Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Echocardiographic Evaluation of Asymptomatic Type 2 Diabetes Mellitus Patients for Cardiovascular Disease in a Tertiary Care Hospital

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Abstract

Introduction: Diabetes mellitus (DM) is one of the most common diseases in the world and is acquiring epidemic proportions. Its prevalence is growing in both developed and developing countries. It is a major risk factor for cardiovascular diseases (CVD) and CVD is the leading cause of morbidity and mortality in people with diabetes. The diastolic abnormalities are present in diabetic patients without overt diabetic complications of the cardiovascular system; It is the earliest and specific functional abnormality in diabetic cardiomyopathy and can affect patients who are free of macrovascular complications. Left ventricular diastolic dysfunction (LVDD) thus represents the first stage of diabetic cardiomyopathy preceding changes in systolic function, reinforcing the importance of early examination of ventricular function in individuals with diabetes.

Material and Methods: It is an observational, Hospital-based Cross-Sectional study. It was carried out among outpatient and inpatient with type 2 DM as per the American Diabetes Association's guidelines attending the General Medicine department of AGMC and GBP Hospital. Sample size was 100 patients.

Results: Of 100 types 2 DM study participants 40.0% were female and 60.0% were male. Mean age of patients was 52.8000 ± 6.2829. About 64.0% patients had LVDD out of 100 patients. 93.8% had LVDD grade 1 and 6.3% patients had LVDD grade 2. 8.0% patients had left ventricular systolic dysfunction among 100 patients. Diastolic dysfunction is significantly associated with increasing age, duration of diabetes, and glycemic index assessed by glycosylated haemoglobin (HbA1c).

Conclusion: the prevalence of LVDD in type 2 Diabetic Mellitus without any cardiovascular symptoms is much higher than previously suspected. Diastolic dysfunction is significantly associated with increasing age, duration of diabetes, and glycemic index assessed by HbA1c. Early diagnosis and treatment for LVDD in diabetic patients without any cardiac symptoms will reduce morbidity and improve outcomes by preventing future development of heart failure.

Key words: Diabetes, Left ventricular Diastolic dysfunction

INTRODUCTION

Diabetes mellitus (DM) is one of the most common diseases in the world and is acquiring epidemic proportions. Its prevalence is growing in both developed and developing countries. Its incidence is increasing rapidly, and by 2030, this number is estimated to be almost double. The greatest increase in prevalence is, expected to occur in Asia and Africa.

India has more diabetics than any other country in 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 of onset is 42.5 years.[1]

DM is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia with disturbance of carbohydrate, fat, and protein metabolism. It results from defects in insulin secretion, insulin action, or both. The effect of DM includes long-term damage, dysfunction, and failure of various organs such as eyes, kidneys, nerves,

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Month of Submission : 11-2021
Month of Peer Review : 12-2021
Month of Acceptance : 12-2021
Month of Publishing : 01-2022

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heart, brain, and blood vessels. Several distinct types of DM are caused by complex interaction of genetics and environmental factors.

The persistence of these metabolic disturbances leads to permanent and irreversible functional and structural changes in the cells of the body which in turn lead to the development of "diabetic complications," characteristically affecting, the cardiovascular system, eye, kidney, and nervous system mainly.

Diabetes is a life-threatening condition, It is a major risk factor for cardiovascular diseases (CVD) and CVD is the leading cause of morbidity and mortality in people with diabetes. Four million people die each year as a result of diabetes and a high proportion of these deaths are attributable to CVD complications such as heart attack and stroke.

Given that people with diabetes are at greater risk of CVD, increasing their knowledge and awareness of CVD at the right time can reduce the chances of developing diabetes complications and thus help to reduce diabetes morbidity and mortality.

The existence of a diabetic cardiomyopathy was first proposed by Rubler *et al.* in 1972 on the basis of post-mortem findings. In 1974, Framingham study showed that heart failure was more common in diabetes due to diabetic cardiomyopathy. The Framingham Study demonstrated that patients with diabetes had a greater likelihood of developing clinical heart failure. The relative risk of developing heart failure was 3.8 in diabetic men and 5.5 in diabetic women compared with non-diabetic patients. The study also revealed a marked increase in congestive heart failure, coronary artery disease, and myocardial Infarction in diabetic patients.[2]

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). DHF is observed in 40% of patients with other heart failure. DM is one of the major risk factors for DHF. The mortality rates among the patients with DHF ranges from 5 to 8% annually as compared with 10 to 15% among patients with systolic heart failure.[3]

In the Framingham heart study, it was shown that patients with DM carry an increased risk for coronary heart disease (CHD). Framingham data suggest that hyperglycemia as such is an independent risk factor.

The leading cause of left ventricular systolic dysfunction (LVSD) and congestive heart failure in developed countries is CHD with a prevalence in the recent multi-center heart failure trials of 66%. Thus, CHD often contributes to the manifestation of heart failure, and the progression 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 the use of established primary and secondary prevention guidelines, including control of blood pressure, use of statins and aspirin, smoking cessation, and implementation of angiotensin-converting enzyme inhibitor therapy in persons with diabetes and cardiovascular risk factors.

Despite similar LVSD, patients with diabetes have more pronounced heart failure symptoms, use more diuretics, and have an adverse prognosis compared with those without diabetes; one putative explanation for these discrepancies is diastolic dysfunction of the left ventricle in DM.[4]

Left ventricular diastolic dysfunction (LVDD) thus represents the first stage of diabetic cardiomyopathy preceding changes in systolic function, reinforcing the importance of early examination of ventricular function in individuals with diabetes.[5,6] Its timely recognition may help to avoid or significantly delay the concept of CHF.

The diastolic abnormalities are present in diabetic patients without overt diabetic complications of the cardiovascular system;[7] It is the earliest and specific functional abnormality in diabetic cardiomyopathy and can affect patients who are free of macrovascular complications, even in newly diagnosed DM patients or in those with a disease duration of <1 year.[8]

Diastolic dysfunction refers to a condition in which abnormalities in mechanical function are present during diastole. The causes of diastolic dysfunction may be subdivided into a decrease in passive myocardial diastolic compliance, and an impairment in active left ventricular relaxation. Abnormalities in diastolic function may occur in the presence or absence of a clinical syndrome of heart failure and with normal or abnormal systolic function. Therefore, whereas diastolic dysfunction describes an abnormal mechanical property, DHF describes a clinical syndrome.

Currently, the only available surrogate measure of diastolic function is echocardiography. Assessment of mitral valve inflow using pulsed wave Doppler is used routinely in clinical practice to noninvasively identify the five progressive filling categories: normal, abnormal relaxation, pseudo-normal, reversible restrictive filling and non-reversible restrictive filling, based upon early (E) and late (A) peak filling velocities and E deceleration time.

In view of the above facts, this study is designed and proposed to be conducted for the 1st time at AGMC and GBP Hospital to study echocardiography of type 2 DM patients who do not have any cardiovascular symptoms, as this kind of study has never been conducted earlier in any tertiary care hospitals of Tripura, India.

Aim and Objectives

Aim

To study echocardiography of type 2 DM patients who do not have any cardiovascular symptoms.

Objectives

1. To assess the cardiac status of type 2 DM patients by echocardiography, who are otherwise asymptomatic clinically of any cardiovascular symptoms.
2. To determine the association of diastolic dysfunction with the socio-demographic factors (age and sex), duration of DM, glycemic control, and obesity indices.

MATERIALS AND METHODS

Study Design

Hospital-based Cross-Sectional study.

Type of Study

Observational study.

Study Setting

Department of General medicine, AGMC and GB Pant Hospital.

Study Duration

1 ½ year.

Study Population

Outpatient and inpatient with type 2 DM as per American Diabetes Association's (ADA) guidelines attending the General Medicine department of AGMC and GBP Hospital and following exclusion and inclusion criteria were included in the study.

Sample Size

100.

Sample Technique

Systemic random sampling.

Operational Definitions

- Diagnosis of type 2 DM was made as per ADA guidelines
- Diagnostic criteria (American diabetes association)
- FBS ≥126 mg/dl
- 2 h plasma glucose ≥200 mg/dl during an OGTT.
- RBS ≥200 mg/dl with symptoms (polyuria, polydipsia, polyphagia, and weight loss) Glycosylated hemoglobin
- HbA1C >6.5%.

Body Mass Index (BMI)

BMI Was derived from the weight (kilograms) and height (metres) by using formula - weight(kilograms)/[height(metres)]^2. Using this the patients were categorized as underweight (BMI <18.5 kg/m^2), normal weight (BMI between 18.5 and 22.9 kg/m^2), overweight (BMI between 23.0 and 24.9 kg/m^2), and obese (BMI ≥25 kg/m^2) based on revised consensus guidelines for India. The mean BMI (mean ± s.d) of patients was 24.5268 ± 2.7819.

Diagnosis of LVDD

Reduction in peak velocity of early mitral flow (E), increase over peak velocity of late mitral flow (A), with E/A ratio of <1, and increase in left atrial (LA) size with preserved ejection fraction were considered as the evidence of LVDD.

Inclusion Criteria

Patients of both sex aged above 30 years, with type 2 DM with no clinical symptoms of cardiovascular involvement and blood pressure <130/80 mm Hg with normal ECG, without renal impairment and without any neurologic impairment.

Exclusion Criteria

Patients with type 2 DM with evidence of CHD, Congenital heart disease, valvular heart diseases, cardiomyopathies, hypertensive patients, patients with previously diagnosed LVSD, age more than 60 years, Those who did not give consent to participate in the study.

Method of Data Collection

All the cases were selected consecutively during the study period when they are presented following the inclusion and exclusion criteria. The data were collected from type 2 DM patients attending AGMC and GBP Hospital, Agartala.

All the patients were personally subjected to detailed history regarding name, age, sex, occupation, socio-economic status, educational status, chief complaints, present illness, past illness, general physical examination, and systemic examination. These findings were recorded in a predesigned and pretested proforma.

Investigations

The following investigations were undertaken immediately after admission Complete hemogram, random blood sugar, fasting blood sugar, Post-prandial blood sugar, HbA1c, renal function test, serum electrolytes, fasting lipid profile, urine routine, and microscopy, fundoscopy, electrocardiogram, chest radiography, liver function tests, and 2D echocardiography.

The diastolic function was evaluated using M mode and two-dimensional transthoracic echocardiography and color flow Doppler examination.

In the Doppler study following values were evaluated.

a. E- peak velocity of early mitral flow
b. A- peak velocity of late mitral flow
c. E/A ratio
d. LA size: Reduction in E velocity, increase in A velocity,
e. E/A <1 and increase in LA size is considered as the evidence of LVDD.

Consent for collecting the required data was obtained. A pre-structured proforma was used to record the relevant information from each individual subjects selected for the study.

Data Management

After completion of data collection, the obtained data were coded and entered into Microsoft excel worksheet and was subjected for statistical analysis using Statistical Package for the Social Sciences (SPSS) software.

For categorical data, comparison was done by chi-square test or Fisher's exact test and for continuous data *t*-test or Z- test was applied.

Statistical Analysis

For statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample *t*-tests for a difference in mean involved independent samples or unpaired samples. Paired *t*-tests were a form of blocking and had greater power than unpaired tests. One-way analysis of variance (one-way ANOVA) was a technique used to compare means of three or more samples for numerical data (using the F distribution). A Chi-squared test (χ^2-test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualifications, "Chi-squared test" often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. Explicit expressions that can be used to carry out various *t*-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a *t*-distribution under the null hypothesis is given. Furthermore, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test. Once a *t* value is determined, a *P*-value can be found using a table of values from Student's t-distribution. If the calculated *P*-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis. $P \leq 0.05$ was considered for statistically significant.

RESULTS

In our study, 6 (6.0%) patients were 30–40 years old, 34 (34.0%) patients were 41–50 years old and 60 (60.0%) patients were 51–60 years old. The mean age (mean ± s.d.) of patients was 52.8000 ± 6.2829 Figure 1.

In our study, 40 (40.0%) patients were female and 60 (60.0%) patients were male Figure 2.

In our study, 24 (24.0%) patients had normal weight, 44 (44.0%) patients were obese, 30 (30.0%) patients had over weight and 2 (2.0%) patients had under weight Figure 3.

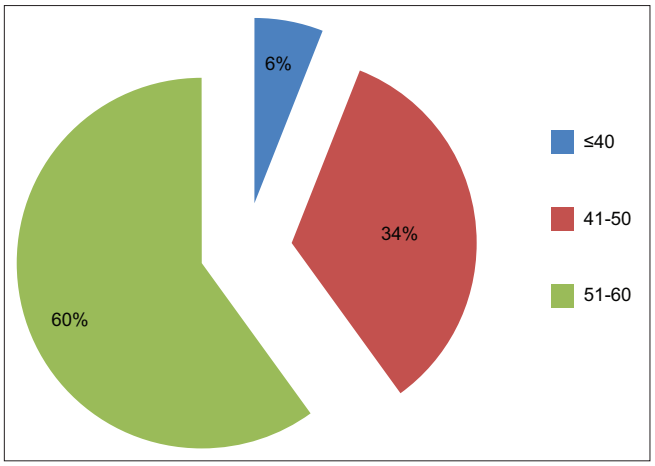

Figure 1: Distribution of age

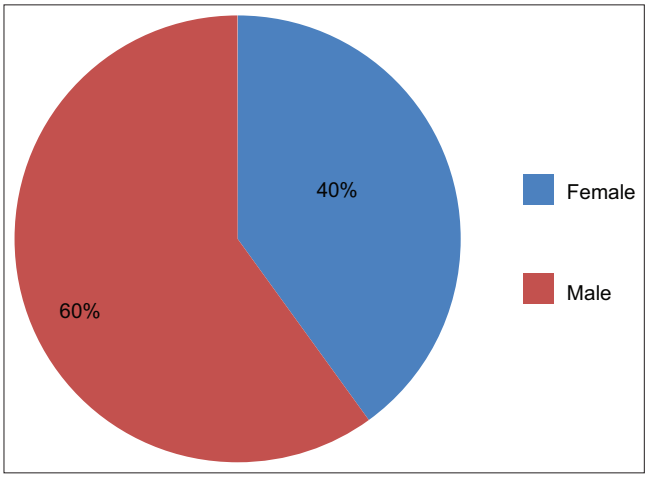

Figure 2: Distribution of sex

In our study, 18 (18.0%) patients were in <10 years duration of diabetes, 82 (82.0%) patients were in >10 years duration of diabetes. The mean duration of diabetes in years (mean ± s.d.) of patients was 16.5800 ± 6.2671 Figure 4.

In our study, 36 (36.0%) patients were HBA1c level 6.5–8.0, 44 (44.0%) patients were HBA1c level 8.1–10.0 and 20 (20.0%) patients were HBA1c level >10.0. The mean HBA1c (mean ± s.d.) of patients was 8.7572 ± 1.5427 Figure 5.

The mean FBS (mean ± s.d.) of patients was 152.5920 ± 46.3410. The mean PPBS (mean ± s.d.) of patients was 286.6580 ± 73.8340. The mean EF (mean ± s.d.) of patients was 62.5160 ± 7.4088 Table 1.

In our study, 64 (64.0%) patients had LVDD Figure 6 and Table 2.

In our study, 60 (93.8%) patients had LVDD grade 1 and 4 (6.3%) patients had LVDD grade 2 Figure 7 and Table 3.

In our study, 8 (8.0%) patients had LVSD Figure 8 and Table 4.

In our study, 12(12.0%) patients had Concentric left ventricular hypertrophy (LVH) Figure 9.

In LVDD, 2 (3.1%) patients were 30–40 years old, 14(21.9%) patients were 41–50 years old and 48(75.0%)

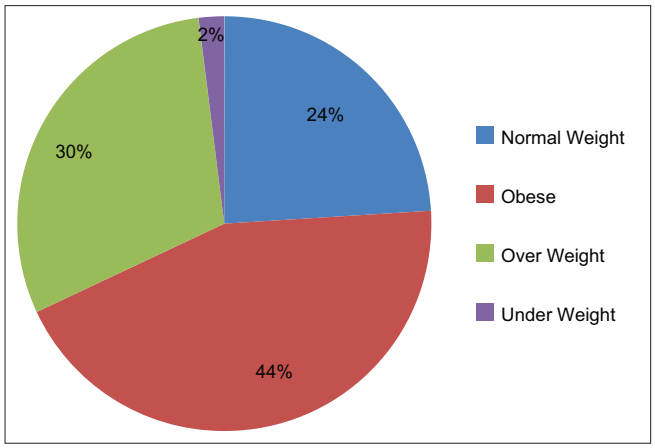

Figure 3: Distribution of body mass index

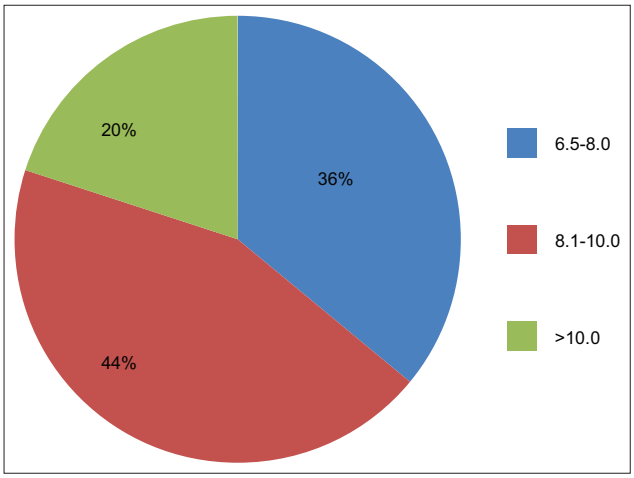

Figure 5: Distribution of glycosylated hemoglobin

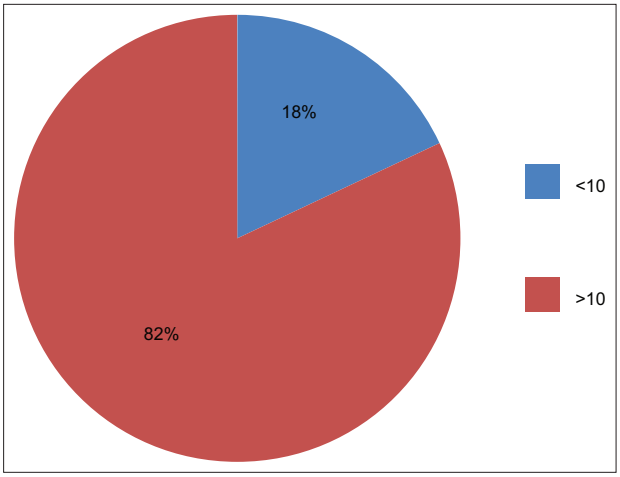

Figure 4: Distribution of duration of diabetes

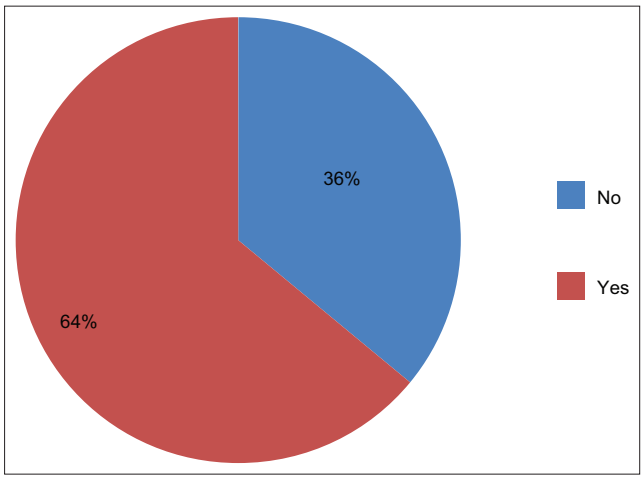

Figure 6: Distribution of left ventricular diastolic dysfunction

Table 1: Distribution of LVDD

LVDD	Frequency	Percent
No	36	36.0
Yes	64	64.0
Total	100	100.0

Table 2: Distribution of LVDD grade

LVDD grade	Frequency	Percent
Grade 1	60	93.8
Grade 2	4	6.3
Total	64	100.0

patients were 51–60 years old. Association of Age with LVDD was statistically significant ($P = 0.0002$) Figure 10.

In LVDD, 22(34.4%) patients were female and 42(65.6%) patients were male. The association of sex with LVDD was not statistically significant ($P = 0.1257$).

In the LVDD Group, 14(21.9%) patients had normal weight, 16(25.0%) patients had over Weight, 32(50.0%) patients were obese, and 2(3.1%) patients had under weight. Association of BMI with LVDD was not statistically significant ($P = 0.2218$) Figure 11.

In the LVDD Group, 2 (3.1%) patients were in <10 years duration of diabetes, 62 (96.9%) patients were in >10 years duration of diabetes. The Association between duration of diabetes and LVDD was statistically significant ($P < 0.0001$) Figure 12.

In LVDD, 6 (9.4%) patients were HBA1c level 6.5–8.0, 38 (59.4%) patients were HBA1c level 8.1–10.0 and 20 (31.3%) patients were HBA1c level >10.0. Association of HBA1c with LVDD was statistically significant ($P < 0.0001$) Figure 13.

DISCUSSION

The present study was carried out as an observational type hospital-based Cross-Sectional study at the Department

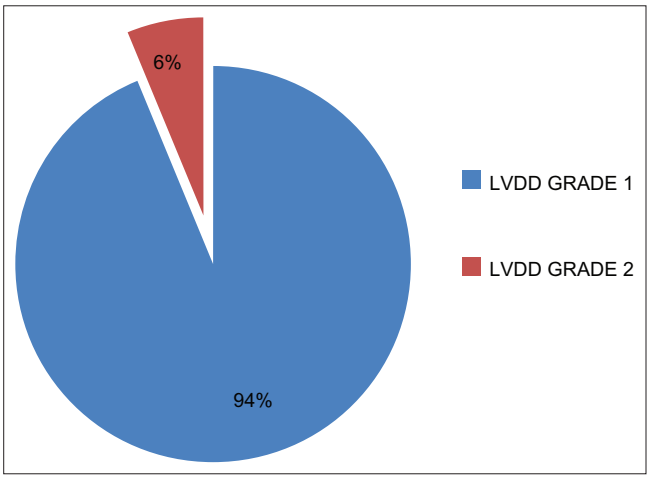

Figure 7: Distribution of left ventricular diastolic dysfunction grade

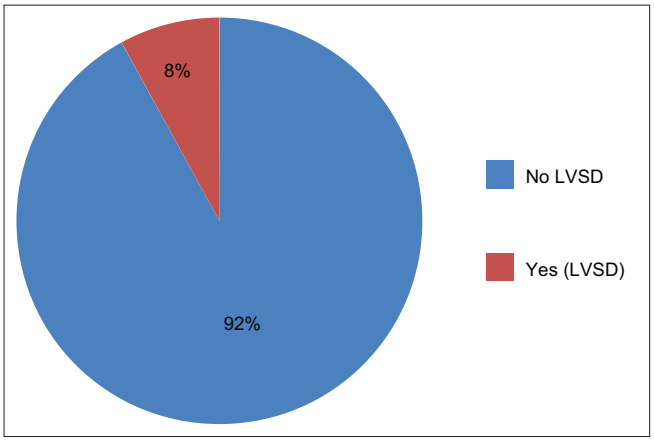

Figure 8: Distribution of left ventricular systolic dysfunction

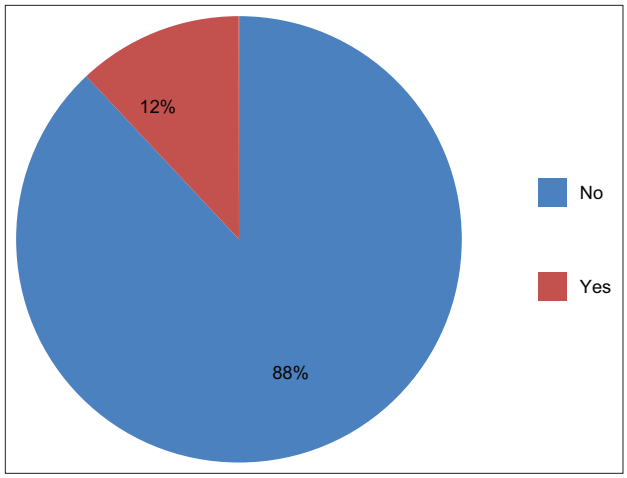

Figure 9: Distribution of concentric left ventricular hypertrophy

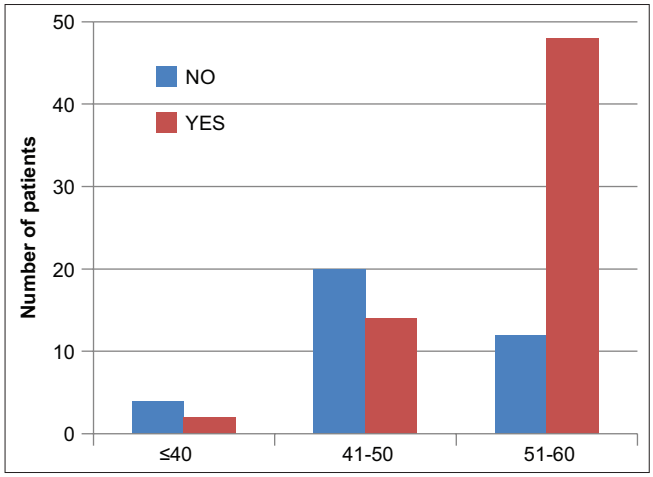

Figure 10: Association between age and LVDD

Table 3: Distribution of LVSD

LVSD	Frequency	Percent
No	92	92.0
Yes	8	8.0
Total	100	100.0

Table 4: Distribution of concentric LVH

Concentric LVH	Frequency	Percent
No	88	88.0
Yes	12	12.0
Total	100	100.0

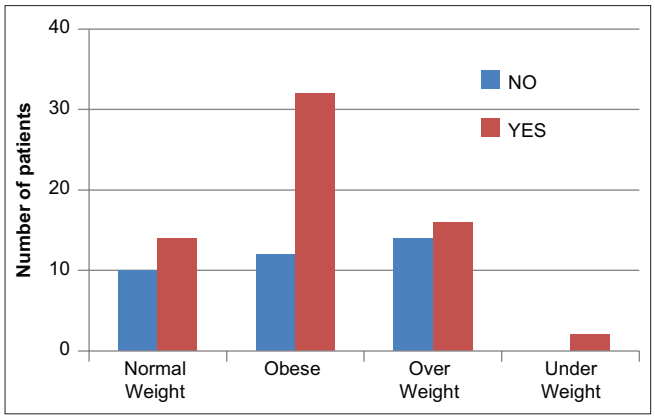

Figure 11: Association between BMI and LVDD

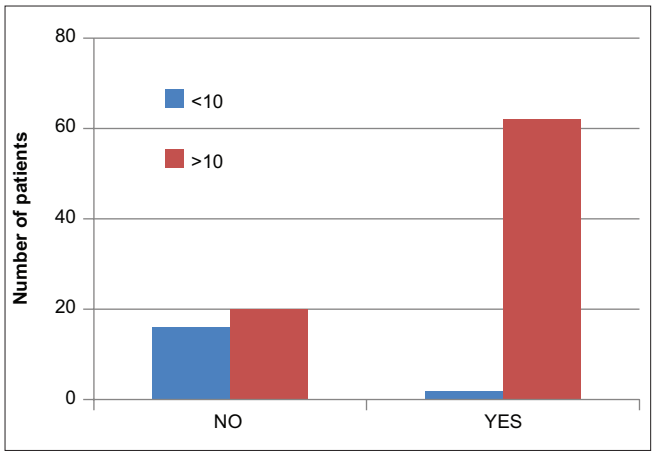

Figure 12: Association between duration of diabetes and left ventricular diastolic dysfunction

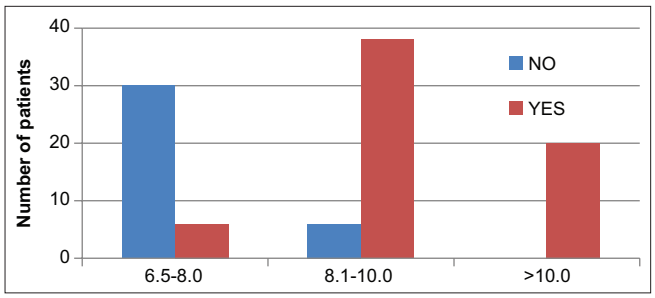

Figure13: Association between HBA1c and LVDD.

of General Medicine, AGMC, and GB Pant Hospital and taken 1 ½ years. We have collected data from Outpatient and inpatient with type 2 DM, as per ADA guidelines, attending the General Medicine department of AGMC and GBP Hospital as per the exclusion and inclusion criteria. A total of 100 patients was taken in our study.

In our study, out of 100 patients, 6.0% were ≤40 years old, 34.0% were between 41 and 50 years old and 60.0% were between 51 and 60 years old. 40.0% of patients were female and 60.0% patients were male out of 100 patients. About 18.0% were in <10 years duration of diabetes Group, 82.0% were in >10 years duration of diabetes group out of 100 patients. Our study found that 24.0% had normal weight, 44.0% were obese, 30.0% were over weight and 2.0% were under weight. Of 100 patients 36.0% had HBA1c level 6.5–8.0, 44.0% HBA1c level 8.1–10.0 and 20.0% had HBA1c level >10.0.

In our study, 64.0% of patients had LVDD out of 100 patients. Patil *et al.*[9] in their study observed LVDD in 64% of their patient, which is similar to our study. Ayman *et al.*[10] in their study observed LVDD in 61% of their patient, which is similar to our study. In our study, 93.8% had LVDD grade 1 and 6.3% of patients had LVDD grade 2, among LVDD patients. Arora *et al.*[11] in their study observed mild, moderate, and severe LVDD among 41%, 10%, and 2% of the subjects respectively, which is similar to our study. In our study, 8.0% of patients had LVSD among 100 patients. Arora *et al.*[11] 38% of patients were detected with LVSD. The finding in their study is not similar to our study. Kumar *et al.*[12] in their study assessed systolic function by fractional shortening (FS) and EF. EF though it is reduced in diabetes patients, it is within normal limits with a mean of 57.98 ± 2.1. The finding in their study is similar to our study. About 12.0% patients had Concentric LVH.

In our study we observed that among the patients with LVDD, 3.1% patients were between 30 and 40 years old, 21.9% patients were between 41 and 50 years old and 75.0% patients were between 51 and 60 years old. Association of Age with LVDD was statistically significant ($P = 0.0002$). Arora *et al.*[11] found Type II DM has a significant impact on the functioning of the left ventricular. This effect increases with the advancing age. Patil *et al.*[9] found there was a linear progression of diastolic dysfunction with the increase age group. Mahesh *et al.*[13] found that Diastolic dysfunction was found to be significantly higher among elderly individuals (60%) when compared to young study participants. The above three studies have similar findings as our study. Incidence of LVDD increases with increasing age. In our study, we found LVDD is more common among male patients (65.6%) compared to female patients (34.4%). In our study, we found among LVDD patients, 21.9% of patients had Normal Weight, 50.0% of patients were Obese, 25.0% of patients had over weight and 3.1% patients had under weight. The Association of BMI with LVDD was not statistically significant ($P = 0.2218$).

In our study we found, in LVDD Group, 3.1% of patients were in <10 years duration of diabetes, 96.9% patients were in >10 years duration of diabetes. The Association of duration of diabetes with LVDD was statistically significant ($P < 0.0001$). Patil *et al.*[9] found the prevalence of diastolic dysfunction increased with longer duration

of diabetes. **Ayman** *et al.*[10] found Diastolic dysfunction is highly prevalent in patients with newly diagnosed DM and is positively correlated with HbA1c level, obesity, dyslipidemia, and the duration of diabetes. Arora *et al.*[11] in their study observed that with the duration of the diabetes, the incidence of LVDD was increased. The findings from the above studies are similar to our finding, the incidence of LVDD increases with duration of diabetes.

In patients with LVDD, 9.4% patients were HBA1c level 6.5-8.0, 59.4% patients were HBA1c level 8.1–10.0 and 31.3% patients were HBA1c level >10.0. The Association of HBA1c with LVDD was statistically significant ($P < 0.0001$). Patil *et al.*[9] found Diastolic dysfunction was significantly associated with uncontrolled diabetes as assessed by HbA1c levels. Ayman *et al.*[10] found that LVDD was more prevalent in diabetic patients with HbA1c ≥ 8.1 (75%). The findings of the above studies are similar to our finding.

CONCLUSION

We found that most of the patients were 51–60 years old. In our study male population was higher than the female population. LVDD is found in 64% of patients. It was found that HBA1c was significantly increased in patients with LVDD. We found that the duration of diabetes >10 years was mostly observed in patients with LVDD which was statistically significant. In our study patients with Obese BMI were more observed with LVDD. Our study showed that the duration of diabetes and HBA1c were significantly increased in patients with LVDD.

From the present study, it can be concluded that the prevalence of LVDD in type 2 Diabetic Mellitus without any cardiovascular symptoms is much higher than previously suspected. Diastolic dysfunction is significantly associated with increasing age, duration of diabetes, and glycemic index assessed by HbA1c.

Early diagnosis and treatment for LVDD in diabetic patients without any cardiac symptoms will reduce the morbidity and improve the outcomes by preventing future development of heart failure. Hence, it can be suggested that all patients of diabetes should routinely undergo echocardiographic evaluation to assess cardiac function regardless of any clinical cardiac symptoms for long-term management.

LIMITATIONS

In spite of every sincere effort, my study has lacunae.

The notable shortcomings of this study are:

1. The sample size was small. Only 100 cases are not sufficient for this kind of study.
2. The study has been done in a single center.
3. The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out.
4. Ongoing COVID 19 pandemic and lockdown have further hampered the study.

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How to cite this article: Sarkar P, Debbarma BK. Echocardiographic Evaluation of Asymptomatic Type 2 Diabetes Mellitus Patients for Cardiovascular Disease in a Tertiary Care Hospital. Int J Sci Stud 2022;9(10):81-88.

Source of Support: Nil, **Conflicts of Interest:** None declared.