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"A Study of Left Ventricular Dysfunction in Patients with Diabetes Mellitus"

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Abstract: *Diabetes mellitus is one of the most common diseases in the world and is acquiring epidemic proportions. Indians are genetically more susceptible to diabetes compared to other races. Cardiovascular complications are the main cause of morbidity and death in diabetic patients.* ***The objective*** *of this study was to find out abnormalities in left ventricular function in patients of diabetes mellitus by echocardiographic measures, its correlation with glycemic control and the duration of diabetes and to compare the left ventricular function of diabetic patients with normal patients. There is an increased rate of ischemic heart disease and cardiomyopathy which may lead to heart failure (Diastolic and systolic heart failure) Left ventricular diastolic dysfunction represents an early stage of heart failure, without any clinical manifestations. In the view of these above facts the present study was done to assess the diastolic and systolic dysfunction in diabetic patients by echocardiography.*

The present study is of 75 patients, 50 diabetics and 25 control who had undergone echocardiography to estimate LV function. Diabetic patients were selected according to WHO criteria. Diabetic patients of Type 2 are selected either on insulin or oral treatment. Patients with following conditions were excluded from the study which were likely to impair LV function. The conditions were age more than 65 years, morbid obesity, hypertension, valvular/congenital/ischemic heart disease, heart failure, renal failure and cerebrovascular disease. Patients with altered renal function test and heavy smokers and alcoholics were also excluded from the study. Patients with resting ECG without any evidence of ischemia, infarct or bundle branch block, LVH were included and patients with echocardiograms showing regional wall motion abnormality were excluded from the study.

Heart rate and blood pressure were comparable in both groups. Glycatedhaemoglobin (HbA1c) was significantly higher in diabetic patients i.e. 7.92 %. HbA_1c has inverse relationship with systolic and diastolic left ventricular function. FBS has linear correlation with systolic blood pressure and S. cholesterol in diabetes. The mean S. cholesterol and S. triglyceride in diabetes patients was 210.52 mg/dl and 202.36 mg/dl respectively higher compare to controls 180.32mg/dland 122.60 mg/dl respectively. Only 16% diabetes patients had acceptable glycemic control as measured by glycated hemoglobin.(HbA1c %).

Systolic dysfunction was found in 36% of diabetic patients. The LV ejection fraction (LVEF %) was 49.40 % in diabetics, significantly lower than in control 57.00%. Diastolic dysfunction was found in 76% of diabetic patients by Doppler transmitral flow velocity curve. The mitral 'A' Vmax was significantly higher in diabetics 0.76 m/sec than control 0.57 m/sec. The VE / VA ratio was significantly lower in diabetics 0.86compared to 1.20 in control. The LV systolic and diastolic functionwere correlated with duration of diabetes and glycemic control.

Key words: *Left ventricular function, Diabetes mellitus, Glycemic control, Control group.*

I. Introduction:

Diabetes mellitus is one of the most common diseases in the world and is acquiring epidemic proportions. More than 5 % of adults has this disease, with prevalence of about 1 % in the youth to 13 % in those older than 60 years. The epidemic of diabetes represents a major burden to health care systems around the world. Both type 1 and type 2 diabetes are increasing in children and adolescents. More alarming is the increase in type 2 Diabetes in the youth related to obesity and physical inactivity.[1,2]

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future.[3]

Cardiovascular complications are known to be the main cause of morbidity and mortality in diabetic patients[4].Other cardiovascular risk factors like hyperlipidemia, hypertension and obesity are common in diabetic patients[5]. Atherosclerosis of the coronary arteries is by far the most common cause of cardiac involvement in diabetes Diabetic cardiomyopathy has been proposed as an independent cardiovascular disease, and many mechanisms, such as microvascular disease, autonomic dysfunction, metabolic disorders, and interstitial fibrosis, have been suggested as causative factors[5]. The evidence indicates that myocardial damage

in diabetic patients affects diastolic function before the systolic function. Left ventricular diastolic dysfunction thus represent the first stage of diabetic cardiomyopathy preceding changes in systolic function, Reinforcing the importance of early examination of ventricular function in individual with diabetes[6,7]. It is the earliest and specific functional abnormality in diabetic cardiomyopathy and can affect patients who are free of macro vascular complications, newly diagnosed diabetes mellitus or even in those with a disease duration of less than 1 year[8]. Also the relationship between the clinical features of diabetes and LV function are linear[9]. Knowledge of abnormalities of cardiac function in the preclinical phase will aid in understanding the disease and its prognosis[10]. It will also help in directing efforts towards patients in this high risk group and find a new way to find the possibility of preventing its occurrence at all[11].

Echocardiography especially Doppler Echo is simple, non – invasive and reproducible. It identifies large number of diabetic patients who have asymptomatic left ventricular dysfunction before abnormalities are detected with ECG or by clinical examination.

II. Material And Methods:

This study of left ventricular function in a selected group of diabetics (50) and control (25) group attending the outpatient department of NIMS hospital, Jaipur was done using echocardiographic measures from 2011-2013. It was a case – control type of analytical cross sectional study.

The diabetic group of 50 patients, 32 male and 18 female was selected. The inclusion criteria were patients with age between 40-65 years with diabetes mellitus diagnosed as per WHO criteria. The control group were a random sample of 25 patients 17 male and 8 female was selected. The criteria for inclusion were age, sex, body mass index and blood Pressure were comparable to the study group like FBS < 126 mg/dl, PPBS < 200 mg/dl, Glycosylated Haemoglobin (HBA1c) < 6.5%, S .cholesterol < 240 mg/dl, S. Triglyceride < 150 mg/dl. Patients not fit into inclusion criteria and with other cardiac problem were excluded from study. All the patients and the control subjects underwent a thorough clinical examination Control of diabetes was decided on basis of GlycolsylatedHaemoglobin (HBA1c),

Under good Control : 6.0 - 7.0%
Diabetic Under fair Control : 7.1 - 8.0%
Diabetic Under Poor Control : $\geq$ 8.1%
Treatment received: OHA and/or insulin

General Examination, Cardiovascular, respiratory system examination was done to exclude any clinical abnormality. Indirect Ophthamoscopy was dpne to find out retinopathy and arteriosclerosis respectively. Laboratory investigations like renal function test : blood urea, s creatinine and electrolytes, urine analysis qualitative : microalbuminuria (dipstick method), cholesterol and s triglyceride estimation, fasting blood sugar after an overnight fast, post prandial blood sugar 2 hours after lunch other investigation like resting 12 lead conventional ECG, Chest X ray PA projection to exclude cardiomegaly, Echocardiography was done on all subjects at M mode, two dimensional and Doppler ultrasound were obtained.

a. LV Systolic function was measured using ejection fraction (EF%), the value < 50% was taken as index of systolic dysfunction.
b. LV Diastolic function was assessed by VE ^{a}/VA^{b} and the ratio < 1 was taken as index of diastolic dysfunction.

a=Peak velocity of early LV filling (V maxE)
b=Peak velocity of late LV filling (V max A)

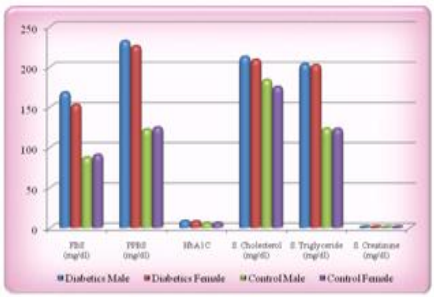
III. Results And Discussion:

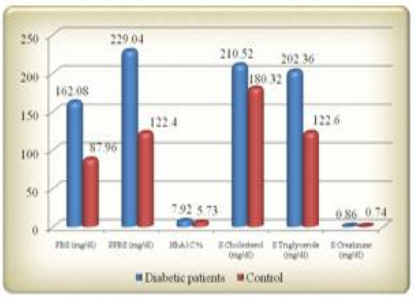
Table 3. 1. Comparison of Anthropometric & Clinical Data of Diabetic patients and Control

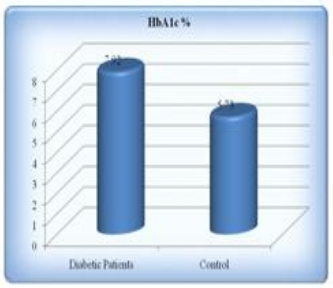
Clinical & Anthropometric Data	Diabetic patients(n=50)			Control (n=25)			P value
	Male (n=32)	Female (n=18)	Total (n=50) Mean	Male (n=17)	Female (n=8)	Total (n=25)	
Age (Years)	54.19 ±7.07	58.11 ±5.39	55.60 ±6.73	54.47 ±7.36	55.75 ±5.78	54.88 ±6.80	0.665
Heart rate (beats/min)	81.50 ±5.63	84.00 ±7.64	82.40 ±6.46	81.65 ±5.49	81.00 ±6.41	81.44 ±5.67	0.530
SBP (mmHg)	129.63 ±8.10	130.22 ±4.39	129.84 ±6.95	128.12 ±7.73	123.75 ±11.49	126.72 ±9.09	0.103
DBP (mmHg)	79.13 ±2.87	79.56 ±4.42	79.28 ±3.47	82.82 ±4.48	83.75 ±4.20	83.12 ±4.32	<0.001
BMI (kg/m^2)	26.39 ±-2.07	26.67 ±1.93	26.49 ±2.00	25.18 ±1.70	25.25 ±1.75	25.20 ±1.68	0.007

Body mass index (BMI) is higher in diabetic patients as compared to control subjects. We found statistically significant difference in BMI and diastolic blood pressure ('p'<0.05)

Chart: 3.2 – (3.2.1, 3.2.2, 3.2.3) . Comparison of Different Laboratory Investigations in Diabetic patients and Control







In our study 'p' value of all 3 parameters Mean FBS, PPBS, and HbA1c , S. Creatinine, total Cholesterol and serum Triglyceride is <0.005. Taken together, there is statistically significant difference ('p'<0.005) noted in above Parameters namely (FBS, PPBS, HbA1c, S.Cholesterol, S.Triglyceride and S.Creatinine) when compared between diabetic patients and control subjects.

3.3 Evaluation of left ventricular function in diabetic patients

In our study of 50 diabetic patients, left ventricular function was evaluated by 2D echocardiography. Systolic function is reflected by ejection fraction (EF%) and diastolic function is reflected by (VE/VA) ratio. EF <50 is taken as systolic dysfunction and VE/VA < 1 is taken as diastolic dysfunction

Table – 3.3.1 Evaluation of left ventricular Diastolic function in Diabetic Patients

Diastolic function (VE/VA)	Male		Female		Total		t – test 'p' value
	No.	VE/VA	No.	VE/VA	No.	VE/VA	
Abnormal (VE/VA <1)	26	72 ± 0.060	12	0.80 ± 0.09	38	0.74 ± 0.08	<0.001
Normal (VE/VA >1)	6	1.25 ± 0.13	6	1.21 ± 0.06	12	1.23 ± 0.09	
Total	32	0.82 ± 0.23	18	0.94 ± 0.21	50	0.86 ± 0.22	

Evaluation of left ventricular Systolic function in Diabetic Patients

Systolic Function (EF - %)	Male		Female		Total		t – test 'p' value
	No.	EF %	No.	EF %	No. %	EF%	
Abnormal (EF < 50)	8	42.5 ± 5.35	10	44.0 ± 2.11	18	43.33 ± 3.83	<0.001
Normal (EF ≥ 50)	24	52.71 ± 2.54	8	53.13 ± 2.59	32	52.81 ±2.52	
Total	32	50.15 ± 5.61	18	48.06 ± 5.19	50	49.40 ± 5.50	

In our study out of total 50 Diabetic Patients 38 (76%) patients have diastolic dysfunction(VE/VA - 0.74 ± 0.08) and 12 (24%) patients have normal diastolic function (VE/VA - 1.23 ± 0.09).
Out of 50 diabetic patients 18 patients (36%) have systolic dysfunction (EF % - 43.33 ±3.83) and 32 (64%) patients have normal systolic function (EF % -52.81 ± 2.52). Mean EF % of patients with abnormal Systolic function is (EF % - 43.33 ± 3.83) and normal systolic function is (EF % -52.81 ± 2.52). 'p' value is < 0.001. There is statistically significant difference in systolic function among patients with abnormal and normal Systolic function (p <0.05).

Table 3.4. Comparison of left ventricular Systolic Function (EF%) between Diabetic Patients and control subjects

Systolic function	Group	N	Mean	Std Dev	'p' Value*
Systolic (EF %) *unpaired t-test	Diabetic patients	50	49.40	5.50	<0.0001
	Control	25	57.00	3.82	

Out of 25 control subjects 1(4%) has systolic dysfunction(EF%<50). 24 (96%) patients have normal systolic function (EF ≥ 50 %). Mean EF % of diabetic patients is 49.40 ± 5.50 .Mean EF of control subjects is 57.00 ± 3.82 . 'p' is <0.0001

Systolic function (EF %) is significantly lower in diabetic patients compared to control subjects. (p<0.05)

Table 3.5 Comparison of left ventricular Diastolic function (VE/VA) between Diabetic Patients and control subjects

Diastolic function(VE/VA)	Diabetic patients		Control	
	No.	%	No.	%
Abnormal (VE/VA <1)	38	76.00	5	20.00
Normal(VE/VA >1)	12	24.00	20	80.00
Total	50	100.00	25	100.00

Chi-Square = 19.138 with 1 degree of freedom; p = 0.000

Table 3.6. Comparison of Mean Diastolic function (VE/VA) between Diabetic Patients and control subjects

Diastolic function (VE/VA	Group	N	Mean	Std Dev	'p' Value*
Diastolic function (VE/VA) *unpaired t-test	Diabetic patients	50	0.86	0.22	<0.0001
	Control	25	1.20	0.31	

In this study, Out of 25 control subjects 5 (20%) have diastolic dysfunction (VE/VA <1) and 20 (80%) patients have normal diastolic function (VE/VA > 1). Mean VE/VA of diabetic patients is 0.86 ± 0.22. mean VE/VA of control subjects is 0.1.20 ± 0.31 'p' is <0.0001. Diastolic function (VE/VA) is significantly lower in diabetic patients compared to control subjects. (p<0.05)

3.7 Correlation of left ventricular function (systolic and diastolic) with duration of diabetes

For co-relating duration of diabetes with LV function, patients are grouped as <2 years, 2-6 years and >6 years of duration of diabetes.

Table 3.7.1 : Correlation Of Diastolic Function (Ve/Va) & Systolic Function (Ef%) ith Duration of Diabetes.

Diastolic function (VE/VA)	Duration of Diabetes	N	Mean	Std Dev	'p' Value*
Diastolic (VE/VA)	<2 Year	14	0.82	0.17	0.696
	2-6 Year	25	0.88	0.24	
	>6 Year	11	0.86	0.28	
Systolic function (EF %) *One way ANOVA	<2 Year	14	49.29	5.50	0.922
	2-6 Year	25	49.20	6.40	
	>6 Year	11	50.00	3.16	

In our study there are there is no statistically significant difference in diastolic function & systolic function among these 3 groups .p value is 0.696 (>0.05) & 0.922 (>0.05).
respectively.

3.8 Correlation of left ventricular function (systolic and diastolic) with glycemic control

For correlating LV function with glycemic control patients are grouped according to values of HbA1c .patients are categorized as Good control (HbA1c 6.1 – 7.0), fair control (HbA1c 7.1 - 8.0), and poor control (HbA1c ≥ 8.1).

Table 3.8.1 : Correlation Of Systolic Function (Ef%) with Glycemic Control

Systolic function (EF %)	Glycemic Control (HbA1c - %)	N	Mean	Std Dev	'p' Value*
Systolic function (EF %)	Good (6.1 – 7.0)	8	48.13	4.58	0.776
	Fair (7.1 – 8.0)	22	49.55	7.06	
	Poor (≥ 8.1)	20	49.75	3.80	
Diastolic function (VE/VA)	Good (6.1 – 7.0)	8	0.92	0.23	0.700
	Fair (7.1 – 8.0)	22	0.85	0.21	
	Poor (≥ 8.1)	20	0.84	0.25	

*One way ANOVA

In our study there is no statistically significant difference in systolic & diastolic function among these 3 groups. p value is 0.776 & 0.700 respectively (> 0.05).

IV. Discussion

Table 4.1 . Comparison of LV Diastolic Function Data in Diabetic Patients of Present Study with Sanchez – Barrigaet al [12]2001

	Barriga et al n=58		Present Study n = 50	
Characteristics	P (n=40)	R(n=18)	P (n=38)	R (n=12)
Age (years)	54	52	55.76±6.17	55.08±8.58
BMI (Kg/m2)	25.5	25.1	26.51±1.97	26.42±2.18
FBS (mg/dl)	203.0	136	171.89±57.68	131.00±29.08
HbA1c%	10	8	7.98±0.81	7.71±0.70
S. Cholesterol (mg/dl)	224	186	214.37±19.55	198.33±11.28
S. Triglyceride (mg/dl)	280	195	207.79±41.56	185.17±53.61
VE/VA	<1	>1	0.74±0.08	1.23±0.09

P = patients with abnormal diastolic function & R = patients with normal diastolic function, *Significant difference ('p' value <0.05).

In Sanchez – Barriga et al 2001, The FBS, HbA1c, S. Cholesterol and S. Triglyceride of group P is significantly more than group R. VE/VA ratio is less than 1 in group P & more > 1 in group R showing diastolic dysfunction in group P.

In the present study, FBS, HbA1c, S. Cholesterol and S. triglyceride is significantly increased in group P i.e. 172.81, 7.96, 218 and 235 respectively than group R. Total 38 patients have diastolic dysfunction (group P). VE/VA ratio is 0.74 ± 0.08 in group P and 1.19 ± 0.09group R, suggesting diastolic dysfunction in group P.

Both studies show strong relationship between hyperglycemia, hypercholesterolemia and left ventricular diastolic dysfunction in diabetics. Thus the present study in comparable with Sanchez – Barriga et al.

Table 4.2 . Comparison of Present Study with Previous Study and Virendra et al [13] 2011.

Characteristics	Virendra et al- 2011		Present Study	
	Diabetics	Control	Diabetics	Control
Age (years)	50	48	55.60±6.73	54.88±6.80
BMI (Kg/m2)	26.8	23.6	26.49±2.00	25.20±1.68
HbA1c%	8.2	5.9	7.92±0.78	5.73±0.51
S. Triglyceride	203	132	202.36±45.22	122.60±12.98
S. Cholesterol	218	141	210.52±19.10	180.32±23.81
EF%	54.5	55.5	49.40±5.50	57.00±3.82
VE/VA	0.8	1.20	0.86±0.22	1.20±0.31
FBS (mg/dl)	142	85	162.08±54.90	87.96±15.33

In Virendra et al study, HbA1c, S. Cholesterol& S. triglyceride is significantly higher in diabetic patients.In Virendra et al study Systolic ejection fraction in diabetic patients is not significantly decreased (54.5%) compared to (55.5%) in normal patient. In present study, there is significant reduction in LVEF% in diabetes (49.40 % ±5.50) than controls (57.00 % ±3.82) ($p<0.05$).

In Virendra et al, there is diastolic dysfunction in diabetics. VE / VA is 0.8. In present study, control group has VE/VA 1.20±0.31 and diabetic patients have diastolic dysfunction VE/VA 0.86±0.22.. Thus the present study is comparable to the Virendra et al study, which shows subclinical left ventricular diastolic dysfunction in asymptomatic diabetic patients related to serum lipids and HBA1c The present study is comparable to the above study.

Table 4.3. Comparison of Present Study with Aldo Study[14] 1995

Characteristics	Aldo Study		Present Study	
	Control n = 25	Diabetics n=24	Control n = 25	Diabetics n=50
Age	58	57	54.88±6.80	55.60±6.73
Women/Men	8/17	10/14	7/18	18/32
BMI	28	28	25.20±1.68	26.49±2.00
HR	65	57	81.44±5.67	82.40±6.46
SBP	139	133	126.72±9.09	129.84±6.95
DBP	89	87	83.12±4.32	79.28±3.47
FBS	97	159	87.96±15.33	162.08±54.90
PPBS	113	246	122.40±10.84	229.04±51.12
EF%	65	60	57.0±3.82	49.40±5.50
VE/VA	1.04	0.86	1.20±0.31	0.86±0.22

In Aldo study and the present study, there is no difference in age, BMI, HR, SBP and DBP variable in control and diabetics. In Aldo study, FBS and PPBS are significantly high than control. In present study, FBS and PPBS are significantly higher in diabetes patients 162.08 and 229.04 respectively than in control 87.96 and 112.40 respectively. In Aldo study, VE/VA in diabetes patients is significantly decreased than control. In present study, LVEF% and VE/VA is 49.40±5.50% and 0.86±0.22 in diabetes patients and 57.0±3.82% in control and ratio is in diabetes patients and 1.20±0.31in control. The Aldo study shows early cardiac abnormality in form of LV diastolic dysfunction in diabetic mellitus. Present study clinically correlates well with Aldo study except for systolic function which is significantly less in diabetic patients compared to control subjects ($p< 0.05$).

V. Conclusion

There is LV systolic dysfunction in36 %.diabetic patients with reduced LV ejection fraction (LVEF <50%)

There is diastolic dysfunction in76 %.diabetic patients with VE/VA<1, due to impaired relaxation and restrictive ventricular filling.

Obesity, hypercholesterolemia, hyper triglyceridemia, hyperglycemia and LV diastolic dysfunction are correlated and may lead to early diabetic cardiomyopathy.

LV systolic and diastolic function is significantly reduced in diabetic patients compared to control subjects.The present study does prove the existence of diabetes specific heart muscle disease.

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