

ECHOCARDIOGRAPHIC EVALUATION OF DIASTOLIC DYSFUNCTION IN ASYMPTOMATIC TYPE 2 DIABETES MELLITUS

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ABSTRACT: INTRODUCTION: Diabetes mellitus is one of the most common diseases in the world and is acquiring epidemic proportions. Its prevalence is growing in both developed and developing countries. India is the Diabetic Capital Of the world. Indians are genetically more susceptible to diabetes compared to other races. Cardiovascular complications are known to be the main cause of morbidity and death in diabetic patients. In diabetic patients there is an increased rate of ischemic heart disease and cardiomyopathy which may lead to heart failure (Diastolic heart failure). Despite similar left ventricular systolic function, patients with diabetes have more pronounced heart failure symptoms, use more diuretics, and have an adverse prognosis compared with those without diabetes; one putative explanation for these discrepancies is diastolic dysfunction of the left ventricle in diabetes mellitus. 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 conducted to assess the diastolic dysfunction in diabetic patients. **MATERIAL AND METHODS:** This cross sectional study comprising 50 cases was conducted in the Department of Medicine, Pt. Jawaharlal Nehru Memorial Medical College and Dr. B.R.A.M. Hospital, Raipur (C.G.) from July 2013 to July 2014 in diabetic patients without evidence of cardiovascular involvement and blood pressure less than 140/90mmHg were studied. Permission of ethical committee was taken. 26 patients were female and 24 were male. LVDD was evaluated by Doppler echocardiography, which included E/A ratio; left atrial size was assessed in relation with age/sex, duration of diabetes and HbA1c level. **RESULTS:** Results showed that diastolic dysfunction was present in 35 (70 %) of the patients. Among males diastolic dysfunction was present in 17 cases (70.83%). Among females diastolic dysfunction was present in 18 cases (69.23%). Diastolic dysfunction was associated with uncontrolled diabetes as assessed by HbA1c levels. Diastolic dysfunction was more common in patients who were on treatment with both oral hypoglycemic agents and insulin. The prevalence of diastolic dysfunction increased with longer duration of diabetes. There was a linear progression of diastolic dysfunction with the increase in age and those with more Left Atrial size. **CONCLUSION:** The findings in our study indicate that myocardial damage in patients with diabetes affects left ventricular diastolic function before systolic function. E/A ratio and Left atrial size are significantly altered in diabetic patients with diastolic dysfunction. Diastolic dysfunction is significantly associated with duration of diabetes, glycemic levels and the type of treatments. Onset of diastolic dysfunction occurs earlier in females as compared to males. Doppler Echocardiography is a simple, noninvasive, cheap, easily available and a valuable tool in diagnosing diastolic dysfunction. In diabetics before they develop cardiac symptoms, Echocardiography should be done routinely on every diabetic patients to assess the cardiac function.

KEYWORDS: Echocardiography, Diastolic Dysfunction, Diabetes Mellitus.

INTRODUCTION: Diabetes mellitus is one of the most common diseases in the world and is acquiring epidemic proportions. Its prevalence is growing in both developed and developing countries. India is

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the Diabetic Capital Of the world.¹ More than 5 % of adults has this disease, with prevalence of about 1% in the youth to 13% in those older than 60 years. Recently the American–Diabetes Association (ADA) and the world health organization (WHO) sharpened the criteria for diagnosing DM, contributing to the increase in the number of diagnosis at an earlier age. Because of the increasing frequency of diabetes in the past 30 years, the importance of cardiovascular disease attributable to diabetes will continue to increase, even as its incidence in the non-diabetic population continues to diminish.²

India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "Diabetes capital of the world". According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with diabetes in India is currently around 40.9million is expected to rise to 69.9million by 2025 unless urgent preventive steps are taken. The so called "Asian Indian Phenotype" refers to certain unique clinical and biochemical abnormalities in Indians which include increased insulin resistance, greater abdominal adiposity i.e., higher waist circumference despite lower body mass index, lower adiponectin and higher high sensitive C-reactive protein levels. This phenotype makes Asian Indians more prone to diabetes and premature coronary artery disease. At least a part of this is due to genetic factors.

However, the primary driver of the epidemic of diabetes is the rapid epidemiological transition associated with changes in dietary patterns and decreased physical activity as evident from the higher prevalence of diabetes in the urban population. Even though the prevalence of microvascular complications of diabetes like retinopathy and nephropathy are comparatively lower in Indians, the prevalence of premature coronary artery disease is much higher in Indians compared to other ethnic groups.³

DIABETES AND HEART: The existence of cardiomyopathy was first proposed by Ruber et al in 1972. In 1974, Framingham study showed that heart failure was more common in diabetes due to diabetic cardiomyopathy.⁴ The Framingham heart study revealed a marked increase in congestive heart failure, coronary artery disease and myocardial Infarction in diabetic patients.⁵

Patients with signs and symptoms of heart failure with preserved left ventricular systolic function i.e., ejection fraction of 60% are said to have diastolic heart failure. Diastolic heart failure (DHF) is observed in 40% of patients with other heart failure. Diabetes mellitus is one of the major risk factors for DHF. The mortality rates among the patients with diastolic heart failure ranges from 5-8% annually as compared with 10-15% among patients with systolic heart failure.⁶

Despite similar left ventricular systolic function, patients with diabetes have more pronounced heart failure symptoms, use more diuretics, and have an adverse prognosis compared with those without diabetes; one putative explanation for these discrepancies is diastolic dysfunction of the left ventricle in diabetes mellitus.⁷

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.⁸

The diastolic abnormalities are present in diabetic patients without diabetic complications of cardiovascular system, it is the earliest and specific functional abnormality in diabetic cardiomyopathy and can affect patients who are free of macro vascular complications and newly diagnosed diabetes mellitus or even in those with a disease duration of less than 1 year.⁹

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Further there is evidence to suggest that a significant proportion of diabetic patients may suffer from diastolic dysfunction, which may contribute to the increased diagnosis of “Idiopathic Cardiomyopathy” in diabetic population. 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.¹⁰

Doppler echocardiography is one of the most useful clinical tools for the assessment of left ventricular diastolic function.⁵

Doppler indices of left ventricular filling are used not only for diagnostic purposes but also for establishing prognosis and evaluating the effect of treatment. Tissue Doppler imaging has provided useful insight in the study of diastolic function. Tissue Doppler imaging has been shown to provide an accurate assessment of diastolic function and appears to be relatively insensitive to the effects of pre-load compensation. Tissue Doppler imaging has markedly improved the echocardiographic detection of diastolic dysfunction in asymptomatic patients with Type 2 diabetes mellitus.¹¹

Therefore, this study was conducted to determine the effect of glycemic status on left ventricular diastolic function in normotensive Type 2 diabetic patients. This study highlights the problem of left ventricular diastolic dysfunction to be taken in consideration while dealing patients with Type 2 diabetes mellitus who were free from symptoms of heart failure.

AIMS AND OBJECTIVES:

1. To assess the diastolic dysfunction in patients with Type 2 diabetes mellitus.
2. To study the correlation of duration of diabetes mellitus with the diastolic dysfunction.
3. To study the age wise and sex wise diastolic dysfunction and its association with duration of diabetes mellitus.
4. To study the correlation of HbA1C level with diastolic dysfunction as a surrogate marker for controlled versus uncontrolled diabetes mellitus.

MATERIAL AND METHODS: This cross sectional study comprising 50 cases was conducted in the Department of Medicine, Pt. Jawaharlal Nehru Memorial Medical College and Dr. B. R. A. M. Hospital, Raipur (C.G.) from July 2013 to July 2014. Permission of ethical committee was taken.

Inclusion Criteria for Study Group:

1. A patient with type 2 diabetes mellitus who clinically had no symptoms of cardiovascular involvement.
2. Blood pressure of less than 140/90 mm of Hg measured on two separate occasions measured at least six hours apart after minimum 15 minutes of rest.

Exclusion Criteria for Study Group:

1. All patients with type 2 diabetes mellitus with cardiac diseases like valvular heart disease, hypertensive heart disease, cardiomyopathies or congestive cardiac failure.
2. All patients who are on antihypertensive medications, or those who have abnormal electrocardiograms.
3. Patients with other chronic illnesses such as chronic kidney disease, thyroid disorders, cerebrovascular accidents were excluded from the study.

Investigations: All 50 patients of type 2 diabetes mellitus who has fulfilled the inclusion/exclusion criteria were enrolled and studied. The patients underwent the following investigations.

- Blood glucose: Fasting and Postprandial.
- Renal function tests including electrolytes.
- Complete blood count.
- Glycosylated haemoglobin (HbA1c).
- Liver function tests.
- Electrocardiography.
- Urine routine and microscopy.
- 2 Dimensional echocardiography.
- Fundus examination.

Lablife (RFCL) H3D automated haematological analyzer and abacus (ark) were used for haematological investigations. Lab 650, fully automated analyser were used for liver function test and renal function test.

- Blood glucose was done using GOD-POD mehod.
- HbA1c was done by A1C NOW+ kit by Bayer.

Doppler Echocardiography: It was done by Mindray M7 echocardiographymachine. Doppler Echo was done in each patient and 3-4 cardiac cycles were analysed to get best phase for better outcome of results.

In Doppler study following values was evaluated.

- a. E-peak velocity of early mitral flow.
- b. A-peak velocity of late mitral flow.
- c. E/A ratio.
- d. Left atrial size.

Reduction in E velocity, increase in A velocity, E/A <1 and increase in LA size were considered as the evidence of left ventricular diastolic dysfunction.

Statical Analysis: Was done by:

Chi Square Test: This was done to find out significance of difference observed between two variables in following steps:

- a) First expected proportion of cases calculated from the observed.
- b) Then X² was applied as;

$$X^2 = \sum \frac{(O-E)^2}{E}$$

The value <0.05 was considered significant, otherwise insignificant. Student t test was used to compare study parameters among patients with diastolic dysfunction to those who have no diastolic dysfunction.

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Age in Years	Females	Males	Total
30-39	3 (6%)	2 (4%)	5 (10%)
40-49	5 (10%)	6 (12%)	11 (22%)
50-59	8 (16%)	10 (20%)	18 (36%)
60-69	9 (18%)	4 (8%)	13 (26%)
>70	1 (2%)	2 (4%)	3 (6%)
Total	26 (52%)	24 (48%)	50 (100%)

Table 1: Age and sex wise distribution of cases

Duration in yrs	Males(%)	Females(%)	Percentage(%)
0-5	12 (24)	13 (26)	25(50)
6-10	10 (20)	7 (14)	17(34)
11-15	2 (4)	6 (12)	8(16)
Total	24 (48)	26 (52)	50(100)

Table 2: Distribution of cases according to duration of diabetes and sex

Duration In Years	Diastolic Dysfunction		Total
	Present	Absent	
0-5	13(26%)	12(24%)	25
6-10	14(28%)	3(6%)	17
11-15	8(16%)	0(0%)	8
Total	35(70%)	15(30%)	50(100%)
P value: Chi square $X^2(df=2)=8.52, p<0.01$			

Table 3: Duration of Diabetes with diastolic Dysfunction

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Type of treatment	Diastolic Dysfunction		Total
	Present	Absent	
OHA	29	14	43
Insulin	2	1	3
Both	4	0	4
Total	35	15	50

P value: Chi square $X^2(df=2)=1.86, p=0.39$

Table 4: Correlation of treatment profile with diastolic dysfunction

Left Atrial size (cm)	Diastolic Dysfunction Present	Diastolic Dysfunction Absent	Total
	2 cm to 3 cm	13	
3cm to 4 cm	19	6	25
More than 4 cms	3	0	3
Total	35	15	50

P value: Chi square $X^2(df=2)=6.37, p=0.04$

Table 5: Correlation of Left Atrial Size with diastolic dysfunction

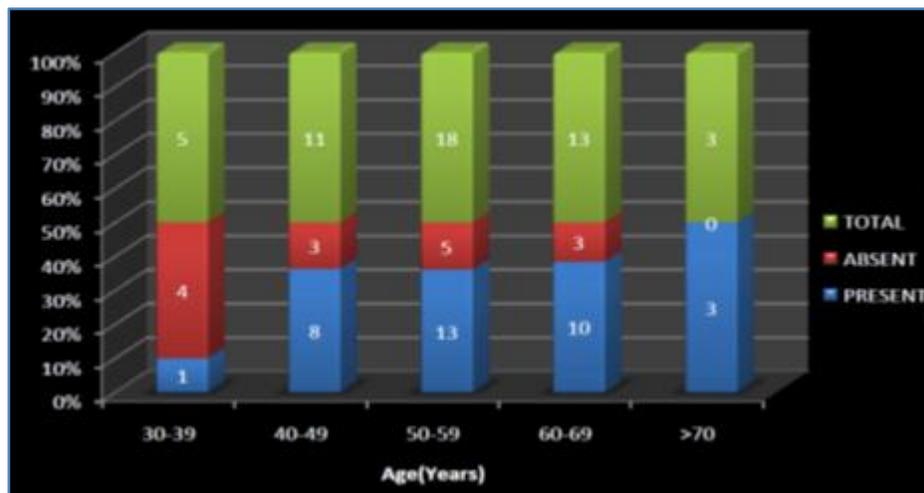


Fig. 1: Age wise prevalence of Diastolic Dysfunction

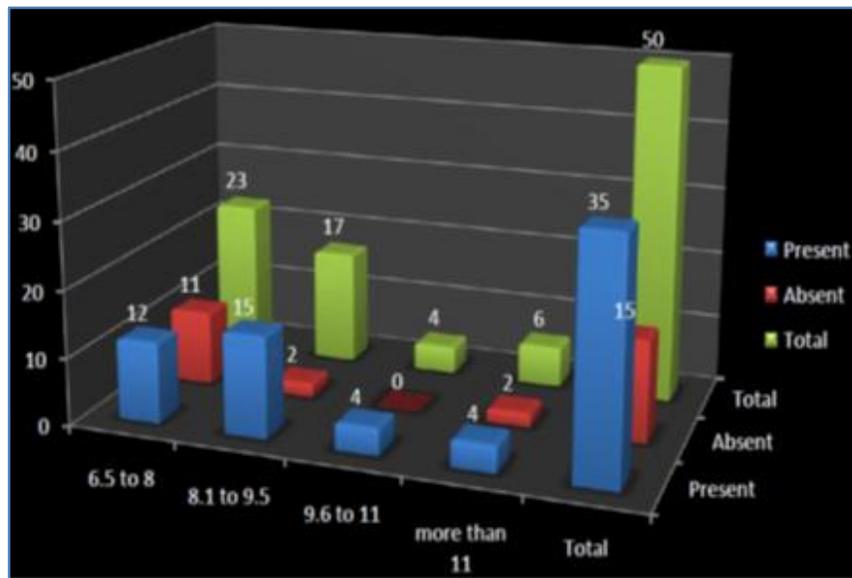


Fig. 2: HbA1c Level with Diastolic Dysfunction

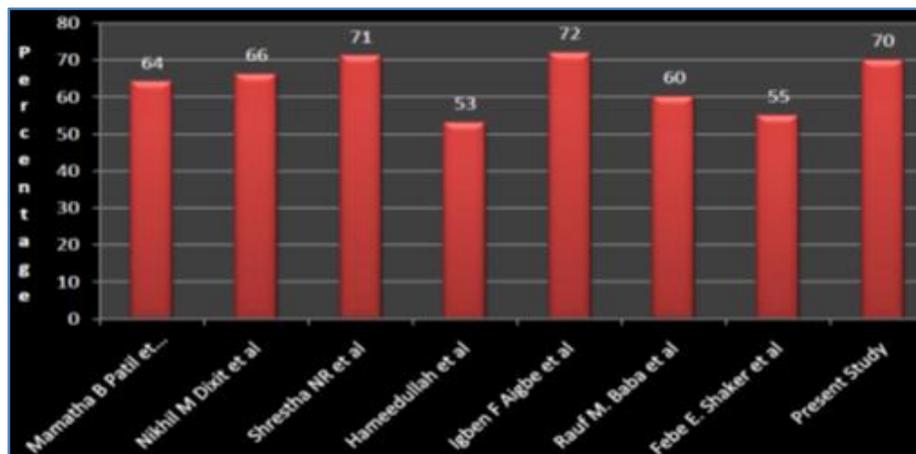


Fig. 3: Comparison of diastolic dysfunction with other studies

RESULTS:

- In our study out of 50 patients, 24 patients (48%) were male while 26 patients (52%) were female.
- Most of the subjects were between 50–59 years of age and comprised 36% of sample size, subjects above 70 years comprised 6 % of sample size with 2 males and 1 female.
- Most of the subjects were having diabetes for less than 5 years comprised 50% of sample size. There was no case having diabetes for more than 15 years.
- Patients receiving OHAs were more 43(86%) as compared to 3(6%) patients who were only on insulin and 4(8%) cases were on OHAs as well as insulin therapy. 27(54%) subjects had HbA1c >8 % which indicated poor glycemic control.

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- Diastolic dysfunction was present in 35(70%) of the cases among them 17 were males, 18 were females. Diastolic dysfunction was almost equally prevalent among female compared to male ($p<0.90$).
- Diastolic dysfunction was prevalent in 20% of patients in age group of 30-39 years and was prevalent in 81.25% of patients with age group more than 60 years. Among the age group of 40 – 49 and 50 – 59 diastolic dysfunction was almost comparable (72%). There was a linear increase in the prevalence of diastolic dysfunction with the increase in age ($p<0.01$).
- In female the diastolic dysfunction was more prevalent at younger age as compared to males (Approx 56yrs for males and 53 for females).
- Prevalence of diastolic dysfunction increased gradually with the rise in HbA1c levels. Diastolic dysfunction was present in 67.5% of patients with HbA1c between 6.5 to 9.5. Among patients with HbA1c level of more than 9.5 diastolic dysfunction was present in 80% cases. Statistically it was not significant ($p<0.71$).
- Patients who were on both insulin as well as OHAs had higher prevalence of diastolic dysfunction as compared who were on either OHAs or insulin.
- Mean E, A and E/A ratio in patients who had diastolic dysfunction was 0.68 ± 0.20 ($p<0.05$), 0.94 ± 0.29 ($p<0.01$) and 0.72 ± 0.12 respectively ($p<0.01$).
- Left atrial size was higher in patients who had diastolic dysfunction($p<0.03$) The mean LA size in centimetres was 3.10 ± 0.48 in those with diastolic dysfunction and 2.78 ± 0.26 who did not have diastolic dysfunction.

DISCUSSION: It is well known that together with other micro vascular complications a specific heart disease termed diabetic cardiomyopathy is present. Left ventricular diastolic dysfunction represents the first stage of diabetic cardiomyopathy preceding systolic dysfunction, reinforcing the importance of early examination of ventricular function in individual with diabetes.

In our study 25 cases had diabetes of duration less than or equal to 5 years. Of those, diastolic dysfunction was present in 13(52% of 25) cases and absent in 12(48%). Out of 17 cases who had diabetes of duration of 6 to 10 years, 14(82.35% of 17) had diastolic dysfunction and 3 cases (17.65%) had no diastolic dysfunction. Of the 8 cases who had diabetes for 11 to 15 years duration diastolic dysfunction was present in all cases (100.00%). Statistically also it was found to be significant ($p<0.01$). Mean duration of diabetes was 5.46 ± 3.95 yrs. Mean duration of diabetes in patients with diastolic dysfunction was 6.71 ± 3.87 yrs. Mean duration of diabetes in patients without diastolic dysfunction was 2.53 ± 2.26 yrs.

In our study most of the subjects were having diabetes of less than 5 years and were between 50-59 years of age group. This was because, as the duration of diabetes increased, other associated comorbid diseases like hypertension, IHD, were also present which were excluded in our study, so the patients with duration of diabetes more than 15 years and above age of 70 years were less. In a study done by Attali et al¹² it was observed that LV diastolic dysfunction was present in patients who were free of cardio vascular disease, had diabetes of less than 5 years.

In another study by Di-Borito et al¹³ it was observed that Diastolic dysfunction could be present in patients having diabetes less than 4 years, and sometimes with less than 1 year.

Febe E. Shaker et al¹³ did a similar study on 40 diabetic patients, of which 22 were having diastolic dysfunction. Also Exiara et al¹⁴ showed 62 patients out of 114 had diastolic dysfunction.

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Virendra C. Patil et al¹⁵ studied a total of 127 subjects with type 2 diabetes of more than five years duration. Patients with a longer duration of DM (Of 11 to 15 years) had a higher prevalence of diastolic dysfunction.

When we co-related the diastolic dysfunction with glycemic study the prevalence of diastolic dysfunction increased gradually with the rise in HbA1C levels. In a study done by Mamatha B Patil¹⁶ in 50 normotensive diabetic patients it was shown that diastolic dysfunction was present in only 3(18.75%) out of 16 patients with HbA1c value of <7%. It was present in all the cases with HbA1c value of more than 10%.

Of the 43 cases who were solely on OHAs, diastolic dysfunction was present in 29 cases (67.44% of 43) and was absent in 14 cases (32.56%). Of the 3 cases who were taking only subcutaneous insulin injections diastolic dysfunction was present in 2 (66.67%) cases and was absent in 1 case. All the 4(100%) cases who were on both OHAs as well as subcutaneous insulin injections had diastolic dysfunction.

When the treatment profile was evaluated most of the patients were on OHAs / OHAs with insulin, most of the subjects had poor glycemic control, reasons are multifactorial Viz., poor compliance of the patient with reference to treatment, lifestyle modifications, inadequate doses, poor regular checkup. In a study by Mamatha B Patil et al,¹⁶ it was shown that diastolic dysfunction was more prevalent in those who were on combined modalities of therapy i.e both insulin and OHAs. There was no difference in diastolic dysfunction in patients who were either on insulin or OHAs.

Considering the left atrial size, 22 cases of left atrial size between 2 to 3cms, 12 cases (59.09%) had diastolic dysfunction and was absent in 10 cases (41.91%). Of the 25 cases with left atrial size between 3 to 4cms, diastolic dysfunction was present in 19 cases (76%) and was absent in 6 cases (24%).

All the three cases with left atrial size more than 4cms had diastolic dysfunction (100%). So diastolic dysfunction is directly related to increase in left atrial size. Statistically also it was found to be significant (p=0.04).

Mamatha B Patil et al¹⁶ compared left atrial size in female and males which was significantly increased in both the sex who had diastolic dysfunction. In another study by Paul Porier 2004,¹⁷ it was shown that higher left atrial sizes were more closely related with diastolic dysfunction.

CONCLUSION: To conclude, the findings in our study indicates that myocardial damage in patients with Diabetes affects left ventricular diastolic function before systolic function. E/A ratio and Left atrial size is significantly altered in Diabetic patients with diastolic dysfunction. Diastolic dysfunction is significantly associated with duration of Diabetes, glycemic control and the type of treatments. Its onset occurs earlier in females as compared to males.

Doppler Echocardiography is simple, noninvasive, reproducible, safe and easily available. It identifies large percentage of Diabetic subjects who have asymptomatic left ventricular diastolic dysfunction before abnormalities are detected with ECG or by clinical examination. Therefore by early detection of diastolic dysfunction we can start early treatment and can retard the progression of LV diastolic dysfunction and its future consequences.

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