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Left Ventricular Diastolic Dysfunction in Patients with Type 2 Diabetes Mellitus at a Tertiary Care Centre in Kanpur: A cross-sectional study

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Abstract-

Introduction- Diabetes mellitus (DM) is a chronic illness with a high morbidity rate due to its complications. According to the data, left ventricular diastolic dysfunction (LVDD) is prevalent in people with type 2 diabetes mellitus (T2DM). Thus in order to postpone or prevent the onset of HF and to provide a methodically targeted intervention aiming at lowering morbidity and mortality in patients with T2DM, this study was planned to evaluate the prevalence and predictors of diastolic dysfunction in T2DM.

Material and method- The current study was a cross sectional study conducted on 300 T2DM patients with age from 30-60years. Vitals and variables like age, sex, body mass index (BMI) and duration of DM were noted. Systemic and respiratory examination was done. Radiographic examination of the diabetics included electrocardiography (ECG) and plane chest x ray. Left ventricular diastolic dysfunction (LVDD) was evaluated by pulsed doppler echocardiography. All the data were noted on a pre-structured proforma and were analyzed by using SPSS-16. The 'p value less than 0.05 was considered statistically significant'.

Result- The present study showed male dominance with mean age of the subjects as 50.08±6.32years. Albuminuria was seen in half of the cases and LVDD was found in 51.6% of

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T2DM patients. The association of sex with LVDD, its grades and albuminuria was statistically significant. The high incidence of diastolic dysfunction in normotensive and asymptomatic T2DM was observed even at the time of diagnosis and this finding showed a positive correlation with HbA1C, age, sex and duration of DM. No significant correlation was found with BMI. LVDD was present significantly in diabetic patients with duration of diabetes >5years.

Conclusion- In our study, LVDD was more prevalent in T2DM patients. So our result suggests optimal glycemic control and emphasizes the importance of screening for subclinical diastolic dysfunction in all T2DM patients especially in advanced age.

Keywords- LVDD, Diastolic heart failure, HF, T2DM etc.

Introduction-

Diabetes mellitus (DM) is a chronic illness with a high morbidity rate and a fast rising incidence rate globally. It was estimated that 536.6 million people between the ages of 20 and 79 had diabetes in 2021, with a prevalence of 10.5%. By 2045, that number is expected to rise to 783.2 million, with a prevalence of 12.2%.[1] Several cardiovascular risk factors, including dyslipidemia, hypertension, and obesity, are exacerbated by type 2 diabetes mellitus (T2DM), a metabolic disease marked by hyperglycemia and insulin resistance.[2,3] The term "Left ventricular diastolic dysfunction" (LVDD), "diastolic heart failure" (DHF), or "HF with normal ejection fraction" (HFNEF) was coined to describe patients who exhibit heart failure (HF) symptoms and signs despite having a nearly normal left ventricular (LV) systolic function. LVDD is frequently underdiagnosed in diabetes, in contrast to left ventricular systolic dysfunction (LVSD). In patients with diabetes, LVDD is believed to occur before LVSD does, and as it can progress to LVSD, it is linked to a poor prognosis.[4] According to earlier research, LVDD is common in people with type 2 diabetes.[5] T2DM was shown to be independently linked to asymptomatic LVDD by the Strong Heart Study.[6] Regardless of the impact of pertinent confounders, numerous epidemiological investigations have demonstrated a markedly elevated frequency of heart dysfunction in diabetes individuals. Numerous studies have shown that even in the absence of hypertension and coronary artery disease, diabetics have a high risk of HF (54.33%). It has been found that between 43-75 percent of these patients had impaired LV diastolic function.[7-9] One of the earliest preclinical signs of diabetic cardiomyopathy is

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believed to be LVDD, which can occur before systolic dysfunction and progress to symptomatic HF.[10] In the absence of treatment, diastolic dysfunction can eventually develop into DHF, which is why it's critical to detect it early. According to the data, diastolic dysfunction in diabetics appears before systolic dysfunction. According to many views, cardiac dysfunction in diabetic individuals may be influenced by hyperglycemia. It is unknown what causes this LVDD in diabetics.[11] However, a number of studies have demonstrated that early diastolic dysfunction in T2DM may be linked to poor glycemic management and a longer duration of diabetes.[12,13] A review of the new pertinent echocardiographic criteria and other revisions is therefore warranted because the early echocardiographic diagnosis of LVDD in these patients is of significant practical importance.[14] With few studies conducted on Asian patients, the majority of data on HF in T2DM has come from Caucasian populations. Research to evaluate LVDD in T2DM patients in our population is necessary because of the high prevalence of T2DM, the substantial morbidity and mortality of HF in T2DM, and the variations in clinical characteristics, prevalence, and predictors of HF among Asian ethnic groups. In order to postpone or prevent the onset of HF and to provide a methodically targeted intervention aiming at lowering morbidity and mortality in patients with T2DM, this study was planned to evaluate the prevalence and predictors of diastolic dysfunction in T2DM.

Material and Methods

The current study was a cross sectional study conducted on type 2 diabetes mellitus (T2DM) patients visiting the L.P.S Institute of cardiology, Kanpur, India for 3 years from 2019 to 2021. All normotensive patients diagnosed with T2DM with age from 30 to 60years were enrolled for the study. Patients were considered diabetics based on the American diabetes association (ADA) recommendation. Patients with fasting plasma glucose (FPG) ≥126mg/dl, random blood sugar (RBS) ≥200mg/dl during an oral glucose tolerance test (OGTT) performed as described by the World Health Organization (WHO) or patients with classic symptoms of hyperglycemia or hyperglycaemic crisis with a RBS ≥200mg/dl or with glycosylated hemoglobin (HbA1C) ≥6.5% were considered diabetics. The ethical clearance was obtained from the ‘Institutes Ethics Committee’ and informed consent was taken from all the participants. Patients who were hypertensive, not willing to participate and had valvular heart disease, ischemic heart disease

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(IHD), congenital heart failure (CHF), cardiomyopathies, severe anemia, chronic renal failure, haemoglobinopathy and chronic pulmonary disease were excluded from the study. Thorough general examination of the patients was done especially for the presence of pallor, anasarca and all peripheral pulses. Vitals, blood pressure (BP), respiratory rate (RR), pulse rate (PR), temperature of the diabetics were noted and systemic examination including cardiovascular and respiratory examination was done. Variables like age, sex, height, body weight, body surface area, duration of DM and body mass index ((BMI) were noted. Laboratory investigations included blood and urine analysis. Blood analysis was conducted to analyze haemogram, FPG, post prandial plasma glucose (PPPG), RBS, HbA1C, blood urea, serum creatinine and fasting lipid profile of the patients. Urine analysis was done to analyze urinary albumin creatinine ratio (UACR) and for routine & microscopic examination of the urine. For blood analysis, venous blood was collected after 8 hours fasting using aseptic measures and for urine analysis morning urine sample was collected in a container. Radiographic examination of the diabetics included electrocardiography (ECG) and plane chest x ray. Left ventricular diastolic dysfunction (LVDD) was evaluated by pulsed doppler echocardiography. Pulsed- wave doppler (PWD)-derived transmitral inflow velocities was obtained in the apical 4-chamber view, with the sample volume placed at the mitral valve leaflet tips. Measurements included the transmitral early diastolic rapid filling (E-wave) and atrial contraction late filling (A-wave) velocities to calculate E/A ratio, isovolumteric relaxation time (IVRT) and deceleration time (DT). For tissue doppler imaging (TDI), the mitral annulus velocity was obtained with a 2 mm sample volume lateral side and septal side of the mitral annulus. Diastolic dysfunction was labeled according to the standard guidelines. Left ventricular overall ejection fraction (systolic function) was calculated by modified Simpson‘s method; and, LVEF ≥ 50% was considered as normal. All echocardiographic measurements were averaged over three consecutive cardiac cycles, measured by a single investigator blinded to all other variables. The five recommended variables for identifying Diastolic Dysfunction and their abnormal cutoff values were annular/septal e′ velocity <7cm/sec, lateral e′ velocity <10cm/sec, average E/e′ ratio>14, LA volume index >34ml/min^2 and peak TR velocity >2.8m/sec. LVDD was classified into grade I, II and III. In patients with normal EF, if E/A ratio was <0.8 along with peak E velocity of <50 cm/sec, the mean LAP was either normal or low and the patient had grade I diastolic dysfunction. If E/A ratio is >2, LA MAP is elevated and grade III diastolic dysfunction present. If E/A ratio <0.8

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along with a peak E velocity of >50 cm/sec, or an E/A ratio>0.8 but <2, then additional parameter was needed e g- TR jet velocity (>2.8m/sec), average E/e′ (>14) and LA volume index (34 ml/min^2). If more than half of all variable met the cut off value, then LAP was elevated and grade II diastolic dysfunction was present. If only one of 3 available variables met the cut off value, then LAP was normal and grade I diastolic dysfunction was present. All the data were noted on a pre-structured proforma. Data were analyzed for mean, percentage, standard deviation, student t- test, fisher‘s exact test, by using SPSS-16 (Statistical Package for the Social Sciences). The t-test and fisher‘s exact test were applied to study quantitative and qualitative data, respectively and ‘p value less than 0.05 was considered statistically significant’.

Result-

The current study was done on 300 normotensive T2DM patients with age from 30-60years. The mean age of the subjects was 50.08±6.32years. As seen in figure 1, age was further divided into three groups with maximum patients were in the age group of 50-60years i.e. 180(60%) followed by 40-49years and 30-39years with 108(36%) and 12 (4%) patients respectively.

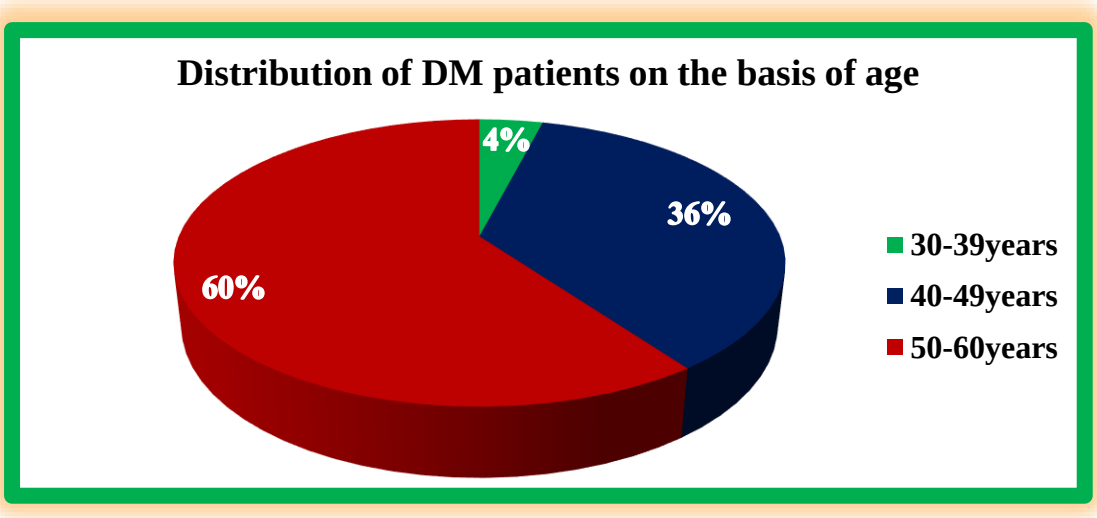

Figure 1- Distribution of DM patients on the basis of age

Table 1 shows mean of the study variables. The mean age of males in present study was 50.70±5.73years and of females was 48.91±6.99years. The mean FPG, HbA1c, BMI and duration of DM was 183.77±29.74mg/dl, 7.48±0.77%, 25.43±2.56 kg/m^2 and 5.91±3.46years respectively.

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Table 1 – Mean of the study variables.

Variable		Mean±SD
Age (years)		50.08±6.32
Mean age (years)	**Males**	50.70±5.73
	Females	48.91±6.99
FPG (mg/dl)		183.77±29.74
HbA1c (%)		7.48±0.77
BMI (kg/m^2)		25.43±2.56
Duration of DM (years)		5.91±3.46

The present study showed male dominance with 180(60%) males and 120(40%) females.

Table 2 clearly shows that LVDD was present in 155(51.66%) T2DM patients. Out of 155 LVDD patients, 118(76.12%) were males and 37(23.87%) were females.

Table 2- Distribution of patients based on different parameters

Parameter	Male	Female	Total
LVDD present	118	37	155 (51.66%)
LVDD absent	62	83	145 (48.34%)
Total	180	120	300 (100%)

Table 3- Sex wise distribution of T2DM patients based on different parameters. LVDD was observed in 118(65.55%) males and 37(30.83%) females. However the rest 62(34.44%) T2DM males and 83(69.16%) females did not report any LVDD. Further LVDD had two grades i.e. grade I and II as detected by 2D echocardiography. Grade I LVDD was assessed in 110(61.11%) males and 26(21.66%) females whereas grade II was seen in 08(4.44%) males and 11(9.16%) females. Albuminuria was seen in half of the T2DM patients. Out of 180 males, 130(72.22%) reported the presence of albuminuria and in rest 50(27.77%), it was absent. Maximum females i.e. 100(83.33%) did not report albuminuria, whereas in 20(16.66%) females, it was found to be present. The association of sex with LVDD, its grades and albuminuria was statistically significant. As far as age groups are concerned, maximum i.e. 110(61.11%) males were from the age group of 50-60years followed by 40-49years and 30-39years with 60(33.33%) and

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10(5.55%) males respectively. Females also mainly belonged to age group of 50-60years with 70(58.33%) females followed by 40-49years and 30-39years with 48(40.00%) and 02(1.66%) females respectively. However the association of age groups with sex was not statistically significant.

Table 3- Sex wise distribution of T2DM patients based on different parameters

Parameters		Males n(%) n=180	Females n(%) n=120	P value
LVDD	Present	118(65.55%)	37(30.83%)	**0.0000**
	Absent	62(34.44%)	83(69.16%)	
LVDD grade	Grade I	110(61.11%)	26(21.66%)	**0.0002**
	Grade II	08(4.44%)	11(9.16%)	
Albuminuria	Present	130(72.22%)	20(16.66%)	**0.0000**
	Absent	50(27.77%)	100(83.33%)	
Age group	30-39years	10 (5.55%)	02(1.66%)	0.5223
	40-49years	60(33.33%)	48(40.00%)	
	50-60years	110(61.11%)	70(58.33%)	

Figure 2 depicts sex wise distribution of T2DM patients based on the type of albuminuria. Microalbuminuria was mainly observed in our study with102(56.66%) males and 14(11.66%) females. Where as macroalbuminuria was seen in 28(15.55%) males and 6(5.00%) females. The association of type of albuminuria with sex was not significant with p value of 0.4001.

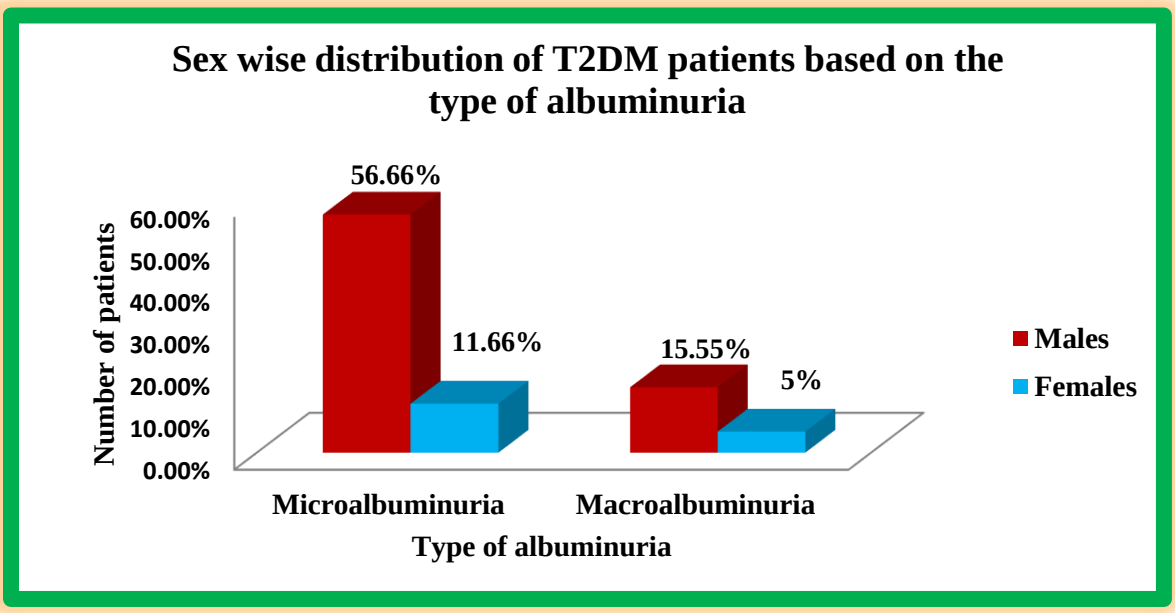

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Figure 2- Sex wise distribution of T2DM patients based on the type of albuminuria

Table 4 compares different parameters between patients with and without LVDD. Mean FPG of population with LVDD was 189.85±30.92mg/dl and that of population without LVDD was 174.45±29.81mg/dl This shows that FPG was positively associated with the incidence of LVDD in population as mean of FPG of population with LVDD was higher as compare to population without LVDD and correlation was found very significant (p=0.0140). The mean HbA1C of population with LVDD was higher i.e. 7.67±0.90% as compare to population without LVDD i.e. 7.24±0.64%. Correlation was found significant using unpaired t test (p value =0.0057). This signifies that higher the value of HbA1C at the time of diagnosis, higher will be the incidence of LVD. Mean age of population with LVDD was 52.46±5.59years and that of population without LVDD was 48.42±6.15years. Age was positively associated with the incidence of diabetic LVDD in population as mean of age of population with LVDD was higher as compare to population without LVDD and correlation was found very significant (p=0.0057) Mean body mass index of population with LVDD was 25.89±2.64kg/m² and that of population without LVDD was 24.95±2.45kg/m². BMI was not positively associated with the incidence of diabetic LVDD in population as mean BMI of population and correlation was not significant (p=0.0702). Mean duration of diabetes of population with LVDD was 7.200±3.200years and that of population without LVDD was 3.200±1.600years. Correlation was found very significant between duration of diabetes and LVDD using t test (p value =0.0001).This correlation suggests that the higher the duration of DM, higher the incidence of LVDD. Out of 150 albuminuria T2DM patients, 102(68%) had LVDD and 48(32%) were without LVDD. 53(35.33%) T2DM patients with LVDD and 97(64.66%) without LVDD did not report any albuminuria. The association of albuminuria with LVDD was statistically significant with p value of 0.0001

Table 4- Comparison of parameters among patients with and without LVDD

Parameters		With LVDD	Without LVDD	P value
No. of Patients		155(51.66%)	145(48.33%)	----
FPG (mg/dl)		189.85±30.92	174.45±29.81	**0.0140**
HbA1C (%)		7.67±0.90	7.24±0.64	**0.0057**
Age (year)		52.46±5.59	48.42±6.15	**0.0012**
BMI (kg/m²)		25.89±2.64	24.95±2.45	0.0702
Duration of DM (years)		7.20±3.20	3.20±1.60	**0 .0001**
Albuminuria	**Present**	102(68%)	48(32%)	**0.0001**
	Absent	53(35.33%)	97(64.66%)	

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Figure 3 clearly shows that LVDD patients with duration of T2DM from 0-5years were 45(15%) and 110(36.66%) with duration of diabetes >5years. Patients without LVDD with duration of T2DM from 0-5years were 101(33.66%) and 44(14.66%) with duration of diabetes >5years. LVDD was present significantly in diabetic patients with duration of diabetes >5 years with p value of 0.0010.

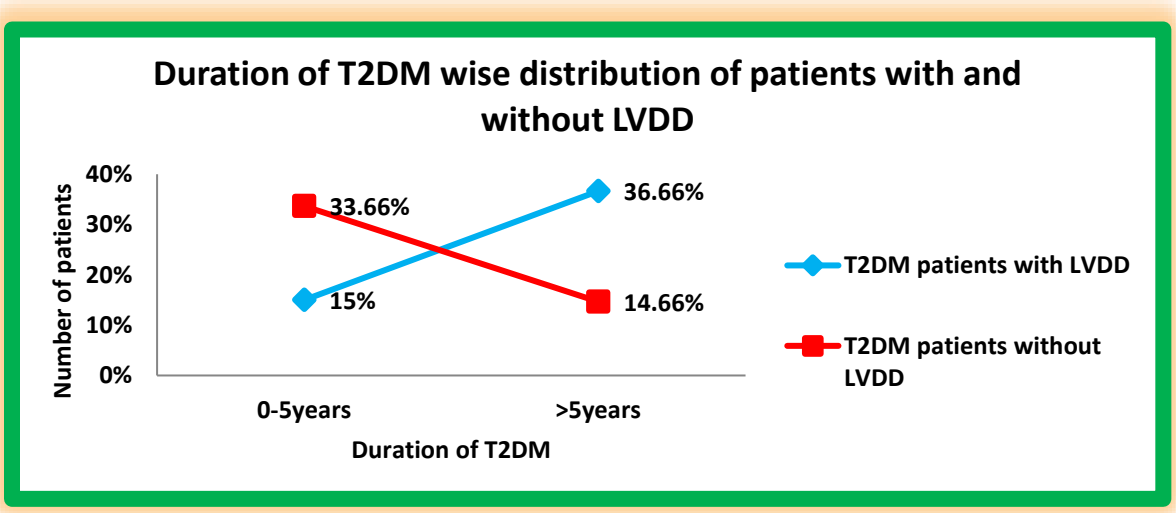

Figure 3- Duration of T2DM wise distribution of patients with and without LVDD

Discussion-

Diabetes Mellitus is a multifactorial disease, associated with a number of microvascular and macrovascular complications. Type 2 DM is likely to remain undiagnosed for years. The gap between the onset of the disease and clinical diagnosis of diabetes leads to the development of these chronic complications, which are the leading causes of premature mortality among diabetic patients. We assessed the incidence of cardiovascular changes and their correlation with various parameters like glycosylated haemoglobin (HbA1C), FPG, age, body mass index (BMI), duration of DM in 300 normotensive type 2 diabetic patients between the age of 30 to 60 years. The mean age of the subjects in our study was 50.08±6.32years. However the study by Srivastava PM et al.[15] and Khalil SI et al.[16] found mean age to be 60±1years and 40.79±7.65years respectively. Maximum patients of our study were in the age group of 50-

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60years. This finding is in contrast to the study by Sawan Kumar Shukla et al.[17] as they found, the prevalence of diastolic dysfunction in the 41-50-year-old group to be approximately 80%. In present study, LVDD was found in 51.6% of T2DM patients. This finding is strongly supported by Patil et al.[18] as in their study, 54% of patients with T2DM had asymptomatic LVDD. In a study from Nepal, Yadava et al. also found a fairly similar prevalence of 47.8% for LVDD in T2DM patients[19] Bouthoorn et al. also found a comparable prevalence for LVDD in a comprehensive systematic analysis, in 48% of hospitalized T2DM patients and 35% of community-dwelling T2DM patients.[20] Sawan Kumar Shukla et al.[17] reported the prevalence of LVDD as 56.66% in T2DM patients. This suggests that all patients with T2DM should undergo screening for LVDD. Mishra et al.[21] due to high incidence of LVDD in diabetics, documented T2DM as a strong independent predictor of asymptomatic LVDD. However, in contrast to our study, Poulsen et al.[22] and Jain et al.[23] found a much lower prevalence of 40% and 30% respectively for LVDD in T2DM.

Our study showed a predominance of Grade I LVDD (45.3%) evidenced by delayed relaxation time pattern in pulsed doppler echocardiography. No case of LV systolic dysfunction was found. This outcome is in harmony with the study by K. M. Hassan Ayman et al.[24] as they reported 52% to have grade I LVDD. Our study demonstrated that presence of albuminuria which can be a risk factor for earliest cardiovascular changes like increased LV mass and LVDD. These correlations are supported by similar findings in a study done by Soichi Kurioka et al.[25] in Japan by studying relationship of severity of nephropathy and LVDD in T2DM. The current study demonstrates high incidence of diastolic dysfunction in normotensive and asymptomatic T2DM, even at the time of diagnosis and this finding had a positive correlation with HbA1C, age, sex and duration of DM. No significant correlation was found with BMI. Our findings are supported by Kumar et al.,[26] Jain et al.,[27] and Suresh et al.[28] as they documented, patients with increased HbA1c to have higher prevalence of diastolic dysfunction. Yadava et al. also found an association between LVDD and advanced age and longer duration of T2DM, however they could not find any association with increased HbA1C.[19] Sawan Kumar Shukla et al.,[17] and Srivastava PM et al.[15] in their study, stated that advanced age in T2DM is a risk factor for diastolic dysfunction. However, in a study done by Hassan Ayman KM et al., diastolic dysfunction was not associated with age, but was linked to duration of DM[24] Our observations are in agreement with Patil et al.[18] who reported a strong correlation between LVDD and DM

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duration and HbA1c, however they also found correlation with obesity. Virendra C Patil et al.[29] also found incidence of LVDD to be positively correlated to BMI unlike our study. Presence of other confounding variable could be a cause of this dissimilarity. LVDD was present significantly in diabetic patients with duration of diabetes >5 years. Similarly, From AM et al.[30] observed that a duration of diabetes >4years to be independently associated with LVDD. Accordingly, early detection of LVDD at the time of DM diagnosis and competent control of hyperglycaemia could interfere with the progression to overt HF and might even improve the prognosis of such patients.

Conclusion-

In our study, LVDD was more prevalent in T2DM patients. The majority of patients with LVDD were grade I. The occurrence of albuminuria, longer duration of type 2 diabetes, worse glycemic control, and advancing age were all linked to the LVDD. Our result suggests optimal glycaemic control and emphasizes the importance of screening for subclinical diastolic dysfunction in all T2DM patients especially in advanced age, even those who do not have a history of cardiovascular disease or hypertension. Frequent screening and monitoring for any cardiac dysfunction can aid in the early identification and prompt, effective therapeutic management of LVDD in diabetics, which will lower the morbidity and will improve disease outcomes. To determine the connection between LVDD and T2DM and related complications, more longitudinal research is required.

Conflict o interest: None

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