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Original Research Article

Left ventricular dysfunction in patients with type 2 diabetes mellitus

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ABSTRACT

Background: Diabetes mellitus (DM) is on the increase globally. Cardiovascular complications, such as left ventricular dysfunction is a major cause of death in patients with type II DM. Prior to the development of symptomatic heart failure, subclinical left ventricular dysfunction (systolic and diastolic) may exist for some time. Aim of this study is to find out abnormalities in left ventricular function in patients of type 2 diabetes mellitus with help of 2D Colour Doppler Echocardiography. To find its correlation with glycemic control on the basis of glycosylated haemoglobin (Hba1c).
Methods: Total 100 Patients of type 2 Diabetes Mellitus of duration more than 10 years of both sexes were included in the cross-sectional study conducted from Jan 2018 to Aug 2019.All the patients were assessed through clinical examination and 2-D echocardiography and control of diabetes determined on the basis of HbA1c.
Results: Study consisted of 100 patients with type 2 DM, 55(55%) were females and 45(45%) males. Majority of patients were in the age group of 4th to 6th decade of life. Diastolic dysfunction was present in 81(81%) patients. systolic dysfunction was present in 14(14%) patients. There was a linear increase in prevalence of diastolic dysfunction with increasing age, increased FPG, increased BMI. There was also significant correlation between LV diastolic dysfunction (LVDD) and LA size. While no statistical correlation found between gender, duration of diabetes, HbA1c with diastolic and systolic dysfunction.
Conclusions: LV diastolic dysfunction is an early manifestation of diabetic cardiomyopathy. LVDD contributes significantly to morbidity of congestive heart failure in diabetic patients. Echocardiography is a very useful non-invasive tool in detecting LVDD and systolic dysfunction in type 2 DM patients.

Keywords: 2-D echocardiography, Diabetes mellitus, Diastolic dysfunction, Heart failure, Systolic dysfunction

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system.[1]

Diabetes mellitus is associated with a multitude of cardiovascular complications, e.g., increased incidence of atherosclerotic coronary artery disease, myocardial infarction, congestive heart failure, coronary microangiopathy, systemic arterial hypertension and cardiomyopathy.[2]

Diabetic cardiomyopathy refers to a disease process which affects the myocardium in diabetic patients causing a wide range of structural abnormalities eventually leading to LVH [left ventricular (LV) hypertrophy] and diastolic and systolic dysfunction or a combination of these. Diabetic cardiomyopathy can be subclinical or apparent on the presence of symptoms and signs. There appears to be a long subclinical course in

most patients before the development of symptoms. Diabetic cardiomyopathy is thought to result from microangiopathy, deposition of collagen, decreased myofilament $Ca2^+$ sensitivity.[3]

The Framingham Heart study has shown that the incidence of congestive cardiac failure in diabetic patients occurs irrespective of coronary artery disease or hypertension.

In overt heart failure, diastolic dysfunction often co-exists with systolic dysfunction as a consequence of ischemic heart disease, but diastolic dysfunction is a frequent finding in type 2 diabetes mellitus without signs and symptoms of heart disease and is presumably due to diabetic cardiomyopathy. Left ventricular diastolic function (LVDF) is affected earlier than systolic function in the development of congestive cardiac failure. Therefore, left ventricular diastolic dysfunction may represent the first stage of diabetic cardiomyopathy.[4]

In the clinical definition most often used, diastole is delineated by the time interval between closure of the aortic valve and closure of the mitral valve. It has been advocated, that only diastasis and atrial contraction represent true diastole physiologically.[5]

Currently, echocardiography is the best noninvasive way to evaluate diastolic function and to estimate filling pressures. M-Mode, two-dimensional, and Doppler (blood flow, tissue, and color) echocardiography are all helpful in evaluating diastolic function.

Diastolic filling is usually classified initially on the peak mitral flow velocity of the early rapid filling wave (E), peak velocity of the late filling wave caused by atrial contraction (A), E/A ratio, and deceleration time (DT), which is the time interval for the peak E velocity to reach zero baseline.

Comprehensive assessment of diastolic filling and estimation of filling pressures by echocardiography require color M-mode of mitral inflow for propagation velocity-sometimes with an alteration in a loading condition. The Valsalva maneuver is used most frequently to decrease venous return by increasing intrathoracic pressure.[6]

Diabetes has been implicated as an important determinant of left ventricular mass in most population-based studies. An adaptive response has been shown to diverse degrees of altered carbohydrate metabolism, as in Cardiovascular Health Study and in The Strong Heart Study cohort, where diabetes, impaired glucose tolerance and insulin levels were associated with increased LV mass. Although associated with an increase in left ventricular mass, hyperinsulinemia and insulin resistance show a stronger association with concentric remodeling.[7]

The objectives of this study were to find out abnormalities in left ventricular function in patients of type 2 diabetes mellitus with help of 2D Colour Doppler Echocardiography and to find its correlation with glycaemic control.

METHODS

A total of 100 Patients of type 2 Diabetes Mellitus of duration more than 10 years of both sexes were studied. This was a cross-sectional study conducted out at OPD/IPD of SGRD Hospital, Vallah, Sri Amritsar over a period of 1.8 years from Jan 2018 to Aug 2019. written consent for the trial was obtained from all patients after examining them in detail.

Inclusion criteria

- Patients of type 2 diabetes mellitus of duration more than 10 years of either sex with either on OHA or insulin treatment were included.

Exclusion criteria

- Morbid obesity.
- Patients with history of Hypertension.
- Patients with history of Congenital/valvular/coronary artery disease.
- Renal failure
- Chronic smokers and Chronic Alcoholics.
- patients on steroids, anticancer drugs.

Patients were verified after fulfilling inclusion criteria and ruled out for presence of exclusion criteria. all patients and their relatives were informed about the study in their vernacular language. written consent was taken. a detailed history of each patient was taken. complete clinical examination was done and all the routine investigations like complete blood count, fasting plasma glucose, HbA1c, renal function test, urine complete examination, fasting lipid profile (serum cholesterol, serum triglyceride), serum electrolytes- Na^+, K^+, liver function tests, ECG, chest X-ray, USG abdomen were done.

All subjects were subjected to an echocardiogram to assess the presence of diastolic dysfunction. Echocardiographic assessment was done in 2D mode, M-mode, and Doppler mode using colour flow mapping.

Each patient was examined in left lateral recumbent position using standard parastomal, short axis, and apical views. From the pulsed doppler spectrum of mitral flow, the following measurements were made: -

- Peak velocity of early filling (E).
- Peak velocity of atrial filling (A).
- Ratio of E/A.
- Left atrial size.

Diastolic filling abnormalities were graded as follows:

- Grade 1: Impaired relaxation pattern with normal filling pressures
- Grade 2: Psuedonormalized pattern
- Grade 3: Reversible restrictive
- Grade 4: Irreversible restrictive pattern.

Diastolic dysfunction was considered to be present if E/A ratio was <1 or >2M-mode echocardiographic measurements of the following left ventricle function parameters was taken: Left ventricular internal dimensions: EDD and ESD (mm), Interventricular septal thickness in systole and diastole: IVSS and IVSD (mm),Left ventricular posterior wall thickness in systole and diastole: LVPWS and LVPWD (mm),Ejection fraction: EF (%), Fractional shortening: FS (%). Systolic dysfunction will be indicated by Ejection fraction <50%; Fractional shortening; Regional wall motion abnormalities.

The data collected was compiled and analysed statistically. Statistical analysis was done using percentages, mean values, standard deviation, Pearson Chi-square test. The level of significance used was 0.05 level for the corresponding degree of freedom to draw the inference. A p-value <0.05 was considered statistically significant and a p>0.05 was considered as not statistically significant.

RESULTS

A total of 100 patients who were type 2 diabetes mellitus were selected for cross-sectional study by simple random sampling method. All patients were evaluated for left ventricular dysfunction both diastolic as well as systolic.

Majority of the patients belonged to 4th to 6th decades of life with mean age of study was 56.07±0.90 years (Figure 1).

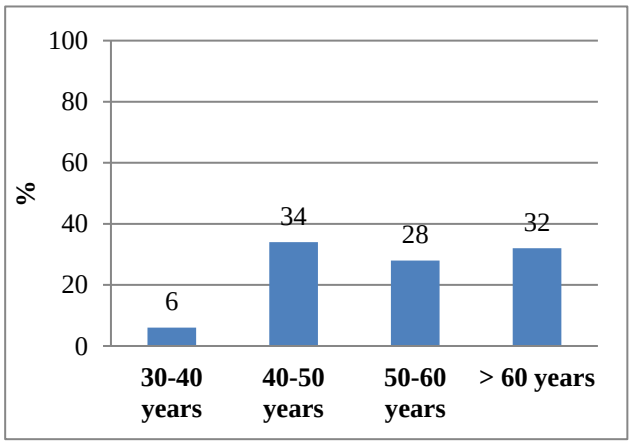

Figure 1: Age distribution of the study population.

The most common age group affected from diastolic dysfunction was >60 years accounting for 35.8% (29 out of 81) of patients affected by dysfunction. In this study there was significant correlation seen between age of patients and prevalence of LV diastolic dysfunction with p value of 0.012 (Table 1). In this study there was no significant correlation seen between age of patients and prevalence of LV systolic dysfunction.

Table 1: Prevalence of diastolic dysfunction in relation to age.

Variables	Diastolic Dysfunction		Total
Age	No	Yes	
30-40 years	4	2	6
	66.7%	33.3%	100.0%
40-50 years	6	28	34
	17.6%	82.4%	100.0%
50-60 years	6	22	28
	21.4%	78.6%	100.0%
> 60 years	3	29	32
	9.4%	90.6%	100.0%
Total	19	81	100
	19.0%	81.0%	100.0%
p-value	0.012* (Sig.)		

Out of 100 patients there were 45 males and 55 females (Figure 2). It was observed that diastolic dysfunction was present in 81(81%) of studied population, out of which 35(43.2%) were males and 46(56.7%) were females, 35 out of 45 (77.8%) male patients had diastolic dysfunction while 46 out of 55(83.6%) female patients had diastolic dysfunction, although prevalence of LVDD was higher in females as compared to males, but the result was not statistically significant with p value 0.458.

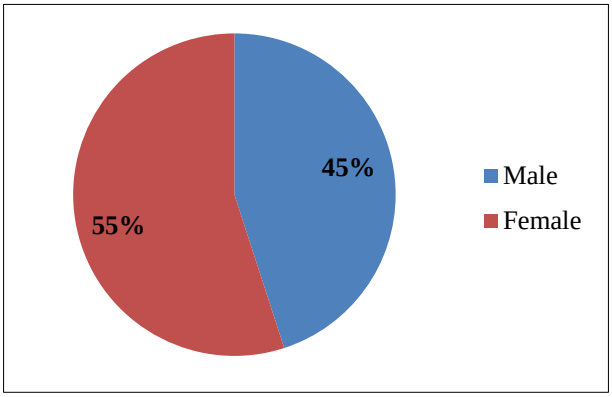

Figure 2: Sex distribution of patients.

Diastolic dysfunction was present in 81(81%) cases, while 19(19%) had no diastolic dysfunction. Out of patients who had diastolic dysfunction 59(72.8%) cases had grade I dysfunction, 17(20.9%) cases had grade II and 5(6.17%) cases had grade III/IV dysfunction (Table 2).

Systolic dysfunction was present in 14(14%) cases while 86(86%) had no systolic dysfunction (Figure 3).

Table 2: Distribution of subjects according to grade of diastolic dysfunction.

Grades of diastolic dysfunction	Frequency	Percent
Normal	19	19.0
Grade I	59	59.0
Grade II	17	17.0
Grade III/IV	5	5.0
Total	100	100.0

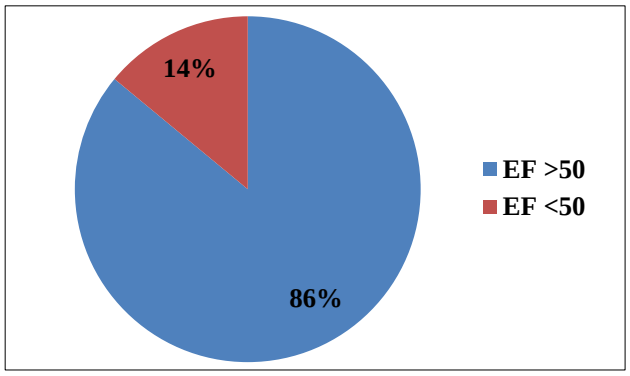

Figure 3: Distribution of subjects according to systolic dysfunction.

Majority of patients were between 10-15 years of duration of diabetes accounting for 90% of cases with mean duration 12.85± 3.88. In this study there was no statistically significant correlation found between duration of diabetes and diastolic dysfunction with p value 0.649. In this study there was no statistically significant correlation found between duration of diabetes and systolic dysfunction with p value 0.352.

In this study majority of patients had HbA1c >8% accounting for 67% of cases with Mean±SD of 9.89±2.62. In this study there was no statistically significant correlation found between HbA1c and diastolic dysfunction with p value 0.974. Patients who had HbA1c between 6.1-7%, had 8 out of 10(80%), HbA1c between 7.1-8% had 19 out of 23(82.6%), HbA1c >8% had 54 out of 67(80.65%) accounting for LVDD (Figure 4).

Table 3: Relation of FPG with prevalence of diastolic dysfunction.

Variables	Diastolic dysfunction		Total
FPG	No	Yes	
100-150	11	13	24
	45.8%	54.2%	100.0%
15-200	5	30	35
	14.3%	85.7%	100.0%
>200	3	38	41
	7.3%	92.7%	100.0%
Total	19	81	100
	19.0%	81.0%	100.0%
p-value	0.000 (S)		

Statistically 41% of patients had FPG >200mg/dl with Mean±SD of 192.07±49.34. It was found that majority of cases who had diastolic dysfunction had FPG >200 mg/dl. However, with p value of <0.05, statistical significance was found between FPG and prevalence of LVDD (Table 3).

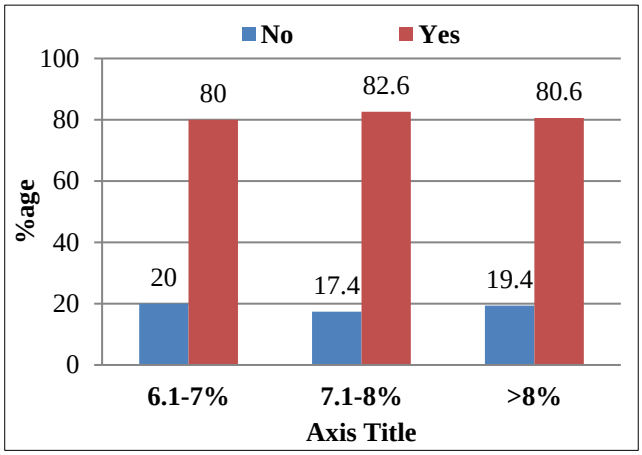

Figure 4: Relation of hba1c with prevalence of diastolic dysfunction.

Table 4: Relation of BMI with prevalence of diastolic dysfunction.

Diastolic dysfunction	BMI			Total
	18.5-22.9	23-24.9	>25	
I	20	25	14	59
	33.9%	42.4%	23.7%	100.0%
II	5	6	6	17
	29.4%	35.3%	35.3%	100.0%
III	0	4	1	5
	0%	80.0%	20.0%	100.0%
No dysfunction	15	4	0	19
	78.9%	21.1%	0%	100.0%
Total	40	39	21	100
	40.0%	39.0%	21.0%	100.0%
p-value	0.003 (Sig.)			

It was found that majority of cases who had diastolic dysfunction had BMI 23-24.9kg/m^2 and accounts for 43.2% of patients affected by diastolic dysfunction with mean BMI was 23.58±1.81. In this study there was statistically significant correlation found between BMI and prevalence of LVDD with p value of 0.003(Table 4), but patients who had BMI >25, 21 out of 21(100%) had diastolic dysfunction, showed prevalence of LVDD was more in patients who had more BMI. There was statistically significant correlation found between BMI and prevalence of systolic dysfunction with p value of 0.010.

Significant correlation found between LA size and diastolic dysfunction with p value 0.025. Total 38 patients out of 100 had LA size >40, 4 out of 5 (80%) had

grade III/IV diastolic dysfunction. In patients who had diastolic dysfunction had increased LA size (Figure 5).

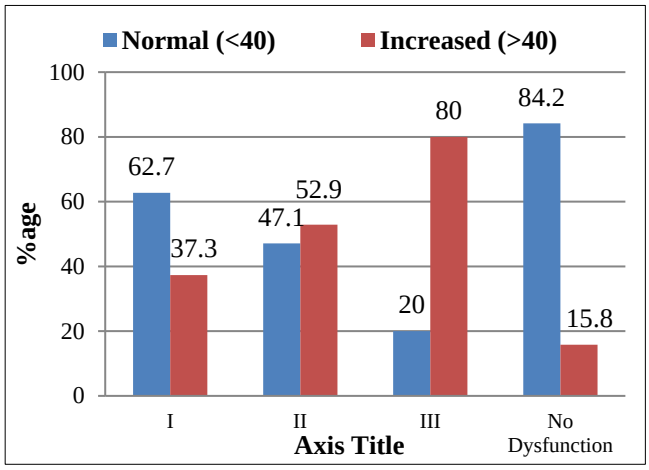

Figure 5: Relation between la size and diastolic dysfunction.

DISCUSSION

Several studies have shown the evidence of left ventricular systolic and diastolic dysfunction in asymptomatic, normotensive type 2 diabetes mellitus patients. In cross-sectional study 100 Patients who were type 2 diabetes mellitus were selected by simple random sampling method. All patients were evaluated for left ventricular dysfunction both Diastolic as well as Systolic after excluding any evidence of hypertension and CAD.in the present study an attempt has been made to evaluate left ventricular function by M-mode, 2-D echo and colour doppler studies in type 2 diabetes patients who were normotensive.

The role of elevated blood sugar in the causation of various cardiovascular diseases has been investigated by several researchers. 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. Such products have been found to accumulate in tissues such as heart.8

A reduced E/A ratio has been shown to be independently associated with increased all-cause mortality as well as cardiovascular mortality. These structural abnormalities lead to increased wall stress, increased oxygen demand, Ischemia and the development of left ventricular diastolic dysfunction. It showed diastolic dysfunction results in reduction in active LA emptying.it was showed that a decreased contribution of active LA emptying to ventricular filling during diastole was strongly predictor of adverse events. It showed that BMI associated with high A and low E. In obese, cardiac preload and afterload are increased leading to increased peripheral resistance. Increased pro inflammatory cytokines originating from adipose tissue are suggestive to be important contributors.

Study conducted by Mamantha et al, had mean age of 57.38 ± 11.23 years with most common affected age group was 41-50 years and Boyer J K et al, had mean age 48.9± 6.9 years with most common affected age group was 50-59 years.[9,10] In the present study, mean age of 56.07±10.9 years with most common age group affected from diastolic dysfunction was >60 years accounting for 35.8% (29 out of 81) of patients affected by dysfunction. In this study there was significant correlation seen between age of patients and prevalence of LV diastolic dysfunction with p value of 0.012. Observations of this study were similar to other studies done by Mamantha et al, and Siddiq Ibrahim khalil et al.[9,11]Both studies found higher prevalence of diastolic dysfunction with higher age group and so was observed in this study.

In the study done by Mamatha et al, there were 28 males and 22 females while study done by Madhumathi et al, had 20 males and 30 females in the study population.[12] In Study done by Mamatha et al diastolic dysfunction was present in 32(64%) of cases. Gender wise comparison of LVDD showed 68.1% of female subjects had diastolic dysfunction compared to 60.7 % of males. In Study done by Madhumathi et al, diastolic dysfunction was present in 24(48%) of cases.[12] Gender wise comparison of LVDD showed 53.3% of female subjects had diastolic dysfunction compared to 40% of males. In the present study population, it was observed that number of female patients were higher. Out of 100 patients there were 45 males and 55 females. Gender wise comparison of LVDD showed 83.6% of female subjects had diastolic dysfunction compared to 77.8% of males. Results of above studies were similar with present study with prevalence of diastolic dysfunction was non significantly higher among females.

Mean duration of diabetes was 12.85±3.88 years in the present study which was not comparable to Mamatha et al mean duration 8.6±7.5 years) study and Siddiq Ibrahim Khalil et al, mean duration 6±3.5 years) because in the present study patients with diabetes mellitus of >10 years duration were included. Both of above studies observed significant correlation between duration of diabetes and prevalence of LVDD, but in present study observed any correlation was not observed between duration of diabetes and LVDD.

Prevalence of LVDD was found to be 71% by Shreshta et al, 71.3% by Dike Ojji et al, and 81% in this study.[13,14] In this study total of 81 (81%) patients had diastolic dysfunction. Grade I was most common 59 (72.8%) followed by Grade II 17(20.9%). Only 5 (6.17%) patients were found to have Grade III/IV dysfunction. Dike Ojji et al, observed that total of 87(71.3%) patients had diastolic dysfunction.[14] Grade I was most common 71 (81.6%) followed by Grade II 9(10.3%). Only 7(8.04%) patients were found to have Grade III/IV dysfunction. Results of both studies were similar with Prevalence of Grade I LVDD was more followed by Grade II and III/IV.

Prevalence of systolic dysfunction was found to be 15.56% by Dodiyi-manuel et al, and 14% in this study.[15] The prevalence of systolic dysfunction in diabetic patients was comparable with the study conducted by Dodiyi-manuel et al.

In study done by Nikhil M Dikshit et al, Mean FPG was 180.8± 78.41mg/dl.[16] However Nikhil M Dikshit et al, observed significant correlation between FPG levels and LVDD.[16] In this study 50.6% of patients affected by diastolic dysfunction had FPG >200 mg/dl with mean FPG was 192.07± 49.34 mg/dl. it was found that patients having FPG >200, 92.7% (38 out of 41) had diastolic dysfunction. However, with p value of <0.05, statistical significance correlation was found between FPG and prevalence of LVDD. Similar findings were observed in both studies.

In study done by Nikhil M Dikshit et al, observed significant correlation between BMI and LVDD with mean BMI 24.06± 2.53 kg/m^2.[16] Mean BMI was 23.58± 1.81kg/m^2. It was found that majority of cases who had diastolic dysfunction had BMI 23-24.9kg/m^2 and accounts for 43.2% of patients affected by diastolic dysfunction. However, with p value of <0.05, statistical significance was found between BMI and prevalence of LVDD. Similar findings were observed in both studies.

Mamatha et al, observed 23(74.19%) had HbA1c >8% which was comparable to this study. In study conducted by Mamatha et al it was found that prevalence of diastolic dysfunction increased gradually with rise in HbA1c and it was statistically significant. while In study conducted by Yadava SK et al, there was no statistically significant association found between diastolic dysfunction and HbA1c.[17] In the study 54(66.6%) had HbA1c >8% while there was no significant association found between diastolic dysfunction and HbA1c in this study which was similar to this study.

Significant correlation was found between LA size and diastolic dysfunction, with Total 38 patients out of 100 had LA size >40, 4 out of 5 (80%) had grade III/IV diastolic dysfunction. In patients who had diastolic dysfunction had increased LA size. Similar findings were observed in study conducted by Mamatha et al, both studies were comparable.

Study conducted by Yadava SK et al, found no significant association between diastolic dysfunction and dyslipidemia and similar results were observed in this study.[17]

CONCLUSION

LV diastolic dysfunction is more seen in type 2 DM patients. Alteration of E/A ratio <1 is a sensitive and specific indicator of early diastolic dysfunction and EF<50% Is indicator of systolic dysfunction. LV dysfunction both systolic and diastolic is marker of evolving heart disease among diabetics. Early diagnosis and institution of treatment will reduce the morbidity and improve the outcome of diastolic heart failure. Patients with Type 2 DM should be screened for subclinical LVDD by echocardiography. Conventional echocardiography is a simple economical test for detecting LV dysfunction in type 2 normotensive diabetes mellitus patients.

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