. The data is statistically significant (p=0.0005). S. Cosson et al[11]have demonstrated that patients with mild to severe retinopathy exhibited LV diastolic dysfunction. In the most recent report, a higher prevalence of retinopathy (49%) was encountered in patients with abnormal mitral filling pattern (E/A ratio < 1) compared to patients with a normal diastolic function (20%).

Conclusion:

It can be concluded that the incidence of left ventricular diastolic dysfunction is higher in type II diabetes mellitus patients who are free of clinically detectable heart disease. In the present series the incidence was more in patients with diabetic complications especially retinopathy, those with HbA1c level >7.5. It was also found that the incidence of diastolic dysfunction had a strong correlation with the age of the patient and duration of diabetes. In the present study the incidence of diastolic dysfunction did not show any correlation with gender, BMI, S. cholesterol of the patient.

The diastolic dysfunction is the earliest manifestation of diabetic cardiomyopathy and hence, detecting and treating it in early stages would prevent disease progression to symptomatic cardiac failure. All the diabetic patients should undergo 2D Echocardiographic evaluation for identifying diastolic dysfunction. Patients should be advised strict control of diabetes in order to reduce the risk for developing diastolic dysfunction.

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