**Original Research Article**

**Echocardiographic evaluation of diastolic dysfunction in diabetes mellitus without covert cardiac involvement**

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**ABSTRACT**

**Background**: Diabetic patients develop systolic and diastolic dysfunction without even associated coronary artery disease. But diastolic dysfunction is more prevalent in diabetic patients than systolic dysfunction and usually occurs before onset of symptoms. Recognition of early diastolic dysfunction is likely to make management better and avoids progression of cardiac dysfunction. This study was conducted in patients of Diabetes mellitus without other comorbidities.

**Methods**: The present study which is cross sectional and was carried out among outpatients and inpatients of tertiary care hospital of Armed forces and involved army personnel and their dependents and sample size was 100 patients.

**Results**: The prevalence of diastolic dysfunction among our study participants was found to be 36%. Diastolic dysfunction was found to be significantly higher among elderly individuals (60%) when compared to young study participants. (p<0.0001). Prevalence of diastolic dysfunction was found to be non-significantly higher among males and with longer duration of diabetes as compared to lesser duration and female gender.

**Conclusions**: Diastolic dysfunction, evaluated by echocardiography, was found to be fairly prevalent (36%; 95% CI = 27-45%) among individuals with type 2 diabetes mellitus. Poor Glycaemic control and increasing age were found to be significantly associated with presence of diastolic dysfunction among individuals with diabetes mellitus.

**Keywords**: Diabetes mellitus, Diastolic dysfunction

**INTRODUCTION**

A Diabetes is a chronic disease, which occurs when the body cannot effectively use the insulin it produces, or pancreas does not produce enough insulin. Because of this phenomenon there is hyperglycaemia (increased concentration of glucose in the blood). Adults with diabetes mellitus are 2-3-fold increased risk of developing ischemic heart disease and stroke.¹ Number of people living with diabetes all over the world was 108 million in 1980 and it has steeply risen to 422 million in 2014. The overall prevalence of diabetes mellitus among adults aged 18 years and above rose to 8.5% in 2014 from 4.7% in 1980.² In the year 2012, 1.5 million deaths were directly attributed to diabetes mellitus. Almost half of all deaths attributable to high blood glucose occur before the age of 70 years.² Because of the increasing frequency of diabetes in the past 30 years, the importance of cardiovascular disease attributable, diabetes will continue to increase, even as its incidence in the non-diabetic population continues to diminish.³ Left ventricular diastolic dysfunction is considered to be one of the common complication of CAD and heart failure. It occurs early in the ischemic cascade, preceding detectable
systolic function changes. The evidence indicates that myocardial damage in diabetic subjects affects diastolic function before the systolic function. Diastolic dysfunction thus represents the first stage of diabetic cardiomyopathy preceding changes in systolic function. This also reinforces the need of early examination of ventricular function in individual with diabetes.\textsuperscript{4,5} The reported prevalence of diastolic dysfunction in different cohorts of patients with T2DM was found to vary from 16% to a maximum of 75%.\textsuperscript{6-11}

Currently, the only available surrogate measure of diastolic function is echocardiography. Assessment of mitral valve inflow using pulsed wave Doppler is used routinely in clinical practice to noninvasively identify the five progressive filling categories: normal, abnormal relaxation, pseudo-normal, restrictive filling and non-reversible restrictive filling, based upon early (E) and late (A) peak filling velocities and E deceleration time.\textsuperscript{12,13}

Although there are studies reporting the prevalence of diastolic dysfunction among diabetics, there was a wide prevalence range noted from these studies. Also, early screening and intervention will aid reducing the disease burden. In view of the above facts this study is being done to assess the diastolic dysfunction in asymptomatic Diabetes mellitus without overt cardiac involvement using echocardiography.

**METHODS**

The present study which is cross sectional and was carried out among outpatients and inpatients of tertiary care hospital of Armed forces and involved army personnel and their dependents and sample size was 100 patients.

This proportion was used for sample size calculation, keeping power of the study as 80%, Type I error as 5%. The sample size was calculated using the formula.

$$Z^2pq/d^2$$

Where, 

$Z =$ value of two tailed alpha error; this is 1.96 at 5%, $p =$ expected proportion, $q = 1-p$, $d =$ acceptable deviation. (15% on either side of 0.63 prevalence i.e., 0.0945).

Convenient sampling technique was used to select the study participants and study period was 1\textsuperscript{st} February 2015 to 31\textsuperscript{st} December 2016.

Patients attending medicine OPD or who are admitted in medical ward were initially interviewed regarding their medical history to identify eligible participants for the study based on the pre-defined inclusion and exclusion criteria. Patients having coronary artery disease, LV Systolic dysfunction, heart failure and hypertension were excluded from study.

Conventional echocardiography. Standard and pulsed wave Doppler echocardiograms was obtained in all patients. All subjects were examined in the left lateral decubitus position, using a commercially available ultrasound system Phillips I/E 33 (Bothell, WA, USA) S5-1 phased-array transducer with M-mode, two-dimensional, pulsed and continuous wave, colour-flow, and tissue Doppler capabilities.

Measurements of the different cardiac chambers were made according to recommendations of the American Society of Cardiology. Early (E) and late (A) diastolic myocardial velocities were obtained and their ratio derived. Means and proportions were calculated for continuous and categorical variables respectively. Chi Square test was applied to identify statistical difference between proportions. Independent sample t test was applied to identify statistical difference between means. P value <0.05 is considered to be statistically significant.

**RESULTS**

Majority of the study participants, 55% were in the age group of 30-45 years with mean age of the study participants was 45.97±10.7 years (Figure 1). Males represented 44% and females represented 56% of the overall study participants. Majority of the study participants, 61% were found to have diabetes for a duration of less than 4 years. The mean duration of Diabetes mellitus of our study population was found to be 4.76±2.8 years. The prevalence of diastolic dysfunction among our study participants was found to be 36% (95% CI = 27%-45%), of whom 2/3rd of them were having Grade I and 1/3rd were found to have Grade II. Diastolic dysfunction was found to be highly prevalent among elderly individuals (60%) when compared to young study participants (Figure 2). This association was found to be statistically significant. (p<0.0001) (Table1).

| Table 1: Association between age and diastolic dysfunction (n = 100). |
|----------------|-----------------|----------|----------|----------|----------|
| Age (years) | Diastolic dysfunction | Present | Absent | Total | P value |
|--------------|----------------|---------|--------|-------|---------|
| 20-40        | 5 (12.8) | 34 (87.2) | 39 (100.0) | <0.0001 |
| 41-60        | 25 (49.0) | 26 (51.0) | 51 (100.0) |        |
| 61-80        | 6 (60.0)  | 4 (40.0)  | 10 (100.0)  |        |
| Total        | 36 (36.0) | 64 (64.0)  | 100 (100)   |        |

Prevalence of diastolic dysfunction was found to be high among males (45.5%) as compared to females (28.6%). However, this difference was not found to be statistically significant (p value - 0.096) (Table 2).

The proportion of study participants with diastolic dysfunction was high among those who are having
diabetes mellitus for more than four years as compared to those who have for less than four years. Although this difference was not found to be statistically significant (Table 3).

### Table 2: Association between gender and diastolic dysfunction (n = 100).

| Gender | Diastolic dysfunction | Present n (%) | Absent n (%) | Total n (%) | P value |
|--------|----------------------|---------------|--------------|-------------|---------|
| Males  |                      | 20 (45.5)     | 24 (54.5)    | 44 (100.0)  | 0.096   |
| Females|                      | 16 (28.6)     | 40 (71.4)    | 56 (100.0)  |         |
| Total  |                      | 36 (36.0)     | 64 (64.0)    | 100 (100)   |         |

Higher proportion of study participants were found to have diastolic dysfunction who had poor glycaemic control as compared to those with optimal glycaemic control.

Although this difference was not found to be statistically significant. (Table 4).

### Table 4: Association between glycaemic control and diastolic dysfunction (n=100).

| Glycaemic status | Diastolic Dysfunction | Present n (%) | Absent n (%) | Total n (%) | P value |
|------------------|-----------------------|---------------|--------------|-------------|---------|
| Good             |                       | 2 (100.0)     | 0 (0.0)      | 02(100.0)   |         |
| Optimal          |                       | 17 (33.3)     | 34 (66.7)    | 51(100.0)   | 0.241   |
| Sub-optimal      |                       | 9(32.1)       | 19 (67.9)    | 28(100.0)   |         |
| Poor             |                       | 8(42.1)       | 11 (57.9)    | 19(100.0)   |         |
| Total            |                       | 36 (36.0)     | 64 (64.0)    | 100(100.0)  |         |

The different echocardiographic parameters are as shown in Table 5. E is found to be negatively correlating with age i.e., E value decreased with increasing age but statically not significant. correlation = -0.51; p value = 0.615) A is found to be positively correlating with age i.e., A value increased as the age increased, however this correlation was not found to be statistically significant (Pearson correlation = 0.122; p value = 0.255) IVRT is found to be negatively correlating with age i.e., IVRT value decreased as the age increased, however this correlation was not statistically significant (Pearson correlation = -0.915; p value = 0.05) E/A is found to be negatively correlating with age i.e., E/A ratio decreased as the age increased.

However, this correlation was not found to be statistically significant (Pearson correlation = -0.138; p value = 0.170) E is found to be positively correlating with duration of diabetes mellitus i.e., E value increased as the duration of diabetes mellitus increased. Also this correlation was found to be statistically significant (Pearson Correlation = 0.226; p value = 0.024) A is found to be positively correlating with duration of diabetes mellitus i.e., A value increased as the duration of diabetes mellitus increased, also this correlation was found to be statistically significant (Pearson Correlation = 0.035; p value = 0.737) E/A is found to be negatively correlating with duration of diabetes mellitus i.e., E/A ratio decreased as the duration of diabetes mellitus increased.

However, this correlation was not found to be statistically significant (Pearson correlation = -0.177; p value = 0.248) é is found to be negatively correlating with duration of diabetes mellitus i.e., é decreased as the duration of diabetes mellitus increased. Also, this correlation was found to be statistically significant (Pearson Correlation = -0.226; p value = 0.024) á is found to be positively correlating with duration of diabetes mellitus i.e., á value increased as the duration of diabetes mellitus increased, also this correlation was found to be statistically significant (Pearson Correlation = 0.24; p value = 0.016).

E/A is found to be positively correlating with duration of diabetes mellitus i.e., E/A ratio increased as the duration of diabetes mellitus increased. Also, this correlation was found to be statistically significant (Pearson correlation = -0.28; p value <0.001).

### Table 5: Echocardiographic parameters (n = 100).

| Parameter | Mean   | Standard deviation (SD) |
|-----------|--------|-------------------------|
| E (ms)    | 90.122 | 20.8                    |
| A (ms)    | 89.391 | 25.1                    |
| IVRT (ms) | 106.55 | 62.9                    |
| EDT (ms)  | 203.45 | 44.6                    |
| é (cm/s)  | 8.477  | 2.7                     |
| á (cm/s)  | 11.045 | 7.5                     |
| s (cm/s)  | 8.727  | 1.9                     |
| E/A       | 1.08   | 0.45                    |
| E/é       | 12.731 | 12.3                    |
Table 6: Distribution of study participants based on echo parameters among different gender (n=100).

| ECHO Parameters | Males (n = 44) | Females (n = 56) | Difference in mean (95% CI) | p value* |
|-----------------|---------------|-----------------|-----------------------------|----------|
|                 | Mean | SE  | Mean | SE  |                   |         |
| E (ms)          | 84.2 | 3.1 | 94.8 | 2.7 | 10.6(2.5-18.7)   | <0.011  |
| A (ms)          | 88.0 | 3.3 | 92.1 | 3.4 | 4.1(4.8-13.8)    | 0.398   |
| IVRT (ms)       | 118.6 | 13.8 | 97.1 | 2.4 | 21.5(3.4-46.3)   | 0.09    |
| EDT (ms)        | 206.1 | 6.2 | 201.3 | 6.3 | 4.8(9.0-13.1)    | 0.599   |
| E (cm/s)        | 8.6  | 0.4 | 8.3  | 0.4 | 0.31(0.5-0.7)    | 0.562   |
| á (cm/s)        | 11.4 | 1.6 | 10.7 | 0.4 | 0.7(-2.3-3.7)    | 0.641   |
| s (cm/s)        | 8.9  | 0.3 | 8.5  | 0.3 | 0.38(-0.4-1.1)   | 0.339   |
| E/A             | 1.0  | 0.1 | 1.1  | 0.1 | 0.08(0.09-0.2)   | 0.398   |
| E/é             | 10.1 | 0.4 | 14.8 | 2.1 | 4.6(1.9-9.5)     | 0.037   |

Figure 1: Distribution of study participants based on age (n = 100).

Figure 2: Association between age and diastolic dysfunction (n = 100).

DISCUSSION

The Present study was carried out as a cross sectional descriptive study among 100 overt diabetics in tertiary care hospital of Armed forces with an objective of evaluating diastolic dysfunction in diabetes mellitus without overt cardiac involvement using echocardiography. The prevalence of diastolic dysfunction among our study participants was found to be 36% (95% CI = 27-45%), of whom 2/3rd of them were having Grade I and 1/3rd were found to have Grade II. Senthil N et al measured the prevalence of diastolic dysfunction among asymptomatic diabetic individuals and it was found to be 30%, which are identical to the findings observed in the present study.14 In a study by Chaudhary AK et al the proportion of diabetics’ subjects with diastolic dysfunction was found to be 41%, which is similar to the results of the present study.15

Madhumathi R et al studied patients with type 2 diabetes mellitus who had no symptoms of cardiovascular disease and normal Blood pressure.16 It was observed in the study that the proportion of individuals with diastolic dysfunction was 48%. This was higher to the results as observed in the present study. Patil VC et al in their case control study among 127 individuals stated that the proportion of diabetics subjects with diastolic dysfunction was found to be 54.33%, which was on a higher side when compared to the present study results (36%).17 Chandravanshi S et al in their study observed that prevalence of diastolic dysfunction increased with increasing age and increasing duration of diabetes mellitus.18 Madhumathi R et al in their reported a linear positive correlation between age of the study participants and duration of diabetes mellitus.16 These findings from various other researchers from different parts of the country were similar to the results of the present study in which it was observed that diastolic dysfunction was highly prevalent among elderly individuals (60%) as compared to young diabetics (p value <0.001). However, no significant association was observed between duration of diabetes mellitus and diastolic dysfunction in the present study (p value =0.402). Poor glycaemic control was found to be associated with diastolic dysfunction among patients with diabetes mellitus in present study. However, this association was not found to be statistically significant (p value =0.241). Similar results were observed by various other authors in their research works. Diastolic dysfunction, evaluated by echocardiography, was found to be fairly prevalent (36%; 95% CI = 27%-45%) among individuals with type 2 diabetes mellitus. Poor Glycaemic control and increasing age were found to be significantly associated with presence of diastolic dysfunction among individuals with diabetes mellitus.
CONCLUSION
Diastolic dysfunction, evaluated by echocardiography, was found to be fairly prevalent (36%; 95% CI = 27%-45%) among individuals with type 2 diabetes mellitus. Poor glycaemic control and increasing age were found to be significantly associated with presence of diastolic dysfunction among individuals with diabetes mellitus.

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