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Study on Type 2 Diabetes Mellitus and Left Ventricular Diastolic Dysfunction at a Tertiary Care Centre

Rajat Kumar Tuteja[1], Dashrath Kumar[2] , Niharika Singh[3], Neha bagga[4], S.L .Mathur[5],

[1]Assistant Professor General medicine, Dr. S.N. Medical College, Jodhpur
[2]Assistant Professor General medicine, Dr. S.N. Medical College, Jodhpur
[3]Senior Resident General Medicine AIIMS Jodhpur
[4]Assistant Professor, Department of Pathology, Dr. S.N. Medical College, Jodhpur
[5]Senior Professor, Department of Medicine, Dr. S. N. Medical College, Jodhpur

Corresponding Author: Neha Bagga

Abstract:

Introduction: - Left ventricular diastolic dysfunction (LVDD) represents first stage of diabetic cardiomyopathy. It precedes changes in systolic function and hence highlights the importance of early evaluation of ventricular function in individuals with Diabetes Mellitus type 2 (DM). Presently very few studies have been carried out in India to study the relation of LVDD in DM (type2). So the present study was undertaken to evaluate LVDD in normotensive type 2 DM patients.

Objectives: - To determine the incidence of LVDD in normotensive type2 DM patients and its relation to age, duration of DM and HbA1c.

Materials and Methods:- The study was done on 75 type 2 normotensive diabetes mellitus patients and compared to the control group (75 patients). A detailed clinical history, physical examination and Doppler echocardiography was done to find out the prevalence of diastolic dysfunction.

Results:- Out of total 75 cases 46 (61.33%) showed LVDD and 5 (6.67%) amongst 75 in the control group population showed the LVDD ($P < 0.01$). Patients with a longer duration of DM (>10 years) had a higher prevalence of diastolic dysfunction ($P < 0.001$). Patients with HbA1c > 8.0% had a higher prevalence of diastolic dysfunction than subjects with HbA1c < 8.0% ($P < 0.01$).

Conclusion:- LVDD is prevalent among type II diabetic patients in Western Rajasthan without symptomatic heart disease. Echocardiography is of immense benefit in the management of type II DM patients as this will enhance early detection of left ventricular diastolic dysfunction.

Keywords: Diabetes Mellitus, Left Ventricular Diastolic, HbA1c, IDF

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorder that shares phenotype of hyper-glycaemia. The incidence of diabetes mellitus (DM) is increasing worldwide. The Indian Council of Medical Research-Indian Diabetes Study 2011 (ICMR-INDIAB) estimates that currently India has 62.4 million people with DM. The majority (>90%) of them have Type 2 DM.[1] It is predicted that by 2030 diabetes mellitus may afflict up to 79.4 million individuals in India. According to the International Diabetes Federation (IDF) (2015) 415 million people in the world live with diabetes. [2]

DM is one of the major risk factors for diastolic heart failure (DHF). Over the last three decades, a number of epidemiological, clinical and autopsy studies have proposed the presence of diabetic heart disease as a distinct clinical entity. Diastolic heart failure (DHF) is also referred to as HF, with preserved left ventricular systolic function. Many

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studies have reported that the incidence of heart failure in diabetic subjects is high even in the absence of hypertension and coronary artery disease. Studies have also reported a high prevalence of pre-clinical diastolic dysfunction among subjects with DM. [3]

Left ventricular diastolic dysfunction (LVDD) represents the first stage of diabetic cardiomyopathy preceding changes in systolic function, reinforcing the importance of early evaluation of ventricular function in individuals with diabetes.[4,5] The diastolic abnormalities are present in diabetic patients in absence of diabetic complications of cardiovascular system.[6-8]

Presently very few studies have been carried out in India to study the relation between diastolic dysfunction in DM (type2). So the present study was undertaken to evaluate left ventricular dysfunction in Normotensive type 2 Diabetes mellitus patients.

Objectives: -

1. To determine the incidence of LV diastolic dysfunction in normotensive type2 DM patients and to compare it with normal subjects.
2. To assess the relation of LV diastolic dysfunction with age, duration of DM, and HbA1c.

Material And Methods:-

This study was conducted on 75 Type 2 normotensive diabetes mellitus patients attending the Department of Internal Medicine at DR SN Medical College & AIIMS Jodhpur and compared to the control group (75 patients). Participants after understanding the study protocol and procedures were asked to given their written consents for the study. The study is a hospital based cross-sectional study where the study populations were selected from the Diabetics Clinic, General medical wards and OPD's.

Inclusion Criteria:-

1) All cases of Type 2 DM diagnosed by ADA criteria
2) BP: <130/90 (at least 3 recordings with the highest recording taken into consideration

Exclusion Criteria:-

1) Systemic Hypertension (BP>140/90)
2) Ischemic heart disease (abnormal E.C.G. and RWMA on Echo)
3) Congestive Heart failure
4) Congenital or Acquired valvular Heart Disease
5) Chronic renal failure
6) Palpitation raised JVP
7) PDR/NPDR
8) Chronic pulmonary disease
9) Severe anemia
10) Haemoglobinopathies

The diagnosis of diabetes will make on the basis of clinical evaluation, biochemical and ancillary investigation fasting plasma glucose (FPG)/postprandial plasma glucose (PPPG) and HbA1C according to recent American Diabetic Association (ADA) recommendations.

Criteria for the diagnosis of DM include one of the following:

• Fasting plasma glucose ≥7.0 mmol/L (≥126 mg/dL)

• Symptoms of diabetes plus a random blood glucose concentration ≥11.1 mmol/L (≥200 mg/dL)

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• Haemoglobin A1C >6.5%

A detailed clinical history with specific reference to cardiovascular symptoms, drug intake and smoking was taken. A complete general and systemic examination was carried out. A normal resting electrocardiogram and chest radiograph were prerequisites for participation. Plasma glucose (fasting and post prandial) was measured by the glucose oxidase method and the urine sugar by Benedict's reagent. Biochemical investigations in the form of blood urea, serum creatinine and serum cholesterol were also carried out enzymatically. A standard 12 lead electrocardiogram and a transthoracic echocardiogram in all its modes (M, colour Doppler) were carried out.

Echocardiography:-

All the subjects (all diabetic patients and healthy volunteers) were evaluated by transthoracic 2-D and Doppler Echocardiography to assess left ventricular diastolic function. Echocardiographer was not aware of this study to avoid bias in the interpretation. Measurements of the different cardiac chambers were made according to recommendation of the American Society of Cardiology. All examinations were performed using an ALOKA SSD 2000 machine 2.5MHz transducer.

The following were register on assessment:
1. Ejection Fraction
2. LV mass
3. Mitral Early filling velocity (E), Mitral late atrial filling velocity (A), E/A then derived
4. IVRT (Isovolumic relaxation time)
5. DT (Deceleration time)

Left Ventricular diastolic dysfunction was considered to be present if any of the following findings were seen:
• E/A ratio < 1 or > 2
• DT < 150 or > 220 ms,
• IVRT < 60 or > 100 ms, or
• E/E' ratio > 15 {ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (E')}[9, 10]

Classification of LVDD

Grade1: Delayed relaxation time i.e. E/A

Grade 2: Pseudo normalisation

Grade 3: Reversible restrictive pattern

Grade 4: Irreversible restrictive pattern

Statistical analysis:

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package. Using this software, frequencies, percentage, mean, standard deviation, x2 and 'p' values were calculated.

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Observations and Results:- The present study included 75 patients with type 2 Diabetes mellitus who fulfilled inclusion criteria and were admitted at the Mathura Das Mathur Hospital, attached to Dr. S.N. Medical College, Jodhpur. The data obtained from these cases formed the basis of our study.

Data analysis revealed the results on the following:-

Table 1 Age and Sex Distribution among Case population

Age	CASE DISTRIBUTION		
	F	M	Total
<50	5 (6.67%)	11 (14.67%)	**16 (21.33%)**
50-60	6 (8%)	22 (29.33%)	**28 (37.33%)**
>60	15 (20%)	16 (21.33%)	**31 (41.33%)**
	26 (34.67%)	49 (65.33%)	75 (100%)

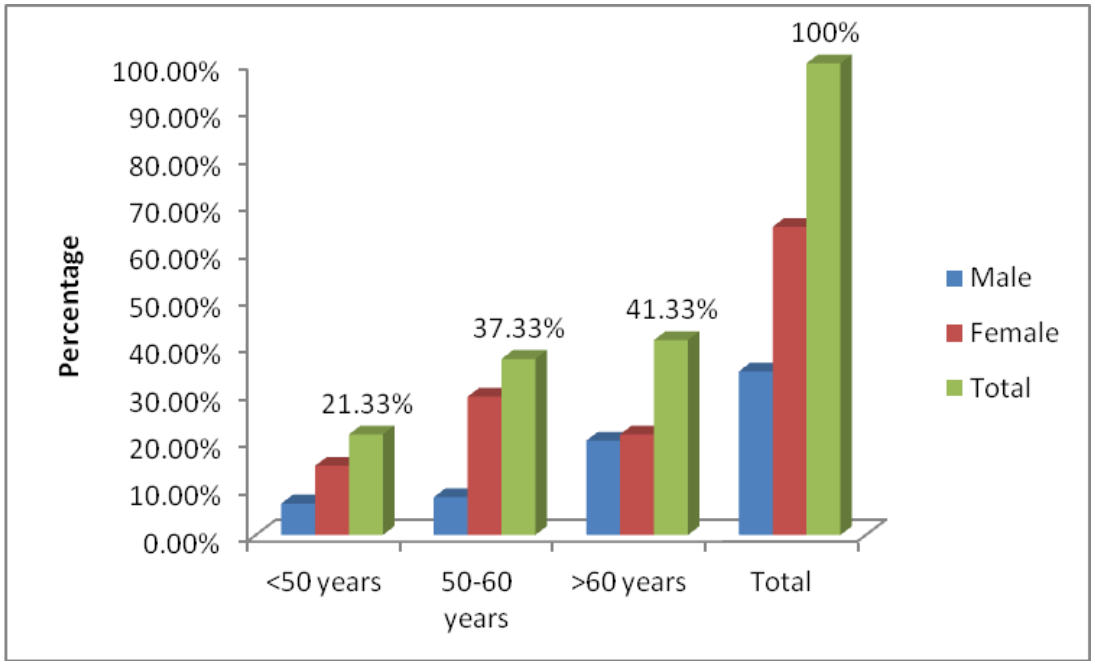

Fig. 1 : Age and Gender distribution among case population

The age distribution among case group (n=75) was : less than <50 years age group 16 out of 75 (21.33%), 50-60 years age group 28 out of 75 (37.33%), more than >60 years age group 31 out of 75 (41.33%).

Table 2: Distribution of Left Ventricle diastolic dysfunction in cases and controls

LVDD (normal EF)	**Cases**	**Controls**
+	46 (61.33%)	05 (6.67%)
-	29 (38.66%)	70 (93.33%)
Total	75	75

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LVDD- left ventricular diastolic dysfunction

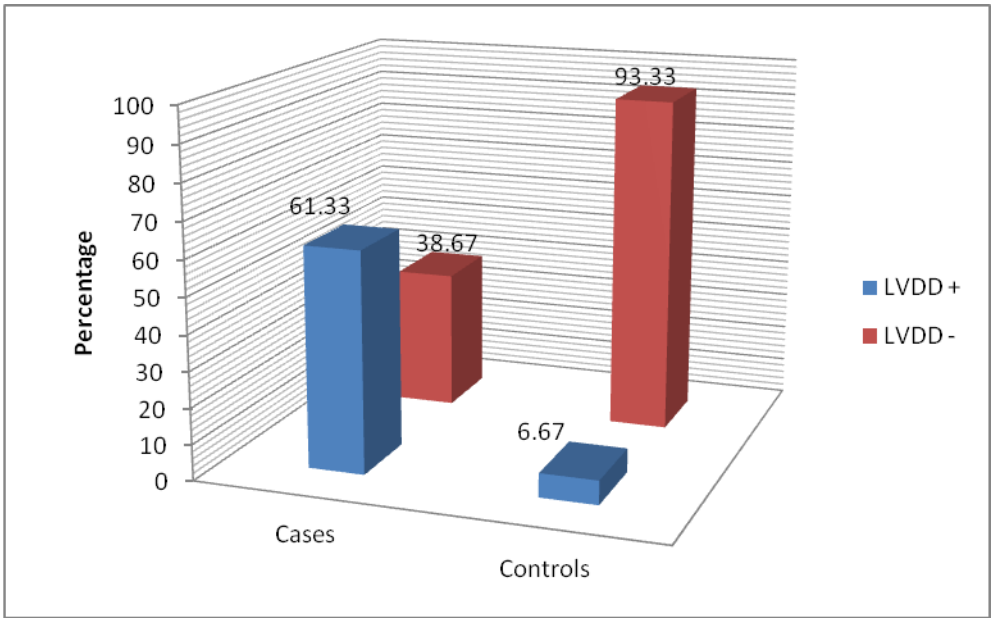

Fig 2: Distribution of diastolic dysfunction in cases and controls

Out of total 75 cases 46 (61.33%) showed LVDD. The results were statistically significant (p< 0.01). Among the control group only 05 (6.66%) showed LVDD.

Table 3: Distribution of LVDD with Age

Variables		Left Ventricle Diastolic Dysfunction Present	Left Ventricle Diastolic Dysfunction Absent	Chi square	p value
Age	<50 (22)	06 (27.27%)	16	15.23	<0.01*
	>50 (53)	40 (75.47%)	13		

*: statistically significant

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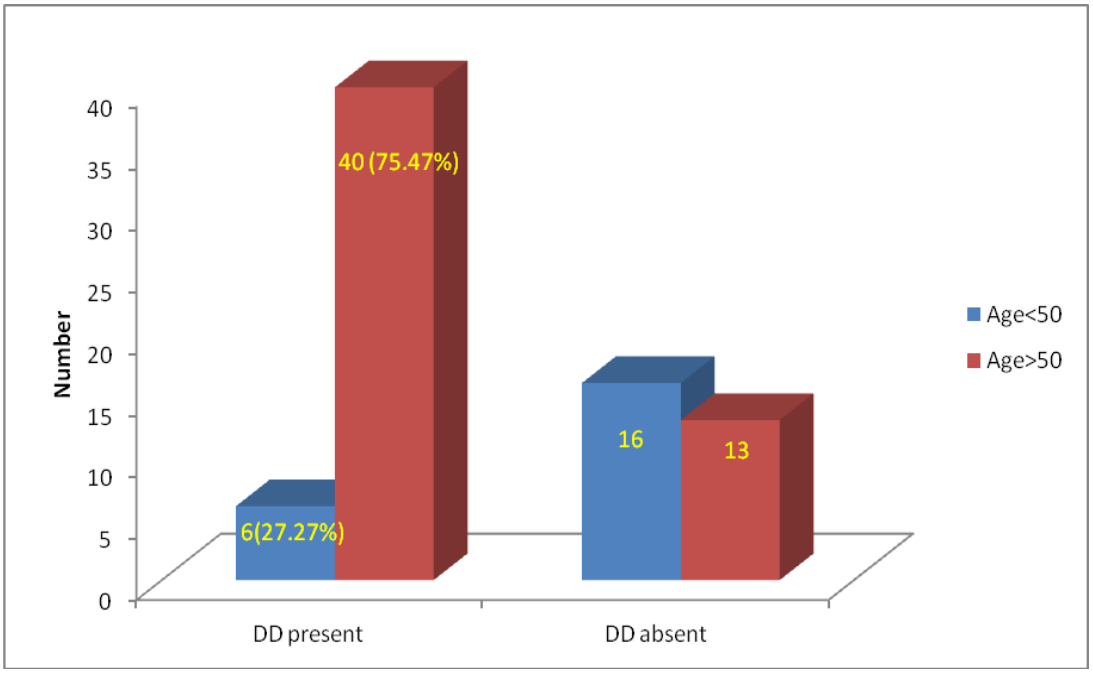

Fig 3- distribution of LVDD with age

Out of 75 cases, 22 cases were < 50yrs and 53 cases were > 50 yrs. LVDD was present in only 06 cases out of 22 (27.27%) who were < 50 yrs. However, 40 (75.47%) cases out of 53 showed LVDD who were > 50 yrs.

Table 4: Relation of HbA1c with LVDD

Variables		Left Ventricle diastolic dysfunction Present	Left Ventricle diastolic dysfunction Absent	Chi square	p value
HbA1c	<8 (35)	12	23	20.24	<0.01*
	>8 (40)	34	6		

*: statistically significant

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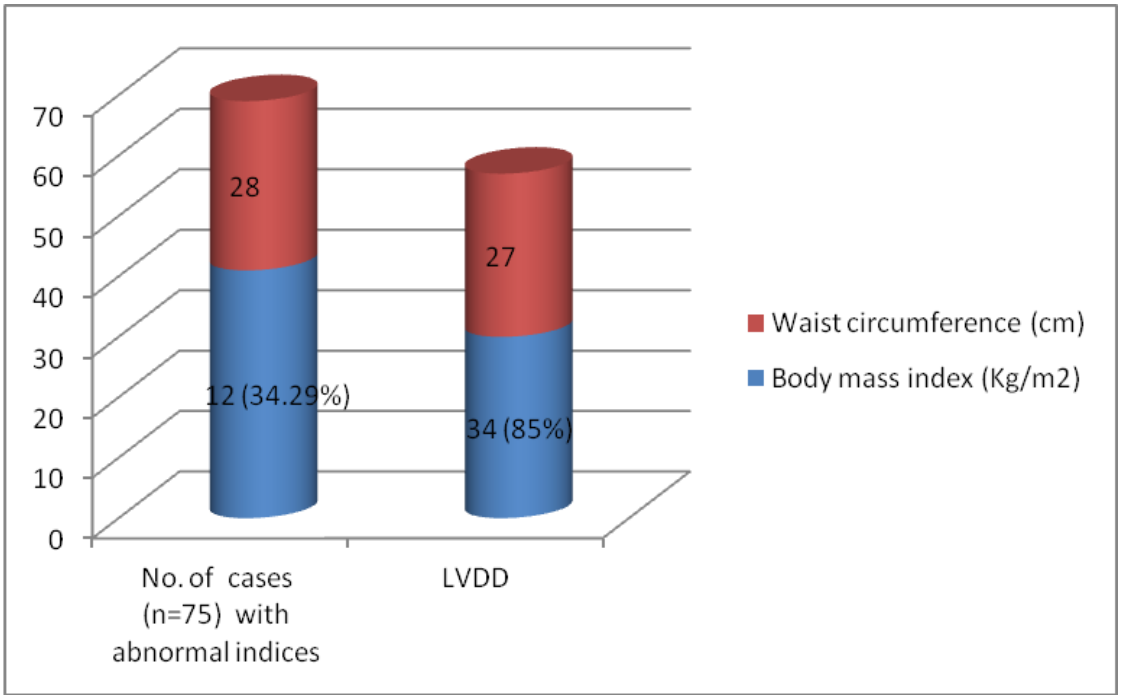

Fig 4: Relation of HbA1c with LVDD

Out of 75 cases, 35(46.67%) had mean HbA1c < 8 and 40(53.33%) cases had mean HbA1c > 8. LVDD was present in 34 (85%) cases with mean HbA1c > 8 compared to only 12 (34.29%) cases with mean HbA1c < 8. the results were statistically significant with p value (<0.01%).

Table 5: **Relation of duration of Diabetes with LVDD**

Variables		Left Ventricle diastolic dysfunction Present	Left Ventricle diastolic dysfunction Absent	Chi square	p value
Duration of diabetes Mellitus	<5 yr (31)	12 (38.70%)	19	13.16	0.001*
	5-10 yr (31)	22 (70.96%)	9		
	>10 yr (13)	12 (92.30%)	1		

*: statistically significant

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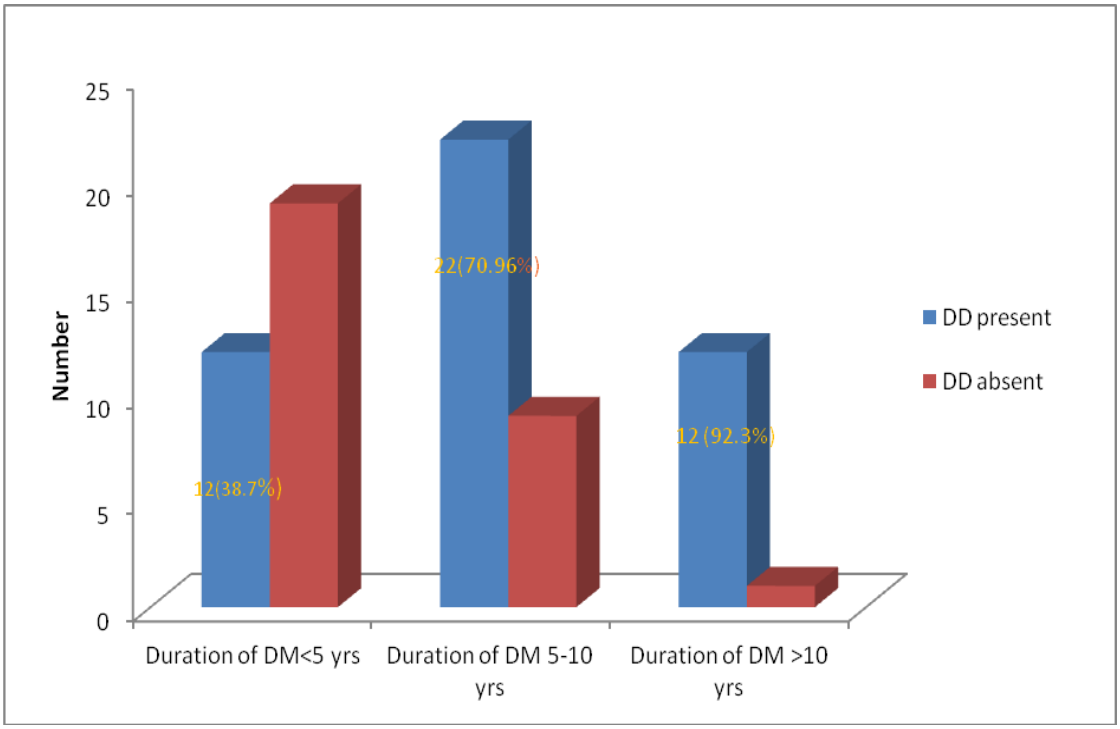

Fig 5: Relation of duration of Diabetes with LVDD

The distribution of total cases (n=75) according to the duration of diabetes were as follows; 31 cases with <5 years duration, 31 cases with duration between 5-10 yrs and 13 cases with duration >10 years. LVDD was present in 12 (92.3%) out of 13 cases with duration of diabetes >10 yrs and the relation was statistically significant (p .001).

Table 6: Echocardiography Parameter in Cases and Controls

Variables	Cases	Controls	t test	p value
	Total Mean±SD	Total Mean±SD		
E(cm/sec)	0.61±0.076	0.61±0.06	0	1
A(cm/sec)	0.7±0.089	0.51±0.09	12.93	<0.01*
E/A	0.89±0.21	1.24±0.17	11.22	<0.01*
DT(msec)	209.28±19.5	168.2±18.14	13.36	<0.01*
IVRT(msec)	76.97±10.51	89.29±8.33	7.96	<0.01*
IVS (mm)	11.6±1.71	11.6±1.71	0	1
LVPW T (mm)	12.09±1.05	12.09±1.05	0	1
EF	59.13±3.14	61.4±3.36	0	1

*: statistically significant

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The various variables studied were E (mitral early filling velocity), A (mitral late Atrial filling velocity), DT (deceleration time), IVRT (Isovolumetric relaxation time), EF (ejection fraction), IVST (inter-ventricular septal thickness), LV PWT (left ventricular posterior wall thickness).

The mean of E/A ratio in case group was significantly lower as compared to control group (p value<0.01).The case group also showed prolonged IVRT and DT in comparison to control as the p value was statistically significant (p<0.01). All subjects' cases and control showed normal systolic function.

Discussion:-

In the present study conducted in Western Rajasthan population, we assessed that left ventricular diastolic dysfunction (LVDD) is common in patients with DM, (a precursor of DCM) and its correlation with duration of diabetes and mean HbA1c. Isolated LVDD has been shown to be effected in early stage of DM when systolic function remains normal.

In the present study, 75 cases with type-2 DM and 75 healthy subjects as controls were included. Mean of FBS, HbA1c in case group was significantly higher as compared to the control group.

Total 46 (61.33%) subjects from the case group had left ventricle diastolic dysfunction compared to only 05 (6.67%) amongst control group showed the left ventricle diastolic dysfunction. Left Ventricle diastolic dysfunction in type 2 diabetes subjects was significantly higher as compared to the control group ('*P*'< 0.001).

Duration of diabetes mellitus of >10 years had more prevalence of left ventricle diastolic dysfunction ('*P*' <0.001). Subjects with HbA1c > 8.0% had more prevalence of left ventricle diastolic dysfunction than subjects with HbA1c < 8.0% ('*P*' <0.01). Left Ventricle diastolic dysfunction was significantly high in patient with age > 50 years compared to age < 50 years ('*P*' <0.01).

We compared our results with various studies.

Patil et al [11] in their study of 127 asymptomatic Type II diabetics found a significant incidence (54.33%) of diastolic dysfunction in diabetics. Dikshit NM et al [12] in their study of 50 asymptomatic Type II diabetics found a significant incidence (66%) of diastolic dysfunction in diabetics. Similarly, in our study, 61.33% diabetics were found to have diastolic dysfunction.

Exiara *et al.* [13] in their study of 114 subjects stated that the prevalence of LV diastolic dysfunction in normotensive, asymptomatic and well-controlled DM type2 patients is high, and increases with age. A total of 63.2% patients had diastolic dysfunction in their study compared to our prevalence of 61.33%.

Comparison with other LVDD studies:-

study / variable	Present Study	Patil VC et al.(11)	Dikshit et al.(12)	Chaudhary AK et al.(14)
Cases	75	127	50	100
LVDD	46 (61.33%)	69 (54.33%)	33 (66%)	41 (41%)
P Value	<0.01	<0.001	<0.01	-

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HBA1C	>8, (85%) P<0.01	>7.5, (81.57%) P<0.02	-	P=0.0057

From the above discussion and comparison of present study findings with various studies, we found that there was high prevalence of left ventricle diastolic dysfunction in subjects with asymptomatic type 2 DM and it was correlated with age, duration of diabetes and HbA1c.

Our study demonstrates that the incidence of LVDD is high in type 2 DM subjects. We also found that there is a significant association between left ventricle diastolic dysfunction and the duration of DM independent of coronary disease or hypertension. Therefore, future studies should be conducted to test the hypothesis that screening and aggressive management of diabetic patients with left ventricle diastolic dysfunction may delay the progression to heart failure.

Summary:-

1) Total of 75 cases with pre-existing type 2 Diabetes Mellitus and 75 healthy controls were taken. Out of total 75 cases, 49 (65.33%) were males and 26(34.67%) were females.
2) Out of total 75 cases 46 (61.33%) showed LVDD. The results were statistically significant (p <0.01).
3) Out of 75 cases, 22 cases were < 50yrs and 53 cases were > 50 yrs. LVDD was present in only 06 cases (27.27%) who were < 50 yrs. However, 40 (75.47%) cases showed LVDD who were > 50 yrs. Relation between increased age and LVDD was statistically significant.
4) The distribution of total cases (n=75) according to the duration of diabetes were as follows; 31 cases with < 5 years duration, 31 cases with duration between 5-10 yrs and 13 cases with duration> 10 years. LVDD was present in 12 (92.3%) out of 13 cases with duration of diabetes > 10 yrs and the relation was statistically significant (p =0.001).
5) Out of 75 cases, 35 (46.67%) had mean HbA1c <8 and 40 (53.33%) cases had mean HbA1c >8. LVDD was present in 34 (85%) cases with mean HbA1c >8 compared to only 12 (34.29%) cases with mean HbA1c <8 the results were statistically significant with p value (<0.01%).
6) The mean of E/A ratio in case group was significantly lower as compared to control group (p value<0.01). The case group also showed prolonged IVRT and DT in comparison to control as the p value was statistically significant (p<0.01). All subjects' cases and control showed normal systolic function.

Conclusion:-

Left ventricular dysfunction is prevalent among type II diabetic patients in Western Rajasthan without symptomatic heart disease. Echocardiography is of immense benefit in the management of type II DM patients as this will enhance early detection of

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left ventricular dysfunction with a view to early treatment in order to reduce morbidity and mortality.

Limitations of the study:- Stress electrocardiography, myocardial perfusion imaging, and coronary angiography were not used to exclude sub clinical coronary disease.

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