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"A Study of Left Ventricular Diastolic Function in Type-2 Diabetic Patients"

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ABSTRACT: ***BACKGROUND: -*** *Patients with diabetes mellitus have high cardiovascular morbidity and mortality. Left ventricular diastolic dysfunction, a basic characteristic of diabetic heart disease (diabetic cardiomyopathy), appears before the development of systolic dysfunction, suggesting that diastolic markers might be sensitive for early cardiac injury.* ***AIMS :-****To study left ventricular diastolic function in diabetic patients by echocardiographic measures and its correlation withAge, BMI,HbA1C, duration of diabetes, diabetic retinopathy ,microalbuminuria .****METHODS:*** *The present study was a hospital based case control study conducted in the Department of General Medicine, GR Medical College Gwalior, from January 2016 to September 2017 with a total of 90 subjects {divided in to case (n=60) and control (n=30)}.All subjects had undergone a standard 12 lead ECG and Doppler 2D- Echo with pulsed Doppler imaging in addition to routine anthropometric and biochemical measurements****Statistical Analysis:*** *All the data analysis was done using IBMSPSS version 20 software. Data is expressed as percentage and mean ± SD. Student t test and analysis of variance was used to tabulate the data. P value of <0.05 is considered as significant.* ***RESULTS:*** *Onechocardiographic evaluation, Left Ventricular Diastolic Dysfunction (LVDD) was recorded in 32 (53.3%) of the patients in Case and 2 (6.7%) of control group.Among cases out of 32 (53.3%) having LVDD, 24 (40%) patients had Impaired Relaxation, 5 (8.3%) Pseudo-Normalization and 3 (5%) had Restrictive Filling. Diastolic dysfunction was highest in patients age group 51-60yrs,57.89% compared to 45.45% in age group 40-50yrs. In patients who had HbA1C >7.5,75% developed diastolic dysfunction. In patients with BMI >30,60% developed diastolic dysfunction. Among cases, in Duration of DM <2 and 2-5 years, 2 (16.67%) and 30 (62.5%) had LVDD respectively. Among cases, patients with Diabetic Retinopathy (DR), 83.33% had LVDD. Among cases, patients withmicro albuminuria,87.9% had LVDD .Cases with Total Cholesterol (TC) > 200 mg/dl, 63.63% had LVDD. Among cases, in patients with TG >150mg/dl, 70% had LVDD.****CONCLUSION:*** *This study has shown that interaction of type 2 diabetics with left ventricular diastolic dysfunction .Older age, high BMI, prolonged duration of diabetes,HbA1C>7.5%,diabetic retinopathy, micro albuminuria hypercholesterolemia, hypertriglyceridemia had a higher prevalence of LVDD and thus this is an indicator of early diabetic cardiomyopathy. Early diagnosis and institution of treatment for LVDD in diabetic patients will reduce the morbidity and improve the outcomes by preventing future development of heart failure.*

KEY WORDS: *Type2 diabetes mellitus, Left ventricular diastolic dysfunction, control group, diabetic retinopathy(DR).*

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I. Introduction

The prevalence of diabetes mellitus (DM) is increasing globally[1,2].It is projected that 366 million people will be diabetic in 2030, 29 million of whom will be living in developing countries[3,4].Diabetes mellitus affect various organs like heart, CNS, Retina, Renal, and Blood vessels. DM is associated with a multitude of cardiovascular complications like CAD, MI, and CHF. In addition structural myocardial involvement diabetic cardiomyopathy may be there.Subclinical abnormalities of left ventricular function are recognized in both Type 1 and Type 2 diabetes mellitus. Studies using Doppler echocardiography have confirmed the findings of abnormal diastolic function as an early indicator of cardiac involvement in asymptomatic patients with Type 1 or Type 2 diabetes mellitus[5]. In Diastolic dysfunction the ventricles become relatively "stiff" Stiff ventricles cannot fully relax during diastole; as a result, the ventricles may not fill completely and blood can "dam up" in the body's organs (mainly the lungs). When diastolic dysfunction is sufficient to produce pulmonary congestion, diastolic heart failure is said to be present. Diabetic subjects have been reported to develop congestive heart failure in the absence of coronary artery disease; hypertension or any known structural heart disease[6].The term „diabetic cardiomyopathy" has been introduced for this condition. It has been suggested that microangiopathic lesions of the myocardium, altered composition and fibrosis of myocardial interstitium and accumulation of lipids in myocardial cells are involved in pathogenesis of diabetic cardiomyopathy[7,8]. Thus, patients with

diabetes are unusually prone to congestive heart failure. Several factors probably underlie diabetic cardiomyopathy, severe coronary atherosclerosis, prolonged hypertension, chronic hyperglycemia, microvascular disease, glycosylation of myocardial proteins, and autonomic neuropathy.5-6 Improved glycemic control, better control of hypertension, and prevention of atherosclerosis with cholesterol-lowering therapy may prevent or mitigate diabetic cardiomyopathy. This diastolic dysfunction can be very easily and early detected by echocardiography**.** Diastolic dysfunction in diabetic patients is believed to represent an earlier stage in the natural history of diabetic cardiomyopathy its timely recognition may help to avoid or significantly delay the onset of CHF[9].

II. Material And Methodology

The present study was a hospital based case control study conducted in the Department of General Medicine, GR Medical College Gwalior, from January 2016 to September 2017 with a total of 90 subjects, 60case and 30control.

Inclusion criteria:

- All newly diagnosed cases of diabetes type 2 (diagnosed as per ADA guideline) and patients with DM type 2 duration <5 years who have given informed consent and are asymptomatic and BP< 130/80 mm hg .
- Healthy controls were included with euglycaemic status without any co-morbid illness who have given the informed consent.

Exclusion criteria

- Patients with known case of cardiac disorder (including IHD, Cardiomyopathy, valvular heart diesase), systemic hypertension, thyroid disorder and pt is on other medications.
- Patients with known cases of arrhythmia anddyselectrolytemia and renal diseases.
- Patients age >60 years ,smokers and alcoholics.

Methodology

- All subjects 40-60 years of age were studied with diagnosis of diabetes mellitus.
- Following history including past history of any heart disease, family history of any SCD, hypertension and diabetes
- CBC, serum creatinine, bilirubin, SGOT, SGPT and BP measurement was done in all the patients. If there was any abnormalities in the above investigation the patients was not been subjected to further study.
- Subjects were examined for weight, height, BMI, waist to hip ratio, blood sugar (FBS and PPBS), HbA1c, Urine for micro-albumin, 12 lead ECG, and fundusexamination.
- All subjects underwent 2D echocardiography with pulsed Doppler imaging for left ventricular diastolic dysfunction.diastolic dysfunction was detected by using variables such as E-peak Velocity of early mitral flow,A- peak velocity of late mitral flow, E/A ratio,IVRT (isovolumeric relaxation time),DT(deceleration time),ratio of E/e' which are used for measuring diastolic dysfunction.

III. Results And Obsevations

TABLE 1: - Left Ventricular Diastolic Function (LVDF) in both Case And Control group

LVDF	Case		Control		T test 'P' value
	No.	%	No.	%	
LVDD	32	53.3	2	6.7	0.006
NORMAL	28	46.7	28	93.3	
Total	60	100	30	100	

Left ventricular diastolic dysfunction (LVDD)was recorded in 32 (53.3%) of the subjects in Case group and 2 (6.7%) of control group (p=0.006).

Table 2: Age Wise Distribution And Correlation With Diastolic Dysfunction

Cohort			LVDD		Total	T test 'P' value
			Present	Absent		
			Count %	Count %		
Cases	Age	40-50	10 (45.45)	12 (54.55)	22 (100)	<0.004
		51-60	22 (57.89)	16 (42.10)	38 (100)	
	Total		32	28	60	
Controls	Age	40-50	0 (0)	12(100)	12(100)	
		51-60	2 (11.1)	16(88.9)	18(100)	
	Total		0	30	30	

Among cases, in age group 40-50 and 51-60 years, 10 (45.45%) and 22 (57.89%) had LVDD whereas among control group, in age group 40-50 none of the patients had LVDD and 51-60 years had 2(11.1%) subjects had LVDD (p<0.004).

Table 3: Correlation Betweenbmi And Diastolic Dysfunction

Cohort			LVDD		Total	**T test 'P' value**
			PRESENT	Absent		
			Count (%)	Count (%)		
Cases	**BMI**	18.5-24.9	5 (41.67)	7 (58.33)	12 (100)	<0.023
		25-30	21 (55.26)	17 (44.73)	38 (100)	
		>30	6 (60)	4 (40)	10 (100)	
	Total		32	28	60	
Controls	**BMI**	18.5-24.9	0 (0)	14 (100)	14 (100)	
		25-30	1 (7.1)	13 (92.9)	14 (100)	
		>30	1 (50)	1(50)	2 (100)	
	Total		2	28	30	

In BMI 18.5-24.9, 25-30 and >30, among cases, LVDD was present in 5 (41.67%), 21 (55.26%)and 6 (60%) patients , whereas in control LVDD present in (0),1(7.1%),1(50%) subjects respectively (p<0.023).

Table 4 : Correlation Between Duration Of Dm And Diastolic Dysfunction

Cohort			**LVDD**		**Total**	**T test 'P' value**
			Present	**Absent**		
			Count (%)	**Count (%)**		
Cases	Duration of DM	<2yrs	2 (16.67)	10 (83.33)	12 (100)	<0.001
		2-5yrs	30 (62.5)	18 (37.5)	48 (100)	
	Total		32	28	60	

Among cases, in Duration of DM <2 and 2-5 years, 2 (16.67%) and 30 (62.5%) had LVDD (p<0.001).

Table 5: Correlation Between Hba1c With Lvdd

				LVDD		**Total**	**T test 'P' value**
				Present	**Absent**		
				Count %	**Count %**		
Cohort	Cases	HbA1C	<7.5%	1 (5.26)	18 (94.73)	19 (100)	<0.001
			>7.5%	31 (75.60)	10 (23.40)	41 (100)	
		Total		32	28	60	
	Controls	HbA1C	<7.5%	2 (6.7)	28(97.3)	30 (100)	
			>7.5%	0 (0)	0 (0)	0 (0)	
		Total		2	28	30	

Among cases, in patients with HbA1c <7.5% and >7.5%, 1 (5.26%) and 31 (75.60%) had LVDD whereas among control group, with HbA1c <7.5% and >7.5%, 2(6.7%) and 0% had LVDD respectively (p<0.001).

Table 6: Correlation Between Micro-Albuminuria With Lvdd

Cohort			**LVDD**		**Total**	**T test 'P' value**
			Present	**Absent**		
			Count (%)	**Count (%)**		
Cases	Micro-albuminuria	Present	14 (87.5)	2 (12.5)	16 (100)	<0.001
		Absent	18 (40.91)	26 (59.09)	44 (100)	
	Total		32	28	60	
Control	Micro-albuminuria	Present	0 (0)	0 (0)	0 (0)	
		Absent	2(6.7)	28 (93.3)	30 (100)	
	Total		2	28	30	

Among cases, in patients with and without micro-albuminuria, 14 (87.9%) and 18 (40.91%) had LVDD respectively(p<0.001).

Table 7: Correlation Between Diabetic Retinopathy With Lvdd

Cohort			LVDD		Total	P
			Present	Absent		
			Count (%)	Count (%)		
Cases	DR	Present	15 (83.33)	3 (16.67)	18 (100)	<0.001
		Absent	17 (40.48)	25 (59.52)	42 (100)	
	Total		33	28		
Control	DR	Present	0 (0)	0 (0)	0 (0)	
		Absent	0 (0)	30 (100)	30 (100)	
	Total		0	30	30	

Among cases, in patients with and without DR, 15 (83.33) and 17 (40.48) had LVDD whereas among control group, in patients with and without DR, none of the patients had LVDD (p<0.001).

Table 8: Correlation Betweentotal Cholesterolwith Lvdd

Cohort			LVDD		Total	T test 'P' value
			Present	Absent		
			Count (%)	Count (%)		
Cases	Total Cholesterol mg/dL	<200	25 (51.02)	24 (48.97)	49 (100)	0.012
		>200	7 (63.63)	4 (36.36)	11 (100)	
	Total		32	28	60	
Controls	Total Cholesterol mg/dL	<200	0	25 (100)	25 (100)	
		>200	2(40)	3 (60)	5 (100)	
	Total		2	28	30	

Among cases, in patients with TC <200 and >200 mg/dl, 25 (51.02%) and 7 (63.63%) had LVDD whereas among control group, in patients with TC<200 mg/dl and >200 mg/dl, 0% and 2(40%) of the patients had LVDD respectively (p<0.012).

Table 9: Correlation Between Serum Triglyceride (T.G.)With Lvdd

Cohort			LVDD		Total	T test 'P' value
			Present	Absent		
			Count (%)	Count (%)		
Cases	TG mg/dL	<150	25 (50)	25 (50)	50 (100)	0.023
		>150	7 (70)	3 (30)	10 (100)	
	Total		32	28	60	
Controls	TG mg/dL	<150	0 (0)	25 (100)	25 (100)	
		>150	2(40)	3 (60)	5 (100)	
	Total		2	28	30	

Among cases, in patients with TG <150 and >150mg/dl, 25 (50%) and 7 (70%) had LVDD whereas among control group, in patients with TG <150 and >150mg/dl, 0% and 2(40%) of the patients had LVDD respectively (p=0.023).

IV. Discussion:-

In our study, we considered it important to assess this parameter in diabetic patients with left-ventricular diastolic dysfunction of the heart.

1) DIASTOLIC DYSFUNCTION:-In present study 32 cases (53.3%) had diastolic dysfunction of which 24 cases(40%) had impaired relaxation 5 cases (8.5%) had pseudo-normalization and 3 cases (5%) restricted filling pattern .whereas control group 2(6.7%)had impaired relaxation type diastolic dysfunction.**Patil et al(2011)[10]**, found the prevalence of diastolic dysfunction in asymptomatic type 2 diabetics as 54.33%, .**Panchal et al**[11]**(2015),**studied 75patients, 50diabetics and 25control who had undergone echocardiography to estimate LV function and reported that diastolic dysfunction was found in 76% of diabetic patients.**Shreshta et al.[12](2009),**studied 100 asymptomatic type 2 Diabetes Mellitus, LVDD was found in 71 subjects of whom 60 had impaired relaxation and 11 had a Pseudo normal pattern.**Paul poinier**et**al[13](2001),**LVDD was found in 60% of whom 32% had impaired relaxation and 28% had a pseudo normalization pattern of ventricular filling.**S. Cossonet al [14](2003),** diastolic dysfunction was present in 69 % of the patients.**Gani et al(2005)[15],** Reported diastolic dysfunction in 65.8% diabetic compared to 33.3% in the control.[80]

2) AGE DISTRIBUTION:-In the present study Among cases, in age group 40-50years ,10 (45.45%) had LVDD and and among age group 51-60 years, 22 (57.89%) had LVDD whereas among control group, patients in age group 40-50years and 51-60 years , 0%and 2(11.1%) had LVDD (p<0.004) .**Chaudhary et al[22](2015)** reported that age of the patients was very significantly associated with incidence of LVDD (p=0.0012), meaning

that older the age at the time of diagnosis, higher the incidence of LVDD.**Patil et al [10](2011)** reported that Diastolic dysfunction was significantly higher in age >45 years compared to age <45 years (pvalue< .05).**Mamatha B patiletal[20](2010),** there was linear increase in the prevalence of diastolic dysfunction with increasing age group.**Ganietal[15] (2005),**concluded that the age of patients had significant correlation with E/A ratio of Trans mitral Doppler flow p<0.01 i.e. patients with higher age group have more diastolic dysfunction.

3) BMI (Body Mass Index):-In the present study- In cases with BMI between 18.5-24.9, 25-30 and >30 , 5 (41.67%), 21 (55.26%) and 6 (60%) patients had LVDD. Whereas in control group, 0%, 1(7.1%) and 1(50%) had LVDD respectively (p<0.023).**Seyfeli, Duru M[16](2006)**in their study, Patients in diabetic group with LVDD in comparison with patients in diabetic group with normal ventricular diastolic function, have a significantly higher BMI.**In the Framingham heart study[17]**, Obesity and BMI has been found to be a strong predictor of sudden cardiac death. [94]**Virendraet al**[11]in their study Total 23 (33.33%) male and 13 (24.41%) female patients had high BMI; and, out of them 16 (69.56%) male and 8 (61.53%) female had diastolic dysfunction.

4)DURATION OF DIABETES:-In the present study:- Among cases with Duration of DM <2 and 2-5 years, 2 (16.67%) and 30 (62.5%) had LVDD (p<0.001).**Gani et al[15]** (2005) in their study in 114 NIDDM patients found that the duration of diabetes was independently associated with diastolic dysfunction. The duration of diabetes had significant correlation with E/A ratio (r= -0.295, p<0.01). **Madhumathi R[21]**(2014) Comparing with duration of diabetes, we had 21(42%) patients with less than 5 year duration of diabetes and 20(40%) patients with 5-10 years duration of diabetes. Statistically it was significant as we had higher percentage of patients with diastolic dysfunction as duration of diabetes increased.

5)MICRO-ALBUMINURIA:-In the present study –Micro albuminuria was recorded in 16 (26.7%) cases.In cases patients with and without Micro-albuminuria, 14 (87.9%) and 18 (40.91%) had LVDD (p<0.001).**Sampson et al [18]** found a gradual decrease in E/A ratio in type 1 diabetic patients according to the presence of micro albuminuria and proteinuria. A significantly higher proportion of abnormal diastolic function (E/A<1) was observed in the group of diabetics with proteinuria.**Rutter MK[19]1980,** Micro-albuminuria is an early marker of glomerular disease that has been shown to predict glomerular injury in early diabetic nephropathy. 25% of type 2 diabetic patients have micro-albuminuria and it is a strong predictor of premature cardiovascular death in them. Diabetic nephropathy is a leading cause of diabetes related mortality and morbidity. [98]

6) DIABETIC RETINOPATHY:-In the Present study - Among cases, patients with and without DR, 15 (83.33%) and 17 (40.48%) had LVDD (p<0.001).**S. Cossonet al [14] (2003)**Diabetic Retinopathy Studies performed in diabetic patients free of coronary artery disease have demonstrated that patients with mild to severe retinopathy exhibited LV diastolic dysfunction (lower E/A values) compared to age-matched controls or patients without retinopathy. In the most recent report, a higher prevalence of retinopathy (49%) was encountered in patients with abnormal mitral filling pattern (E/A ratio < 1) compared to patients with a normal diastolic function (20%).

7) HBA1C :-In the Present study, Most of the patients among cases have HbA1c >7.5% (68.3%). Among cases, in patients with HbA1c <7.5% and >7.5%, 1 (5.26%) and 31 (75.60%) had LVDD whereas among control group, with HbA1c <7.5% and >7.5%,2(6.7%) and 0% of the patients had LVDD (p<0.001).**Virendra C. Patilet al[11] (2011)** Out of 89 subjects with HbA1c < 7.5%, 39 (42.82%) had diastolic dysfunction; and, out of 38 subjects with HbA1c>7.5%, 31 (81.57%) had diastolic dysfunction. Subjects with HBA1c>7.5% had more prevalence of diastolic dysfunction, than subjects with HBA1c < 7.5% ('P' < 0.02).**Mamatha B Patilet al**[20] we co-related the diastolic dysfunction with glycemic status, that the prevalence of diastolic dysfunction increased gradually with the rise in HbA1C levels. This was in accordance with Fiorina who demonstrated that glycemic levels had an impact on diastolic dysfunction.**Madhumathi R et al** [21]**(2014**) 25(50%) subjects had HbA1c >8 %which indicated poor glycemic control .Prevalence of diastolic dysfunction increased gradually with the rise in HbA1c levels and it was statistically significant.**Chaudhary AK [22](2015),** Mean HbA1C level of LVDD group was found higher as compared to those without LVDD.**Celentano et al.[23],** also studied subjects with normal glucose tolerance, with impaired glucose tolerance, and with type 2 DM and found early signs of diastolic dysfunction (assessed by E/A mitral flow ratio), not only in patients with diabetes but also in those with impaired glucose tolerance, independent of the confounding role of ischemia, body weight, and blood pressure.[99]

V. Conclusion:-

The present study has shown that interaction of type 2 diabetics with left ventricular diastolic dysfunction.Older age,prolonged duration of Diabetes, high BMI, diabetic retinopathy, microalbuminuria,poorly controlled diabetes having higher prevalence of LVDD and thus this reflect as an indicator of early diabetic cardiomyopathy.Echocardiography is a very useful noninvasive tool in detecting LVDD in asymptomatic type2 DM patients.

Early diagnoSsis and institution of treatment for LVDD in diabetic patients will reduce the morbidity and improve the outcomes by preventing future development of heart failure.

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