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. 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.

There is an increased rate of ischemic heart disease and cardiomyopathy which may lead to heart failure (Diastolic 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 dysfunction in diabetic patients.

**Methods:** A cross-sectional hospital-based study was done which included 50 asymptomatic patients with type 2 diabetes mellitus without evidence of cardiovascular involvement and blood pressure less than 130/80 mmHg were studied. 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 32 (64 %) of the patients. Diastolic dysfunction was more common among female sex (68.18%) compared to male (60.17%). Diastolic dysfunction was significantly 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 age group.

**Conclusion:** The findings in our study indicate that myocardial damage in patients with diabetes affects diastolic dysfunction 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 disease, glycemic levels and the type of treatments. Doppler Echocardiography is a simple non invasive valuable tool in diagnosing diastolic dysfunction. In diabetics before they develop cardiac symptoms it has to be done routinely on every diabetic patients to assess the cardiac function.

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. 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, diabetes will continue to increase, even as its incidence in the non diabetic population continues to diminish.

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.

**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. The Framingham heart study revealed a marked increase in congestive heart failure, coronary artery disease and myocardial Infarction in diabetic patients. 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 diabetic heart failure ranges from 5-8 % annually as compared with 10-15% among patients with systolic 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 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.

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, newly diagnosed diabetes mellitus or even in those with a disease duration of less than 1 year.
Table 1: Age and sex wise distribution of cases (N= 50)

<table>
<thead>
<tr>
<th>Age in Years</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>40-49</td>
<td>4</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>50-59</td>
<td>8</td>
<td>12</td>
<td>20</td>
</tr>
<tr>
<td>60-69</td>
<td>5</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>&gt;70</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2: Duration of diabetes according to the sex/ correlation with diastolic dysfunction

<table>
<thead>
<tr>
<th>Duration in Years</th>
<th>No of cases</th>
<th>%</th>
<th>Diastolic Dysfunction</th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>12 : 10 = 22</td>
<td>44</td>
<td>9</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>6-10</td>
<td>11 : 5 = 16</td>
<td>32</td>
<td>13</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>11-15</td>
<td>5 : 6 = 11</td>
<td>22</td>
<td>9</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>&gt;15</td>
<td>0 : 1 = 1</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>28 : 22 = 50</td>
<td>32</td>
<td>18</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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.14-18

Methods

This cross sectional study was conducted in K.L.E.S. Dr. Prabhakar Kore Hospital and Medical Research Center, Belgaum, over a period of one year between 1st January 2007 to 31st December 2007.

The study comprised a total of 50 cases of diabetic patients who clinically had no symptoms of cardiovascular involvement and blood pressure < 130/80 mmHg, with normal ECG were included in the study. All patients with type 2 diabetes with other cardiac diseases like valvular heart disease. Ischemic and hypertensive heart disease congestive heart failure, cardiomyopathy were excluded from the study.

Informed consent was obtained from the subjects and the Hospital ethical committee, approved the study. Patients underwent thorough clinical examination supported by relevant investigations.

The patients underwent the following investigations.

a. Blood glucose on admission: FBS PPBS
b. Renal function tests, including electrolytes.
c. Glycosylated hemoglobin (HbA1c)
d. Fasting Lipid profile : ECG, urine routine and microscopy study Fundoscopy, chest radiography, Echocardiography by # Sonos 4500, EAGLENE, # Sonos 7500 – Phillips

Doppler Echo was done in each patient and 3-4 cardiac cycles were analysed to get best phase for better outcome of results. Ejection fraction was calculated in all patients.

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
e. 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 DD.

Statistical analysis was done by estimating the prevalence rate of diastolic dysfunction and co-relating with the demographic variables like age and sex and its application to clinical practice. All data were analysed by using statistical package for social sciences (SPSS) version13 for windows. Chi-square and Fisher exact test was used to find the significance of proportion of diastolic dysfunction in the diabetic patients.

Results

Our study consists of 50 Diabetic patients comprising 28 (56%) males and 22(44%) females, most of the subjects were between 50 – 59 years of age and comprised 40 % of sample size, subjects above 70 years comprised 6 % of sample size, and all were females (Table 1). Most of the subjects were having diabetes for less than 5 years comprised 44% of sample size. There was one case having diabetes for more than 15 years (Table 2). In the study group male subject’s outnumbered female subjects with duration of diabetes 0-10 years; female subjects predominated with duration more than 11 years. Statistically it was not significant. Patients receiving OHAS were more 20 (40%) compared 16 (32%) patients were on insulin and both therapy in 14 cases (28%) (Table 3). 26(52%) subjects had HbA1c >8 % which indicated poor glyemic control (Table 4). Table 5 showing mean value of demographic characteristics in the present study. Diastolic dysfunction was present in 32 (64%) of the cases among them 17 were males, 15 were females.Diastolic dysfunction was more prevalent among female compared to male. Statistically it was not significant.

Diastolic dysfunction was prevalent in 16.67 % of patients in age group of 30 –39 years and was prevalent in 85.7 % of patients with age group more than 60 years. Among the age group of 40 – 49, 50 – 59 diastolic dysfunction was almost comparable. There was a linear increase in the prevalence of diastolic dysfunction with the increase in age group (Graph 1). There was no statistical significance for the above finding. Prevalence of diastolic dysfunction increased with the duration of Diabetes and statistically this was significant as shown (Graph No 2). Prevalence of diastolic dysfunction increased gradually with the rise in HbA1c levels and it was statistically significant as shown in (Table 4). Diastolic dysfunction was present in 18.75% of patients with HbA1c between 6.4 to 7 (good glyemic control).75% of patients between 7.1 to 8 and 85% of patients between 8.1 to 10 HbA1c. In all patients with HbA1c >10 % were having diastolic dysfunction. Statistically it was not significant correlation between treatment profile, with diastolic dysfunction (OHAS, Insulin or both therapy) (Table 3).

There were significant changes in E/A and E/A ratio in patients who had diastolic dysfunction (Table 7). This was statistically
significant. In both sex group E/A ratio was <1, and there is no statistical significance between sex. Left atrial size was higher in female patients who had diastolic dysfunction. The mean LA size was 3.32 ± 0.23 and 2.74 ± 0.29 who did not have diastolic dysfunction. This was statistically significant. And 3.77 ± 0.28 in males who had diastolic dysfunction and 3.10 ± 0.17 in males who did not have diastolic dysfunction. When compared among the sex groups left atrial size was significantly larger in male patients, statistically it was significant.

**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 function reinforcing the importance of early examination of ventricular function in individual with diabetes.\(^{10,11}\) This was in accordance with study done by Schannwell CM et al in 1999 who evaluated 92 type 2 diabetic patients without known cardiac disease and 50 controls with Doppler echocardiography. He had found that diabetic patients with normal systolic ventricular function suffer a diastolic dysfunction which served as a marker of a Diabetes.\(^{12}\) Paul Poirier et al in 2001 evaluated 40 diabetic patients without clinical evidence of cardiac disease by Doppler Echocardiography and came to conclusion that diastolic function in diabetic patients were impaired even though found normal systolic function,\(^{13}\) our findings were similar to the above.

Mean duration of diabetes was 7.31 ± 6.53 years. 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 co-morbid 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. 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 check up.

LVDD was found in 32 (64%) of patients prevalence of diastolic dysfunction was almost comparable with other studies (Table 6). LVDD was compared among gender shows 68.18 % female subjects had diastolic dysfunction compared to male 60.7 %. The strong heart study by Devereuex and colleagues in 2000 also demonstrated the same.\(^{21}\) This could be due to hormonal changes that accompany after menopause. The prevalence of diastolic dysfunction increased with duration of diabetes. The previous studies also confirmed the above findings.

In a study done by Attali et al it was observed that LV diastolic dysfunction was present in patients who were free of cardiovascular disease, had diabetes of less than 5 years, in another study by Di-Borito et al it was observed that Diastolic dysfunction could be present in patients having diabetes less than 4 years, and sometimes with less than 1 year.\(^{22}\) But in our study more of the patients had diabetic dysfunction with duration less than one year. When we co-related the diastolic dysfunction with glycemic study the prevalence of diastolic dysfunction increased gradually with the rise in HbA1C levels. This was in accordance with Fiorina who demonstrated that glycemic levels had an impact on diastolic dysfunction.\(^{23}\) There was one study done by Ann m. Grandi et al, showed a close relationship between glycemic control and left ventricular diastolic dysfunction in 36 type 1 diabetic patients which improved with glycemic control.\(^{24}\)
Hiramastn et al found that a short term glycemic control resulted in a decrease in diastolic dysfunction which was found in 48 out of 246 patients who were randomly selected and treated with insulin for 6 months. Doppler Echo was done twice, at 1 and 6 months after the initiation of insulin treatment and results were comparable.25 Studies done by Beljic et al26 and Gough et al27 found that there was no positive co relation with diastolic dysfunction and HbA1C levels assessed with pulsed wave Doppler. There were no changes in the E/A ratio despite improvements in glycemic control. Study done by Shrestha et al in 100 asymptomatic type 2 Diabetes Mellitus, LVDD was found in 71 subjects of whom 60 had impaired relaxation and 11 had a Pseudo normal pattern of ventricular filling detected by Doppler Echo which included Valsalva Maneuver.28

Diastolic dysfunction was evaluated by Doppler Echocardiography. The transmitral flow were analysed using E and A Parameters. The patients in whom E/A ratio < 1 were considered to have diastolic dysfunction. The mean E/A ratio was 0.72± 0.24 among the patient who had diastolic dysfunction and <1.38 ± 0.21 without diastolic dysfunction statistically it was significant. (P= 4.6E-13). In our study left atrial size was compared in female and males which was significantly increased in both the sex who had diastolic dysfunction. Which was comparable with study done by Paul Porier.29 There was no comparison among the sex in their studies but this is crucially important because left atrial size varies among the sex and it is smaller in females compared to males.

Conclusion

The findings in our study indicate that myocardial damage in patients with diabetes affects diastolic function before systolic function, E/A ratio; Left atrial sizes are significantly altered in diabetic patients with diastolic dysfunction. Diabetic dysfunction is significantly associated with duration of disease, glycemic control.

Doppler Echo is simple, non – invasive and reproducible. It identifies large percentage of diabetic subjects who have asymptomatic left ventricular dysfunction before abnormalities are detected with ECG or by clinical examination. Therefore by early detection we can start early treatment and can retard the progression of LV diastolic dysfunction.

References

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