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# Diastolic Dysfunction in Type 2 Diabetes Mellitus Patients Presenting to Tertiary Care Hospital

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## ABSTRACT

***Objective***: To study the frequency of left ventricular diastolic dysfunction in patients with type 2 diabetes mellitus presenting to a tertiary care hospital.

***Study Design***: Cross sectional study.

***Place and Duration of Study***: Medicine Dept, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Mar to Aug 2022.

***Methodology***: Fifty-one patients between the ages of 30 to 65 years were enrolled, belonging to either gender, presenting to outdoor department, with diagnosed type 2 diabetes mellitus for at least 1 year, on oral hypoglycemic drugs or insulin, and no underlying hypertensive cardiac pathology or diastolic dysfunction. These patients were further analyzed using statistical software based on their 2D echocardiogram findings.

***Results***: Out of 51 type 2 diabetes mellitus patients, there were more males 32(62.7%) as compared to females 19(37.3%), with mean age of 52.25±8.09 years. We observed that 21(41.2%) patients did not have left ventricular diastolic dysfunction at the time of our study, but among these patients, 13(61.9%) had type 2 diabetes mellitus for 1-3 years while remaining 30(58.8%) patients had both type 2 diabetes mellitus and left ventricular diastolic dysfunction, with 13(25.5%) having grade-I, 10(19.6%) having grade-II and 7(13.7%) having grade-III categorization.

***Conclusion***: There was an increased risk of left ventricular diastolic dysfunction in type 2 diabetes mellitus with longer duration of disease and higher HbA1c. Patients with type 2 diabetes mellitus to be followed up for diabetic control and monitored for the presence of asymptomatic left ventricular diastolic dysfunction with measures to be taken to prevent it.

**Keywords**: Diastolic Dysfunction, Diabetes Mellitus, Left Atrial Volume Index, 2D Echocardiography.

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## INTRODUCTION

Diastolic function is the intrinsic filling property of the heart, due to which, diastole is critically related to heart rate (HR), heart rhythm, atrial systole, ventricular compliance, preload, and atrioventricular valve function.[1] During diastole, the heart ventricle remains elastic and compliant, with the capacity to receive incoming blood, to ensure effective filling, thus making the ventricles intrinsic distinctive features useful in the evaluation and quantification of diastolic function,[2] with diastolic dysfunction often noted as compromised left ventricular relaxation and increased left ventricle chamber stiffness, leading to elevated filling pressures,[3] causing Left Ventricle Diastolic Dysfunction (LVDD), which occurs when the myocardium of the left ventricular is non-compliant and unable to receive return blood from the left atrium.[3] While this can be a normal physiological response with an aging heart, it can also be due to elevated left atrial pressures, culminating in symptomatic diastolic congestive heart failure.[4] To assess diastolic function, functional variables of the heart are checked with corresponding pathological cut-off values including Mitral E/A ratio (0.9-1.5), E/e´ ratio (5-10cm/sec), Left Atrial Maximum Volume Index (LAVI) (16-28mL/m2), Deceleration Time (DT) (140-240 msec) and peak Tricuspid Regurgitation (TR) velocity (>2.8m/sec).[4,5] With type 2 diabetes mellitus (T2DM) on the rise globally, Pakistan is among the most vulnerable countries at risk for diabetes-associated mortality.[6,7] As T2DM is associated with vascular complications,[8] there is a close association between DM and cardiovascular disease (CVD), due to shared risk factors such as obesity, hypertension, and dyslipidemias[9] particularly noted on imaging where left ventricular dysfunction, thickened left ventricular wall, and increased left ventricular mass are manifestations of diabetic cardiomyopathy.[9] Thus, the rationale of this study was to assess the presence of Left Ventricular Diastolic Dysfunction occurring concurrently with T2DM, based on 2D echocardiogram.

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## METHODOLOGY

This was a cross-sectional study, done in the Department of Medicine, Pak Emirate Military Hospital, Rawalpindi Pakistan, from March 2022 to August 2022, after gaining approval of the hospital Ethics Committee via letter no. A/28/EC/446/2022. The sample size was calculated using the World Health Organization (WHO) sample size calculator, keeping confidence interval of 95%, margin of error of 5%, and reported prevalence of T2DM as 26.7%[6] after which estimated sample size came out to be 58. We used consecutive non-probability sampling to complete enrollment of required sample size. Patients were advised baseline investigations and 2D Echocardiogram on the basis of being outdoor (OPD) cases and advised follow-up. However, 7 patients out of total 58, were lost to follow-up.

**Inclusion Criteria**: Patients between the ages of 30 to 65 years, belonging to either gender, presenting to Outpatient Department (OPD) during the study period, with diagnosed T2DM for at least 1 year, on oral hypoglycemic drugs or insulin with no underlying hypertensive cardiac pathology, were included.

**Exclusion Criteria**: Patients aged below 30 years or more than 65 years, with pre-existing underlying heart pathology, pregnancy, BMI >30 kg/cm$^2$, chronic debilitating lung pathology, such as, Chronic Obstructive Pulmonary Disease (COPD), Asthma, Tuberculosis or having a terminal illness, were excluded.

Patients were advised baseline investigation including HbA1c, NT Pro-BNP, and 2D Echocardiogram to assess their diastolic function and ejection fraction to categorize patients into LVDD grade. 2-D Echo factors such as the ratio of mitral inflow E to mitral e' annular velocities (E/e'), LV mass index (LAVI), Deceleration Time (DT), and Peak Tricuspid (TR) velocity were visualized for categorization into different grades of LVDD.[10] Variables like age, gender, comorbid conditions, HbA1c, and duration of T2DM were collected on a pre-designed data collection form. The data were summarized as mean, frequency, and percentage and then analyzed via Statistical Package for the Social Sciences (SPSS) version 23.0. Pearson Chi-square was applied and a *p*-value of ≤0.05 was considered statistically significant.

## RESULTS

We analyzed the findings of a total of 51 patients, of which 32(62.7%) were male and 19(37.3%) were female, with a mean age of 52.25±8.09 years. There was no statistically significant relationship found between gender and presence of LVDD ($p$=0.917). Among our patients, 14(27.5%) had T2DM for 1-3 years, 19(37.3%) for 3-5 years and 18(35.3%) for more than 5 years ($p$<0.005). We found that 5(9.8%) patients were on dietary and lifestyle modifications whereas oral hypoglycemic drugs, insulin, and a combination of dietary, oral medication, and insulin were seen in 26(51.0%), 6(11.8%) and 14(27.5%) patients respectively ($p$=0.041). Associated comorbid conditions with T2DM were also seen, with 13(25.5%) individuals having no other comorbid condition whereas dyslipidemia, Hep B/C, and other chronic diseases like osteoarthritis, Inflammatory Bowel Disease (IBD), Acid Peptic Disease were seen in 14(27.5%), 10(19.6%) and 14(27.5%) individuals respectively ($p$=0.001). These are further explored in Table-I.

**Table-I: Patient Characteristics and their Association with Left Ventricular Diastolic Dysfunction (LVDD) (n=51)**

| Variable | | With LVDD | Without LVDD | *p*-value |
|---|---|---|---|---|
| **Gender** | Male: 32(62.7%) | 19(63.3%) | 13(61.9%) | 0.917 |
| | Female: 19(37.3%) | 11(36.6%) | 8(38.1%) | |
| **T2DM Duration (years)** | 1-3 yr: 14(27.5%) | 1(3.33%) | 13(61.9%) | <0.005 |
| | 3-5 yr: 19(37.3%) | 13(43.3%) | 6(28.5%) | |
| | >5 yr: 18(35.3%) | 16(53.3%) | 2(9.5%) | |
| **HbA1c** | 6.5 - 8.5% 17(33.3%) | 7(23.3%) | 10(47.6%) | 0.05 |
| | 8.6 - 10.0% 16(31.4%) | 8(26.6%) | 8(38.0%) | |
| | >10.0% 18(35.3%) | 15(50.1%) | 3(14.2%) | |
| **Comorbid** | Dyslipidemia 14(27.5%) | 8(26.6%) | 6(28.5%) | 0.001 |
| | Hep B/C 10(19.6%) | 8(26.6%) | 2(9.5%) | |
| | Misc: 14(27.5%) | 12(40.2%) | 2(9.5%) | |
| | None: 13(25.4%) | 2(6.6%) | 11(52.3%) | |
| **Medications** | Dietary Control 5(9.8%) | 1(3.33%) | 4(19.1%) | 0.041 |
| | OHGs: 26(51.0%) | 13(43.3%) | 13(61.9%) | |
| | Insulin: 6(11.8%) | 4(13.3%) | 2(9.5%) | |
| | OHGs+Insulin 14(27.5%) | 12(40.1%) | 2(9.5%) | |
| **EF** | 55-60% 20(39.2%) | 7(23.3%) | 13(61.9%) | 0.028 |
| | 50-55% 19(37.3%) | 13(43.3%) | 6(28.5%) | |
| | 40-49% 12(23.5%) | 10(33.3%) | 2(9.5%) | |

Glycosylated hemoglobin (HbA1c) levels were tested in all patients to assess glycemic control following the presence of LVDD. Out of 51 patients, 33(64.7%) had HbA1c in the range of 6.5 - 10.0% whereas 18(35.3%) had HbA1c >10.1% ($p$=0.05). We

observed that out of a total of 51 patients with T2DM, 21(41.2%) did not have LVDD while LVDD was observed in 30(58.8%) patients and classified into grades-I, II, and III with 13(25.5%), 10(19.6%), and 7(13.7%), in each grade, respectively ($p$<0.005).

A high frequency of LVDD was noted with advancing age and longer duration of disease as 30(58.8%) patients had LVDD of different grades, of which 25(83.3%) patients were in the age bracket of 50-65 years as compared to 5(16.7%) who were in the age of 30-49 years ($p$<0.005) as shown in Table-II.

**Table-II: Association of Left Ventricular Diastolic Dysfunction (LVDD) Grades with Age (n=51)**

| Age (years) | LVDD | | | | $p$-value |
|---|---|---|---|---|---|
| | None 21(41.2%) | Grade-I 13(25.5%) | Grade-II 10(19.6%) | Grade-III 7(13.7%) | |
| 30-49 19(37.2%) | 14(73.6%) | 3(15.7%) | 1(5.2%) | 1(5.2%) | <0.005 |
| 50-65 32(62.7%) | 7(21.8%) | 10(31.2%) | 9(28.1%) | 6(18.7%) | |

We found that a longer duration of T2DM poses a greater risk of LVDD and higher grades of dysfunction, as 16(53.3%) patients had T2DM for longer than 5 years ($p$<0.005), 13(43.3%) patients had T2DM for 3 to 5 years and only 1(3.33%) patient who had T2DM for less than one year, developed diastolic dysfunction ($p$<0.005), as shown in Table-III.

In our study, patients with HbA1c levels of more than 8.5% had a higher grade of diastolic dysfunction, with 30(58.8%) patients having LVDD, of which only 7(23.3%) had good glycemic control while 23(76.6%) patients had poor glycemic control, as shown in Table-IV.

## DISCUSSION

According to American Heart Association (AHA), the overall occurrence of LVDD is 47.8% in the presence of T2DM, increasing with advancing age and the duration of disease.[11,12] LVDD can present as symptomatic heart failure, with mid-range ejection fraction 40-49% and worsen to a reduced ejection fraction of EF <40%.[13] T2DM also causes diabetic cardiomyopathy especially when associated with longer duration of disease, poor glycemic control, and advancing age.[14] One study revealed that pooled prevalence for LVDD in patients with T2DM, among in-hospital population and general population, was 48% (95% confidence interval: 38%-59%) and 35% (95% confidence interval: 24%-46%), respectively,[14] similar to our findings. Another study found that, similar to our findings, the prevalence of diastolic dysfunction increased with advancing age, up to 23.1% in patients aged 30-39 years and 65.8% in patients aged 50-60 years ($p$=0.010) with increased risk of LVDD associated with longer duration of diabetes, up to 32.8% in patients with diabetes for <5 years to 75% in patients with diabetes for >10 years ($p$=0.05).[15] One study concluded that LVDD was more prevalent in diabetic patients with higher HbA1c levels (>8.1%), reflecting increased risk with poor glycemic control,[16] similar to multiple other studies which observed that in the population with LVDD, the mean HbA1c was found to be higher as compared to mean population HbA1c with higher grade LVDD as compared to normal or low grade LVDD.[17-19]

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**Table-III: Comparison of Left Ventricular Diastolic Dysfunction (LVDD) Grade with T2DM Disease Duration (n=51)**

| Duration of T2DM (years) | LVDD | | | | | $p$-value |
|---|---|---|---|---|---|---|
| | Absent: 21(41.2%) | Present: 30(58.8%) | | | | |
| | None 21(41.2%) | Grade-I 13(25.5%) | Grade-II 10(19.6%) | Grade-III 7(13.7%) | Total | |
| 1-3: 14(27.5%) | 13(61.9%) | 1(7.6%) | 0 | 0 | 1(3.33%) | <0.005 |
| 3–5: 19(37.3%) | 6(28.5%) | 7(53.8%) | 2(20.0%) | 4(57.1%) | 13(43.3%) | |
| >5: 18(35.3%) | 2(9.5%) | 5(53.8%) | 8(80.0%) | 3(42.8%) | 16(53.3%) | |

**Table-IV: Association of LVDD Grades with HbA1c in T2DM Patients (n=51)**

| HbA1c (%) | LVDD | | | | | $p$-value |
|---|---|---|---|---|---|---|
| | Absent: 21(41.2%) | Present: 30(58.8%) | | | | |
| | None 21(41.2%) | Grade-I 13(25.5%) | Grade-II 10(19.6%) | Grade-III 7(13.7%) | Total | |
| 6.5-8.5%: 17(33.3%) | 10(47.6%) | 5(38.5%) | 2(20.0%) | 0 | 7(23.3%) | <0.005 |
| 8.6-10.0%: 16(31.4%) | 8(38.1%) | 3(23.0%) | 4(30.0%) | 1(14.3%) | 8(26.6%) | |
| >10.1%: 18(35.4%) | 3(14.2%) | 5(38.5%) | 4(30.0%) | 6(85.7%) | 15(50.1%) | |

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## LIMITATION OF STUDY

The study was carried out in a single tertiary care setup with relatively small sample size. Extensive tests like stress electrocardiography, perfusion imaging, and coronary angiography were not done due to limited resources. For future studies, a larger sample size may be conducive in drawing definitive conclusions.

## CONCLUSION

Our study found that there is an increased risk of LVDD in patients with T2DM of longer duration and higher HbA1c due to which they require good glycemic control and timely monitoring for worsening of LVDD with active mitigation measures.

**Conflict of Interest:** None.

**Funding Source:** None.

**Authors' Contribution**

The following authors have made substantial contributions to the manuscript as under:

HAS & SWA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MY & SFZ: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

MH & MU: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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