

Diastolic Dysfunction in Asymptomatic Type 2 Diabetes Mellitus with Normal Systolic Function

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Abstract: ***Background:** The incidence of heart failure in diabetic subjects is high even in the absence of hypertension and coronary artery disease. **Aims:** The purpose of this study was to study the incidence of diastolic dysfunction in diabetic subjects and its relation to age, duration of diabetes mellitus (DM), Glycosylated hemoglobin (HbA1c) levels, obesity indices and diabetic microangiopathies. **Settings and Design:** This was a case control prospective study conducted at the teaching hospital during a one year period. **Materials and Methods:** A total of 75 subjects (case) with type 2 diabetes of more than five years duration were studied. Total 75 healthy subjects were included as the control group. Echocardiography was performed to assess left ventricular diastolic function. **Results:** Out of the total 75 subjects, 43 (57%) from the case group had diastolic dysfunction, and 11% amongst 75 in the control group population showed the diastolic dysfunction ($P < 0.001$). Patients with a longer duration of DM (of 16 to 20 years) had a higher prevalence of diastolic dysfunction ($P < 0.02$). Subjects with high BMI had statistically significant diastolic dysfunction with 'P' =0.001 and 'P' = < 0.02 respectively. Subjects with HbA1c > 7.5% had a higher prevalence of diastolic dysfunction than subjects with HbA1c < 7.5% ($P < 0.02$). **Conclusions:** Present study reveals high incidence of diastolic dysfunction in asymptomatic diabetic; subjects and, this finding was correlated with the duration of diabetes, HbA1c levels, obesity indices. We conclude that early diagnosis and institution of treatment will reduce morbidity and improve the outcomes, and prevent future heart failure.*

Keywords: Diastolic dysfunction, diabetes mellitus, echocardiography, heart failure

1. Introduction

The incidence of diabetes mellitus (DM) is increasing worldwide and rapidly assuming epidemic proportions. 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 (HF) is also referred to as HF, with preserved left ventricular systolic function. Many 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 reported a high prevalence of pre-clinical diastolic dysfunction among subjects with DM.[1] The evidence indicates that myocardial damage in diabetic subjects affects diastolic function before the systolic function. The pathogenesis of this left ventricular (LV) dysfunction in diabetic subjects is not clearly understood. 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.[2] However, the exact etio-pathogenesis of diabetic cardiomyopathy still remains unclear. So far, very few population-based studies have been carried out in India, to demonstrate the prevalence of diastolic dysfunction in diabetic subjects in the Indian patients. The objective of our study was to determine whether there is any association between diastolic dysfunction and type 2DM, even in the asymptomatic subjects. Thus, this prospective case control study was conducted with the aim of determining the prevalence of asymptomatic LV diastolic dysfunction in type 2 diabetes subjects, and its relation to age, duration of DM, HbA1c, obesity indices and other diabetic complications such as microangiopathies.

2. Materials and Methods

The objectives of our study

- To determine the incidence of LV diastolic dysfunction in asymptomatic type 2 DM patients and to compare it with normal subjects;
- and, to quantify the relation of LV diastolic dysfunction with age, duration of DM, HbA1c, obesity indices and other diabetic complications such as microangiopathies.

For the study, we hypothesized that the diastolic dysfunction, [as assessed by the mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (e') (E/e') ratio], worsens with age, duration of DM, HbA1c and obesity indices. A total of 75 normotensive subjects (case), with type 2 DM of more than five years duration with no clinical evidence of cardiac disease were studied. A total 75 apparently healthy subjects with age and sex matched were included as the control group. This case control study was designed to determine the prevalence of asymptomatic left ventricular diastolic dysfunction in type 2 DM subjects and its relation to patient's age, duration of DM, control of diabetes as determined by HbA1c levels, biochemical profile and obesity indices. This was a case -control prospective, observational study conducted out at the Raja Muthiah Medical College and Hospital over a period of one year period from January 2021 to December 2021.

Inclusion Criteria for Case Population

- Age above 30 yrs
- All type 2 DM with patients with duration > 5 years with normal left ventricular systolic function (LVEF: $\geq 50\%$).

Exclusion Criteria for Case Population

- History of any heart disease (ischemic heart disease, valvular disease, chronic heart failure including hypertension)
- History of Alcohol intake (more than one drink in women and 2 drink in men or day)
- History of chronic Liver disease
- History of Kidney disease
- Patient on OHA (pioglitazone)
- History of thyroid disorder.
- BMI >40
- Postmenopausal women with out hormone replacement therapy
- Drugs causing steatohepatitis (glucocorticoids, amiodarone, tamoxifen, valproic acid, zidovudine)

Echocardiography

All the subjects were underwent resting transthoracic 2-dimensional echocardiography and Doppler imaging, to assess left ventricular diastolic function. Pulsed-wave Doppler (PWD)-derived transmitral inflow velocities was obtained in the apical 4-chamber view, with the sample volume placed at the mitral valve leaflet tips.[3] Measurements included the transmitral early diastolic rapid filling (E-wave) and atrial contraction late filling (A-wave) velocities to calculate E/A ratio, isovolumetric relaxation time (IVRT) and deceleration time (DT). For tissue Doppler imaging, the mitral annulus velocity was obtained with a 2 mm sample volume placed at the lateral side and septal side of the mitral annulus. Diastolic dysfunction was labelled according to the standard guidelines. Left ventricular overall ejection fraction (systolic function) was calculated by modified Simpson’s method; and, LVEF ≥ 50% was considered as normal.[3,4] All echocardiographic measurements were averaged over three consecutive cardiac cycles, measured by a single investigator blinded to all other variables [Figure 1].

Diagnostic Criteria

- Dyslipidemia: was defined if TC ≥ 200 mg/dL; LDL cholesterol ≥ 130 mg/dL; HDL cholesterol 40 mg/ dL; and, TG ≥ 150 mg/dL.[5]
- Obesity indices: Cut-off for high Body Mass Index (BMI) was ≥ 25 for females and ≥ 27 for males..[6]
- Diabetes mellitus (DM): If a subject is a known diabetic on treatment, or with any fasting blood sugar level (FBSL) ≥ 126 mg/dL.[6]
- Retinopathy: Microangiopathy was assessed by fundoscopy (direct ophthalmoscopy). The ophthalmologist doing fundoscopy was unaware of this study. Fundoscopic examination was done after dilating the pupil with tropicamide (1%). Retinopathy status was labeled as follow:
 - no evidence of diabetic retinopathy
 - background diabetic retinopathy, defined as presence of one or more microaneurysms, punctate or striate intraretinal hemorrhages, and hard exudates;
 - preproliferative diabetic retinopathy defined as soft exudates, venous beading, and intraretinal microvascular abnormalities;

- proliferative diabetic retinopathy characterized by neovascularization on or within one disk diameter of the disk in extent. After these initial evaluations were completed, 127 diabetic subjects were enrolled into the study protocol. Hundred apparently healthy individuals, matched for age and sex served as control group.[7]
- Diastolic dysfunction: LV diastolic dysfunction was considered to be present if any of the following findings were seen, as previously described:[3,4]
 - E/A ratio < 1 or > 2
 - DT < 150 or > 220 ms,
 - IVRT < 60 or > 100 ms, or
 - E/e’ ratio > 15.

3. Observation and Results

Table 1: Age Distribution

| Age (In years) | Cases | |
|----------------|-------------|-------|
| | No | % |
| UPTO 35 | 6 | 8 |
| 36-45 years | 7 | 9.3 |
| 46-55 | 31 | 41.3 |
| 56-65 | 30 | 40 |
| >65 | 1 | 1.3 |
| Total | 75 | 100.0 |
| Range | 24-68 years | |
| Mean | 51.8 years | |
| S.D | 9 years | |

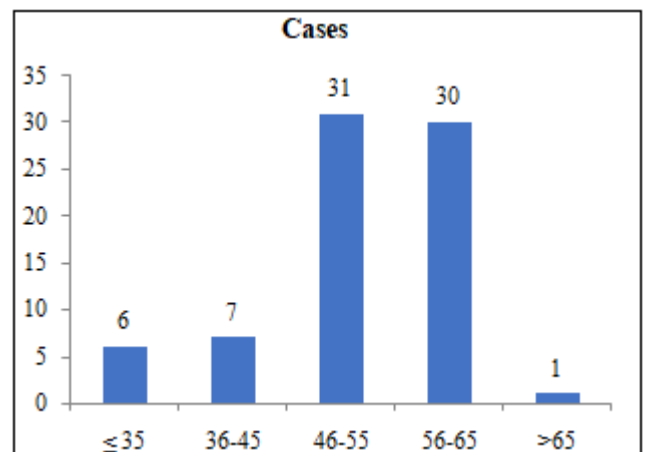


Figure 1: Bar Diagram showing Age Distribution

- Among the participants 6 patients fall under <35 years of age, 7 patients belongs to 36-45 age group, 31 patients fall under <46-55 years of age, 30 patient belongs to 56-65 years of age, 1 patient belongs to >65 years of age.
- From this above table we found more patients belongs to age group under 46-55 years.

Table 2: Distribution of Gender

| | Cases | |
|--------|-------|-------|
| | No | % |
| Male | 53 | 71 |
| Female | 22 | 29 |
| Total | 75 | 100.0 |

- Among 75 patients 53 (71 %) were male and 22 (29%) were female.

Table 3: Distribution of BMI as per WHO

| | Cases | |
|--------------------|-------|-------|
| | No | % |
| 18.5 -24.9 Normal | 8 | 10.7 |
| 25-29.9 overweight | 35 | 46.7 |
| ≥30 obesity | 32 | 42.7 |
| Total | 75 | 100.0 |

- Among the participants 8 patients belongs to normal weight, 32 patients belongs to overweight category, 35 patients belongs to obesity category.

Table 4: Distribution of Duration of Diabetes

| Duration | Cases | |
|----------|-------|-------|
| | No | % |
| 0-5 | 6 | 8 |
| 6-10 | 24 | 32 |
| 11-15 | 23 | 30.7 |
| 16-20 | 13 | 17.3 |
| >20 | 9 | 12 |
| Total | 75 | 100.0 |

- Among the 75 participants 6 patients belongs to 5 years duration, 24 patients belongs to 10 years duration, 23 patients belongs to 15 years duration, 13 patients belongs to 20 years duration, 23 patients belongs to >20 years duration of diabetes.

Table 5: Distribution of HbA1C

| | Cases | |
|--------------------|-------|-------|
| | No | % |
| Upto 6.3 Excellent | 7 | 9.3 |
| 6.4-8.5 Good | 13 | 17.3 |
| >8.5 Poor | 55 | 73.3 |
| Total | 75 | 100.0 |

- Among the 75 patients, 7 patients had excellent glycemic control, 13 patients had good glycemic control, 55 patients had poor glycemic control.

Table 6: Distribution of Total Cholesterol

| | Cases | |
|----------|-------|-------|
| | No | % |
| Normal | 0 | 0 |
| Abnormal | 75 | 100 |
| Total | 75 | 100.0 |

- Among the participants, 21 patients had normal total cholesterol level where as remaining 54 patients had abnormal cholesterol level.

Table 7: Distribution of LDL

| | Cases | |
|----------|-------|-------|
| | No | % |
| Normal | 31 | 41.3 |
| Abnormal | 44 | 58.7 |
| Total | 75 | 100.0 |

- Among the 75 patients, 31 patients had normal LDL levels, 44 patients had abnormal LDL levels.

Table 8: Distribution of TGL

| | Cases | |
|----------|-------|-------|
| | No | % |
| Normal | 4 | 5.3 |
| Abnormal | 71 | 94.7 |
| Total | 75 | 100.0 |

- Among the 75 patients, 4 patients had normal TGL levels, 71 patients had abnormal TGL levels.

Table 9: Distribution of ECHO

| ECHO (diastolic dysfunction) | Cases | |
|------------------------------|--------|-------|
| | Number | % |
| Present | 32 | 43 |
| Absent | 43 | 57 |
| Total | 75 | 100.0 |

- Among the 75 patients, 32 patients had normal ECHO findings, 43 patients had abnormal echo findings.

Table 10: Comparison of Age VS Echo

| Age | ECHO | | Total | P value |
|-------|-----------|-----------|-------|---------|
| | Normal | Abnormal | | |
| | N(%) | N(%) | | |
| ≤35 | 6 (18.8) | 0 | 6 | <0.05* |
| 36-45 | 5 (15.6) | 2 (4.7) | 7 | |
| 46-55 | 10 (31.3) | 21 (48.8) | 31 | |
| 56-65 | 10 (31.3) | 20 (46.5) | 30 | |
| >65 | 1 (3.1) | 0 | 1 | |
| Total | 32 | 43 | 75 | |

* P value <0.05 significant (S) using chi Square Test

- Among the participants, abnormal echo findings seen more in 46-55 years of age.

Table 11: Comparison of BMI vs ECHO

| BMI | ECHO | | Total | P value |
|------------|-----------|-----------|-------|---------|
| | Normal | Abnormal | | |
| | N (%) | N (%) | | |
| Normal | 6 (18.8) | 2 (4.7) | 8 | <0.05* |
| Obesity | 21 (65.6) | 14 (32.6) | 35 | |
| Overweight | 5 (15.6) | 27 (62.8) | 32 | |
| Total | 32 | 43 | 75 | |

*P value <0.05 significant (S) using Chi Square Test/ Fischer Exact Test

- Among the participants, abnormal echo findings seen more in overweight category patient

Table 12: Comparison of Duration of Diabetes vs ECHO

| Duration | ECHO | | Total | P value |
|----------|-----------|-----------|-------|---------|
| | Normal | Abnormal | | |
| | N(%) | N(%) | | |
| 0-5 | 6 (18.8) | 0 | 6 | <0.05* |
| 6-10 | 12 (37.5) | 12 (27.9) | 24 | |
| 11-15 | 6 (18.8) | 17 (39.5) | 23 | |
| 16-20 | 1 (3.1) | 12 (27.9) | 13 | |
| >20 | 7 (21.9) | 2 (4.7) | 9 | |
| Total | 32 | 43 | 75 | |

*P value <0.05 significant (S) using Chi Square Test/ Fischer Exact Test

- Among the participants, abnormal echo findings seen more in 11-15 years of duration of diabetes.

Table 13: Comparison of cholesterol vs ECHO

| | ECHO | | Total | P value |
|----------|-----------|-----------|-------|---------|
| | Normal | Abnormal | | |
| | N(%) | N(%) | | |
| Normal | 17 (53.1) | 4 (9.3) | 21 | <0.05* |
| Abnormal | 15 (46.9) | 39 (90.7) | 54 | |
| Total | 32 | 43 | 75 | |

*P value <0.05 significant (S) using Chi Square Test/ Fischer Exact Test

- Among the participants, abnormal echo findings seen more in high cholesterol levels

Table 14: Comparison of LDL vs ECHO

| | ECHO | | Total | P value |
|----------|---------|-----------|-------|---------|
| | Normal | Abnormal | | |
| | N(%) | N(%) | | |
| Normal | 23 (72) | 8 (18.6) | 31 | <0.05* |
| Abnormal | 9 (28) | 35 (81.4) | 44 | |
| Total | 32 | 43 | 75 | |

*P value <0.05 significant (S) using Chi Square Test

- Among the participants, abnormal echo findings seen more in abnormal LDL levels.

Table 15: Comparison of TGL vs ECHO

| | ECHO | | Total | P value |
|----------|-----------|----------|-------|---------|
| | Normal | Abnormal | | |
| | N (%) | N (%) | | |
| Normal | 4 (12.5) | 0 | 4 | <0.05* |
| Abnormal | 28 (87.5) | 43 (100) | 71 | |
| Total | 32 | 43 | 75 | |

*P value <0.05 significant (S) using Chi Square Test/ Fischer Exact Test

- Among the participants, abnormal echo findings seen in abnormal TGL levels.

Statistical Analysis

Data was analysed for mean, percentage, standard deviation, chi square test, multiple correlation and multivariate analysis, by using SPSS-10 (Statistical Package for the Social Sciences) for Windows (SPSS, Chicago, IL). Variables that were not normally distributed were reciprocally transformed for analysis. The 't'-test and Chi-Square tests were applied to study quantitative and qualitative data, respectively with 'P' value < 0.05 was considered statistically significant. Correlation of various factors was determined using r^2 and multiple linear regression analysis. Correlation (r) findings were describes as follows: $r = 0.8$ (high correlation coefficient); $r = 0.4-0.7$ (moderate correlation); and, $r = 0.3$ and above (low correlation coefficient).

4. Results

A total 75 subjects with type-2 diabetes mellitus (cases) and 75 healthy age and sex matched controls were included in this case-control prospective study. Out of 75 subjects with type -2 DM, 53(71 %) were male and 22 (29%) were female. Total 50 (66.6%) male and 25 (33.3%) female were control healthy subjects. Mean standard deviation of biochemical, anthropometric indices and echocardiographic parameters were obtained [Table 1]. Mean of BMI in the case group was

significantly higher as compared to the control group ('P' < 0.05). Mean of TC in case group was high compared to control group (P <0.05). Mean of TG in the case group was significantly higher as compared to control group ('P' <0.05). Mean of LDL- cholesterol in the case group was higher as compared to the control group (P <0.05). Mean of HDL- cholesterol in the case group was significantly lower as compared to the control group ('P' < 0.05). Mean of HBA1c in the case group was significantly higher as compared to the control group ('P' = 0.01). Total 43 (57%) subjects from the case group had diastolic dysfunction; and, 8 (11%) amongst control group had the diastolic dysfunction. Diastolic dysfunction in type -2 DM subjects was significantly higher as compared to the control group ('P' < 0.001) [Table 1]

Relation of Diastolic Dysfunction with Various Dependent Variables in Type 2 Diabetes Subjects

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). Out of 23 subjects with age < 45 years, 10 (43.47%) had diastolic dysfunction; and, out of 104 subjects with age > 45 years, 61 (58.65%) had diastolic dysfunction. Diastolic dysfunction was significantly high in patients with age > 45 years, compared to age < 45 years ('P' < 0.05). Total 78 (61.41%) subjects were with the duration of diabetes between 6-10 years, and 49 (38.58%) were between 11-15 years. Out of 78 (61.41%) subjects with duration of diabetes between 6-10 years, 32 (41.02%) had diastolic dysfunction. Out of 49 (38.58%) subjects with duration of diabetes between 11-15 years, 37 (75.51%) had diastolic dysfunction. Comparing duration of diabetes of 6 to 10 years and 11 to 15 years with diastolic dysfunction, patients with 11 to 15 years duration of diabetes had more prevalence of diastolic dysfunction ('P' < 0.02) [Table 2 and Figure 2].

Relation of Diastolic Dysfunction with Obesity Indices

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. [Table 3 and Figure 3]

Correlation of echocardiography parameters of diastolic dysfunction with obesity indices, duration of diabetes mellitus and biochemical profile

Age was negatively correlated with E/A ratio (-0.59); and, positively with E/e' ratio (+0.2). Duration of diabetes was negatively correlated with E/A ratio (-0.51); and, positively with E/e' ratio (+0.64). Glycated HbA1c level was negatively correlated with E/A ratio (-0.23); and, positively with E/e' ratio (+0.12). Serum TG level was negatively correlated with E/A ratio (-0.28); and, positively with E/e' ratio (+0.08). Serum HDL cholesterol levels were negatively correlated with E/e' ratio (-0.23); and, positively with E/A ratio (+0.09) [Table 4 and Figure 4]. By multivariate analysis of covariance (MACOVA) and Cox's proportional hazard regression analysis, (after adjustment for age, sex) it was determined that the diastolic dysfunction (measured by E/A ratio and E/e' ratio), was significantly associated with longer duration of DM, HbA1c, serum

5. Discussion

Our current findings demonstrate that pre-clinical diastolic dysfunction is common in patients with DM. Pre-clinical diastolic dysfunction has been broadly defined as diastolic dysfunction in patients with normal systolic function, and no symptoms of heart failure (HF). Present study reveals high burden of diastolic dysfunction in cohort of type 2 DM population. In the present prospective case control study, 75 subjects with type-2 DM as cases; and, 75 healthy subjects as controls, were included. Overall mean of obesity indices like BMI was significantly higher in subjects with type 2 DM compared to the control group. Mean of HbA1c, serum TC, serum TG and LDL cholesterol in case group was significantly higher as compared to the control group. The mean of HDL cholesterol was lower in the case group as compared to the control group. Total 43 (57%) subjects from the case group had diastolic dysfunction, and 8 (11%) amongst control group showed the diastolic dysfunction. Diastolic dysfunction in type -2 diabetes subjects was significantly higher as compared to the control group ($P < 0.05$). E/A ratio negatively correlated with age, duration of DM, HbA1c level and serum TG levels; and, positively correlated with serum HDL- cholesterol. E/e' ratio positively correlated with age, duration of DM, HbA1c level, fasting BSL, and serum TG levels; and, negatively correlated with serum HDL- cholesterol. Duration of diabetes mellitus of 11 to 15 years had more prevalence of diastolic dysfunction ($P < 0.02$). Subjects with HbA1c $> 7.5\%$ had more prevalence of diastolic dysfunction than subjects with HbA1c $< 7.5\%$ ($P < 0.05$). Diastolic dysfunction was significantly high in patient with age > 45 years compared to age < 45 years ($P < 0.05$). We compared our results with various studies. Soldatos et al.[8] in their case control study of 55 individuals with type -2 DM found that Diastolic dysfunction, present in a significant proportion of population with Type 2 DM. Similarly, in the present study, 57% of subjects from the case group had diastolic dysfunction and 8 (11%) amongst control group had the diastolic dysfunction ($P < 0.05$). Van Heerebeek et al.[10] in their study of 36 type -2 DM patients stated that, the cardiomyocyte resting tension is more important when LVEF is normal. Excessive diastolic left ventricular stiffness is an important contributor to heart failure in subjects with DM. Diabetes is presumed to increase stiffness through myocardial deposition of collagen and advanced glycation end products. Similarly, in the present study, 57% of subjects from the case group had diastolic dysfunction with normal LVEF. Masugata et al.[11] in their case control study of 77 normotensive patients found that, the cardiac diastolic dysfunction without LV systolic dysfunction in patients with well-controlled type 2 DM is related neither to hypertension nor LV hypertrophy, but rather to aging and the duration of type 2 DM. Similarly, in the present study, total 57% of subjects from case group without hypertension and CAD had diastolic dysfunction with normal LV systolic function. Mishra et al.[7] in their case control study of 71 subjects with type 2 DM found that asymptomatic diabetic patients have reduced LV systolic and diastolic function as compared with healthy subjects. LV systolic and diastolic abnormalities are correlated with the duration of diabetes. These results are comparable with present study, where 57% of type -2 DM population had diastolic dysfunction and the DM was correlated to

advancing age, increasing duration of DM high obesity indices, HbA1c $> 7.5\%$ and dyslipidemia. From et al.[2] in their study of 484 subjects between 1996 to 2007 year found that a duration of diabetes ≥ 4 years was independently associated with LV diastolic dysfunction ($E/e' > 15$) with odds ratio 1.91. Doppler imaging velocity of the medial mitral annulus during passive filling (E/e') ratio in diabetic patients is associated with the subsequent development of HF and increased mortality. Sohailet al.[13] in their study of 212 diabetic population found that 30.76% patients with type-2 DM had diastolic dysfunction. The LV diastolic dysfunction is much more prevalent in patients with type-2 diabetes mellitus and LV diastolic dysfunction is an early marker of diabetic cardiomyopathy. In our study, prevalence of type 2 DM was 57%. Exiar et al.[14] in their study of 114 subjects stated that the prevalence of LV diastolic dysfunction in normotensive, asymptomatic and well-controlled DM type 2 patients is high, and increases with age. A total of 63.2% patients had diastolic dysfunction in their study compared to our prevalence of 57%. Diamant et al.[15] stated that early (E) acceleration peak, deceleration peak, peak filling rate, and E/A ratio, and all other indices of diastolic function, were significantly decreased in patients with recently diagnosed, well-controlled and uncomplicated type 2 diabetes compared with the controls ($P < 0.02$). Aaron et al.[17] in 1,760 diabetic patients found that, 411 (23%) patients had diastolic dysfunction and diabetic patients with diastolic dysfunction had a significantly higher mortality rate compared with those without diastolic dysfunction. An increase in the TDI velocity of the medial mitral annulus during passive filling (E/e') ratio in diabetic patients is associated with the subsequent development of HF. These findings are comparable with our study. Boyer et al.[18] stated that the prevalence of LV diastolic dysfunction in asymptomatic, normotensive patients with type 2 diabetes disease is high. Diastolic dysfunction was found in 75% subjects. They also found that, TDI detected diastolic dysfunction more often than any other echocardiographic parameter. In our study, prevalence of diastolic dysfunction was 57%. Poulsen et al.[19] in their prospective observational study of 305 patients with type 2 DM found that, abnormal LV filling is closely associated with abnormal myocardial perfusion on myocardial perfusion scintigraphy. Takeda et al.[20] in their population of 544 consecutive Japanese DM patients with ejection fraction $\geq 50\%$, found that diastolic dysfunction (impaired relaxation) plays a crucial role in the induction of HF with normal systolic function in DM patients, regardless of the severity of DM and renal dysfunction. These findings are partially comparable with our study where diastolic dysfunction was more prevalent with HbA1c > 7.5 . Poanta et al.[21] Hameedullah et al.[23] in their study population of 60 patients with type 2 DM found that there was strong correlation between HbA1c level and diastolic indices ($P < 0.05$). Diastolic dysfunction was more frequent in poorly controlled diabetic patients, and its severity is correlated with glycaemic control. Similarly in our study, HbA1c $> 7.5\%$ had higher prevalence of diastolic dysfunction compared to HbA1c $< 7.5\%$. C.M. Schannwell et al.[24] in their study population of 87 subjects concluded that even young subjects with diabetes mellitus suffer from a diastolic dysfunction, while systolic ventricular function is normal. From the above discussion and comparison of present study

findings with various studies, we found that there was high prevalence of diastolic dysfunction in subjects with asymptomatic type 2 DM, and it was correlated with age, duration of diabetes, HbA1c, dyslipidemia and obesity indice.

Our study demonstrates that the incidence of pre-clinical diastolic dysfunction is high in type 2 DM subjects. Furthermore, we found that there is a direct correlation between the duration of DM and diastolic dysfunction; and, that significant diastolic dysfunction occurs > 5 years after the onset 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 pre-clinical diastolic dysfunction may delay the progression to heart failure.

6. Study Limitations

The study was conducted on Indian general population. Thus, these findings need to be examined in different racial and ethnic groups. Homeostatic model assessment (HOMA) index for investigating fasting insulin concentration is not calculated in the present study due to resources limitations. HOMA index is considered as an independent factor for diastolic dysfunction.

7. Conclusion

Overall prevalence of diastolic dysfunction was 57% in asymptomatic type 2 DM subjects in the present study. Asymptomatic type 2 DM had significantly high prevalence of diastolic dysfunction as compared to healthy subjects. LV diastolic abnormalities were correlated with the duration of diabetes and with diabetic microangiopathies, like retinopathy and autonomic neuropathy. In the present study, DM was the strongest independent factor for LV diastolic dysfunction. This study confirms that asymptomatic diastolic dysfunction is more prevalent in subjects with type 2-DM. There was a significant correlation of LV diastolic dysfunction with the duration of diabetes, glycated HbA1c levels, obesity indices (BMI) and hypertriglyceridemia, as determined by multivariate analysis. We conclude that early diagnosis and institution of treatment for diastolic dysfunction in the form of ACE inhibitors, angiotensin II receptor blockers, aldosterone antagonists, diuretics etc. depending on clinical scenario, will reduce the morbidity and improve the outcome of diastolic HF. In order to improve the current poor prognosis in subjects with DM, the treatment of diastolic HF must be optimised. Subjects with DM type 2 should be screened for sub clinical diastolic dysfunction by echocardiography

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