



## DIASTOLIC DYSFUNCTION IN PATIENTS OF TYPE 2 DIABETES MELLITUS

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### ABSTRACT

This study was aimed to know cardiac dysfunction in patient type II diabetes mellitus. 100 patients of type II diabetes mellitus of more than 5 years duration attending medical OPD and admitted in New Civil Hospital Surat were taken for study. ECG and 2D ECHO with doppler was done to know the cardiac dysfunction and other routine investigations related to the subject were done. Mean age of diabetic patients was 57.17 years, Ratio of male to female was 1.17:1, As the age of diabetic patients increases, LV diastolic function decreases. Mean EF% was found lower in 60-75 years group (47.39%) as compared to 51.66% of 40-49 years age group. Mean  $V_e/V_a$  was found lower in 60-75 years group (0.84) as compared to 0.88 of 40-59 years age group. As BMI increases, LV diastolic dysfunction increases. It is concluded that left ventricular dysfunction was present in significant proportion of asymptomatic diabetic patients.

**KEYWORDS:** *Diastolic dysfunction, type 2 Diabetes mellitus, 2D ECHO, Ejection fraction*



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## INTRODUCTION

Diabetes is now emerging as a worldwide epidemic. Type 2 diabetes mellitus (12DM) is the predominant form of diabetes worldwide, accounting for 90% of cases globally. All forms of diabetes, both inherited and acquired, are characterized by hyperglycemia, a relative or absolute lack of insulin. Diabetes mellitus is one of the leading public health problems and has a profound effect on CVS. The risk of cardiovascular complications is increased by twofold to sixfold in subject with diabetes. Overall, life expectancy is about 7 to 10 years shorter than for people without diabetes mellitus because of increased mortality from diabetic complications. All morbidity in DM is related to Cardiovascular dysfunction (CAD, Hypertension, cardiomyopathy, renal failure secondary to micro vascular disease). Diabetes itself can confer 75% to 90% of the excess risk of coronary disease in these diabetic subjects, and it enhances the deleterious effects of the other major cardiovascular risk factors. It is now well established that metabolic syndrome (hypertension, dyslipidemia, obesity, insulin resistance) tends to occur together in patients with diabetes. It also appears that diabetes interacts synergistically with the other risk factors to more sharply increase risk as the number of total risk factors increases.<sup>1</sup> Once heart failure develops little benefit can be done to the patient. Also the relationship between the clinical features of diabetes and LV function are linear.<sup>2</sup> Knowledge of abnormalities of cardiac function in the preclinical phase will aid in understanding the disease and its prognosis.<sup>3</sup> 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.<sup>4</sup> On a cellular level, both hyperglycemia and insulin resistance have direct negative effects on myocardial metabolism. Collectively, these various abnormalities potentiate the characteristic left ventricular remodeling of diabetes, clinically manifested as serial wall motion changes, reduced regional ejection fraction, and increased end-diastolic and end-systolic volumes.<sup>5</sup>

### Types of diabetic heart disease

Diabetes affects the heart by many mechanisms: Heart muscle - diabetic cardiomyopathy, Blood supply - coronary artery disease<sup>6</sup>, Hypertensive heart disease<sup>7,8</sup>, Hypertrophic cardiomyopathy and abnormal LV fillings<sup>9</sup>, Nerve supply - cardiac autonomic neuropathy

### Preclinical abnormalities

Diabetes without clinical heart disease has been found to have a spectrum of abnormalities of LV function, both diastolic and systolic as found with invasive and noninvasive studies. Abnormalities may be in the form of, Decreased early to late peak filling ratio, Left ventricular asynergy on 2D echo<sup>10</sup>, Reduction of peak diastolic filling ratio, Abnormal LV ejection fraction in response to exercise<sup>11</sup>, Evidence of diastolic dysfunction even in normotensive diabetes<sup>12</sup>. There is insufficient data to establish the frequency of progression of subclinical

dysfunction to congestive heart failure. But in early stages of diabetes, with optimum glycemic control, the changes are reversible.<sup>13,14</sup>

### Risk factors for cardiovascular disease in diabetic patients

The increase in cardiovascular morbidity and mortality appears to related to synergism -of hyperglycemia with other cardiovascular risk factors. Risk factors for CVD in diabetic individuals include:<sup>15</sup> Hyperglycemia, Dyslipidemia, Hypertension, Obesity, Reduced physical activity, Cigarette smoking.

### Analysis of left ventricular diastolic function<sup>16,17</sup>

Diastolic dysfunction may be an early sign of cardiac disease in diabetes, often antedating clinical and echocardiographic evidence of systolic dysfunction.

## MATERIALS AND METHODS

Total 100 patients were studied. Human ethical clearance certificate was obtained from Dean, Govt. medical college, Surat and the number is- MCS/STU/ETHICS/APPROVAL/26393/13.

### Inclusion criteria

Adults patients of type II Diabetes mellitus of more than 5 years duration, Age > 18 years of age, Patients On Following Antidiabetic Medications Will Be Included 1. All Types Of Insulin Preparations (Example. Inj. Human Mixtard), 2. All Sulfonylureas (Example. Tab. Glipizide), 3. All Biguanides (Example. Tab. Metformin) & 4. Alpha Glucosidase Inhibitors (Example. Acarbose, Voglibose).

### Exclusion criteria

Patients Of Hypertension, Patients Of Ischemic Heart Disease, Chronic Alcoholic Patient, Patients Taking Rosiglitazone And Pioglitazone, Patients having hyperlipidemia (ie deranged lipid profile).

**Control-** A random sample of 30 patients 19 male and 11 female was selected. The criteria for inclusion were: Age and Sex were comparable to the study group, FBS < 126mg/dl, PPBS < 200 mg/dl, S. cholesterol < 200 mg/dl, S. Triglyceride < 150 mg/dl. 100 adult patients fulfilling our inclusion criteria and who visited the hospital from 2012 to 2015 were studied. Among them 54 were male and 46 were female. Assessment of left ventricular diastolic functions<sup>16</sup> was done by Digitalized M echocardiography and Doppler echocardiography

## RESULTS & DISCUSSION

Total 100 patients were studied Out of that 54 were male and 46 were female. **Probable** reasons of diastolic dysfunction are diabetic cardiomyopathy, coronary artery disease<sup>6</sup>, Hypertensive heart disease<sup>7,8</sup>, Hypertrophic cardiomyopathy and cardiac autonomic neuropathy. Various results related to age, sex, left ventricular function, diabetes, echocardiography etc....are shown in

following tables.

**Table 1**  
**Age and sex wise distribution of Diabetic cases**

Age	Male	Female	Total
40-49	6	6	12
50-59	20	20	40
60-69	25	20	45
>70	3	0	3
	54	46	100

**Table 2**  
**Mean Age in various study groups**

Study Group	Mean Age in Years
Vinereanu et al (n=70)	57
Aldo Study (n=49)	59
Kyong et al (n=103)	60
Donbouchi et al (n=100)	51.3
Our Study (n=130)	57.17

- Mean age of patients in our study was 57.17 years as compared to 57 years in the cohort used by Vinereanu et al<sup>18</sup> and 59 years and 60 years in the study carried out by Aldo et al and Kyong et al<sup>19</sup> respectively. Average age in study by Donbouchi et al was 51.3 years.

**Table 3**  
**Relationship between age and left ventricular diastolic function in diabetics**

Age in years	Diabetics (n=100)		Control (n=30)	
	Mean EF%	Mean VE/VA	Mean EF%	Mean VE/VA
40-49	51.66%	0.88	57.5%	1.35
50-59	47.62%	0.88	57.08%	1.26
60-69	47.39%	0.84	56.78%	0.99

- Mean EF% of 40-49 years age group was 51.66% as compared to 47.62% and 47.39% of 50-59 and 60-75 years age group respectively. Mean EF% was found lower in 60-75 years group (47.39%) as compared to 51.66% of 40-49 years age group. Mean EF% of the control group was higher as compared to diabetics of the same age group and mean EF% of control group didn't show decline with advancing age.
- Mean Ve/Va of 40-49 years age group was 0.88 which was similar to ve/va of 50-59 years group. Mean Ve/Va was found slightly lower in 60-75 years group

(0.84) as compared to 0.88 of 40-59 years age group. Mean VE/VA of control group was higher as compared to diabetics of the same age group. Mean VE/VA of control group decreases as age advance. This is due to effects of advancing age on the diastolic function of the heart.

- With advancing age diabetics showed poor systolic as well as diastolic function. This can also be explained on a basis that with increasing age of diabetic patients, duration and complications of diabetes also increases which may be responsible for poor LV function.

**Table 4**  
**Sex ratio of Diabetes Cases in Various studies**

Study Groups	Sex Ratio-M:F
Vinereanu et al (n=70)	1.70:1
Aldo Study (n=49)	1.40:1
Kyong et al (n=103)	0.80:1
Donbouchi et al (n=50)	0.85:1
Mohammd et al (n=80)	0.82:1
Our Study (n=130)	1.17:1

Sex ratio in study by Vinereanu et al<sup>18</sup> was 1.7:1, while sex ratio in studies by Kyong et al<sup>19</sup>, Donbouchi et al<sup>20</sup> and Mohammd et al<sup>21</sup> was 0.82:1, 0.85:1 respectively .

**Table 5**  
**Comparison of Clinical Data of Diabetics and control in various Study Groups**

Study Group	Heart Rate (Beats/Min)		Systolic Blood Pressure		Diastolic Blood Pressure	
	Diabetes	Control	Diabetes	Control	Diabetes	Control
Vinereanu et al (n=70)	74	72	145	133	83	76
Aldo Study (n=49)	65	57	139	133	89	87
Kyong et Al (n=103)	70	68	124.4	118.5	77.1	76.5
Donbouchi et al (n=50)	75	68	145.3	125.2	85.8	78.1
Mohammad et Al (n=80)	75	72	124	118	82	78
Present Study (n=130)	82.20	78.38	131.52	122.19	81.06	79.67

Mean systolic blood pressure in a study carried out by Vinereanu et al group was 145 mm of Hg as compared to control 133 mm of Hg. Mean systolic blood pressure in studies carried out by Aldo et al, Kyong et al<sup>19</sup>, Donbouchi et al and Mohammad et al<sup>20</sup> was 139 mm of Hg, 124.4 mm of Hg, 145.3 mm of Hg and 124 mm of Hg

respectively, which was higher as compared to respected control groups. Mean heart rate and DBP in study by Donbouchi et al were 75 beats / minute and 85.8 mm of Hg as compared to 68 beats/minute and 78.1 mm of Hg in control group.

**Table 6**  
**Relationship between duration of diabetes & LV Function**

Duration of diabetes	Number of patients	Mean EF %	Mean VE/VA
Upto 5 years	43	52.26%	0.91
6-10 years	41	46.70%	0.84
>10 years	16	40.58%	0.78

- 43 patients out of 100 had diabetes duration upto 5 years 41 patients had duration of diabetes between 6 to 10 years, while 16 patients had diabetes duration more than 10 years.
- Mean EF% of patients with diabetes duration more than 10 years was 40.58% which was markedly lower than 52.26% of patients with less than 6 years duration.

- Mean VE/VA of patients with diabetes with less than 6 years duration. This shows that with increase in duration of diabetes due to its effect at cellular level and the micro vascular complications, LV systolic as well as diastolic function deteriorates.

**Table 7**  
**Comparison of BMI in various Study Groups**

Study Groups	BMI	
	Diabetes	Control
Vinereanu et al <sup>18</sup> (n=70)	27	26
Aldo Study (n=49)	28	28
Kyong et al <sup>19</sup> (n=103)	25.6	23.4
Donbouchi et al <sup>20</sup> (n=100)	26.1	25
M Usitupa te al (n=70)	28.7	26.4
Present Study (n=130)	26.25	22.77
p=0.0069(HS)		

- Mean BMI of diabetic patient was 26.25 as compared to 22.77 of control groups. Mean BMI is statically significantly higher (p=0.0069) than control group. Mean BMI in study carried out by Kyong et al<sup>19</sup> was 25.6 as compared to control 23.4 which is almost similar to our study.

- Similarly, as BMI increases, LV diastolic function also deteriorates, showing linear relationship. Mean Ve / Va was lower (0.74) in more than 35 BMI group as compared to 0.90 in normal BMI group.

**Table 8**  
**Comparison of Echocardiographic indices of Diastolic Function in Diabetics and Control**

Echo Parametres	Diabetics (n=100)		Control (n=30)	
	Male (n=54)	Female(n=46)	Male (n=54)	Female(n=46)
VE (m/sec)	0.67	0.72	0.68	0.70
VA(m/sec)	0.83	0.82	0.6	0.6
Mean VE/VA	0.82	0.90	1.18	1.09

Mean Ve/Va in diabetic male (0.82) and female (0.90) was lower than control group male (1.18) and female (1.09) respectively. Ve/Va<1 is indicative of LV diastolic dysfunction.

**Table 9**  
**Comparison of Echocardiographic indices of Diabetics patient's Diastolic Function in various Study**

Study	VE/VA
Vinereanu et al <sup>18</sup> (n=70)	0.820
Donbouchi et al (n=100)	0.900
Mohammd et al <sup>20</sup> (n=80)	0.890
Kyong et al <sup>19</sup> (n=103)	0.870
Aldo et al (n=49)	0.860
Present Study (n=130)	0.855

Mean Ve/Va in study by Mohammad et al<sup>20</sup> was 0.890. In Aldo et al and in study by Kyong et al it was 0.86 and 0.87 respectively, which is similar to our study (0.855).

**Table 10**  
**Relationship between Systolic and Diastolic Function in Diabetes**

EF%	Number	VE/VA(<or=0.75)	VE/VA(>0.75-<1.5)	VE/VA(>or=1.5)
>=55	48	30	17	1
45-54	33	12	15	6
35-44	7	4	2	1
<34	12	10	2	0

48 diabetic patients had normal systolic function (EF>=55%). Out of which, 30 patients had mild diastolic dysfunction, 17 patients had moderate diastolic dysfunction and 1 patient had severe diastolic dysfunction. 33 diabetic patients had mild systolic dysfunction (EF <55and>=45) Out of which, 12 patients had mild diastolic dysfunction, 15 patients had moderate diastolic dysfunction and 6 patients had severe diastolic dysfunction. 7 diabetic patients had moderate systolic dysfunction (EF<45 and>=35). Out of which, 4 patients

had mild diastolic dysfunction, 2 patients had moderate diastolic dysfunction and 1 patient had severe diastolic dysfunction. 12 diabetic patients had severe systolic dysfunction (EF<35). Out of which, 10 patients had mild diastolic dysfunction and 2 patients had moderate diastolic dysfunction. These findings suggested that diabetic patients with preserved EF may have diastolic dysfunction and similarly, patients with severe systolic dysfunction may not have severe diastolic dysfunction

**Table 11**  
**Prevalence of diastolic Dysfunction in Diabetic Patients**

VE/VA	Diabetics		
	Male	Female	Total
<or=0.75 & >or=1.5	38	26	64
0.75 to 1.5	16	20	36

Out of 100 diabetic patients studied, 64 patients had LV diastolic dysfunction, out of which 38 were male and 26 were female. 36 diabetic patients had normal LV diastolic function.

• **Z TEST for effect of diabetes on Diastolic Function of heart**

	TEST	CONTROL
EF% MEAN	X <sub>1</sub> = 0.85	X <sub>2</sub> = 55.17
STANDARD DEVIATION	SD <sub>1</sub> = 0.26	SD <sub>2</sub> = 0.32
NUMBER OF SUBJECT	N <sub>1</sub> = 100	N <sub>2</sub> = 30

Z test value for this is 3.92 that corresponds to p value of <0.0001. This shows association of diabetes with LV diastolic dysfunction at significance level of 99.99% this

shows strong relationship between diabetes and left ventricular diastolic function. 64% of diabetic patients had diastolic dysfunction, while 52% diabetic patients had

systolic dysfunction. In our study, the prevalence of diastolic dysfunction in diabetic patients was found more than systolic dysfunction.

## CONCLUSION

It was concluded that left ventricular dysfunction was present in a significant proportion of asymptomatic diabetic patients and related to duration and control of diabetes and frequently associated in patients with

microvascular complications. If early left ventricular dysfunction could be detected by simple noninvasive 2D echocardiography, then high risk patients could be detected early and treated more vigorously.

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