Original Research Article

Observational Study To Evaluate the role of LV Diastolic Dysfunction as An Earliest Marker of Diabetic Cardiomyopathy and Correlate with HbA1c, age and duration of diabetes in normotensive asymptomatic Type 2 diabetes mellitus (T2DM) patients

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Abstract

Objective and AIM: Over the last two decades worldwide the prevalence of type 2 diabetes (T2D) has almost doubled and increasing in a rapid progression. Among cardiovascular complications of diabetes, Heart Failure (HF) considered as most common one. The main objective of this study was to evaluate the role of LV diastolic dysfunction asan earliest marker of diabetic cardiomyopathy and correlate with HbA1c, age and duration of diabetes in normotensive asymptomatic Type 2 diabetes mellitus (T2DM) patients**Material and Method:** This is a retrospective observational study conducted at a primary diabetes and cardiology clinic OPD among 75 patients whose clinical records are well maintained or fully available at the clinics registry. After getting individual patient consent the data collected and analysed to draw a study conclusion. **Results:** Average mean age of the participants were 55.72±16.7 years with average duration of diabetes of 7.87±7.13 years. Left ventricular diastolic dysfunction was present in 47 patients. To detect diastolic dysfunction among participated patients E/A ratio < 1 were considered. 0.74±0.12 were the mean E/A ratio among the patient who had diastolic dysfunction and without diastolic dysfunction it was 1.34±0.19. In female and males left atrial size was compared in this study and found to be significantly increased in both the sex who had diastolic dysfunction. Mean HbA1c of 8.93±1.6 % were found in patient with diastolic dysfunction. with diastolic dysfunction average age for patients of patients were 57.29±14.3. **Conclusion:** Diastolic function affects before systolic function in patients with diabetes because of myocardial damage during the process. In diabetic patients with diastolic dysfunction, E/A ratio is significantly altered. Before actual clinical manifestation appears early detection of myocardial injury and diagnosing diastolic dysfunction can retard the progression of further myocardial injury.

Keywords:LV Diastolic Dysfunction, Type 2 diabetes mellitus, Diabetic Cardiomyopathy. Glycemic control.

Introduction

Diabetes is well known to be associated with multiple complications that contribute to its significant morbidity and mortality. The microvascular complications, including retinopathy and nephropathy, are widely recognized as are the microvascular complications, cardiovascular disease (CVD) is the major contributor representing the largest cause of morbidity and mortality and related costs of diabetes care [1]. CVD is the leading cause of death among individuals with diabetes, accounting for about 65% of all death [2]. Individuals with diabetes have high rates of CVD. Diabetes represented the largest single risk factor, with 57.3% of women and 67.1% of men with diabetes developing CVD compared with 16.3% and 30.2% of age-matched women and men without diabetes [3]. In a study of participants drawn from the Framingham Heart Study, the lifetime risk of CVD was asses in patients with and without diabetes and stratified by obesity. At 30 years of follow-up, 67.1% of women with diabetes had developed CVD compared with 38% of women without diabetes [4]. There have been multiple interventional studies on the association between tight glycemic control and CVD. The Diabetes Control and Complications Trial (DCCT) had shown that intensive treatment group experienced significant less microvascular disease [5]. Among cardiovascular complications of diabetes, Heart Failure (HF) considered as most common one [6]. Type 2 Diabetes mellitus (T2DM) when uncontrolled lets to influence changes in myocardial structural, functional and metabolic condition and thus contribute to the development of HF. Five-year survival reduces to 12.5% and mortality risk increases tenfold when in established in T2D patients over the age of 65 HF diagnosed [7]. Thus we can profoundly describes diabetic heart disease as metabolic, structural and functional changes which is multi-faceted and spans. In diabetic cardiomyopathy, cardiac metabolism may play a central role. Left ventricular diastolic dysfunction is considered as first stage of diabetic cardio-myopathy followed by systolic dysfunction. Therefore, in every diabetic patient early examination of ventricular function is important [8,9]. Echocardiography is generally considered as best option for early and definite detection of diastolic function. The main objective of this study was to evaluate the role of LV diastolic dysfunction asan earliest marker of diabetic cardiomyopathy and correlate with HbA1c, age and duration of diabetes in normotensive asymptomatic Type 2 diabetes mellitus (T2DM) patients

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Material and Methods

This is a retrospective observational study conducted at a primary diabetes and cardiology clinic OPD among 75 patients whose clinical records are well maintained or fully available at the clinic's registry. After getting individual patient consent the data collected and analysed to draw a study conclusion.All Type 2 diabetic patients Without any clinical symptoms of cardiovascular involvement, blood pressure <130/80mmHg and having normal ECG were included in the study. All Type 2 diabetes patients with other cardiac diseases like ischemic and hypertensive heart disease, cardiomyopathy, congestive heart failure and valvular heart disease. Outcome

measures of the treatment of T2DM included BMI (body mass index), SBP (systolic blood pressure), DBP (diastolic blood pressure), FPG (fasting plasma glucose), HbA1c (glycosylated hemoglobin level), Fasting Lipid profile, Urine routine and microscopy, ECG,Fundoscopy, Chest X-ray, Echocardiography (E/A ratio; left atrial size was assessed) were noted from the clinical records of the participants. evidence of left ventricular diastolic dysfunction were considered as the E/A <1 and increase in LA size. All study patients were described by demographic variables, background variables, and other variables with appropriate statistics: frequency tables (count and percent) for categorical variables and/or descriptive statistics (mean, SD, minimum, median, mode, and maximum) for continuous variables. The analysis was carried out by using SPSS version 20.0 and MS-Excel. T- Test was applied for continuous data.

Result

70 patient's data were analysed in this observational study. Average mean age of the participants were 55.72±16.7 years with average duration of diabetes of 7.87±7.13years. Left ventricular diastolic dysfunction was present in 47 patients .With duration of diabetes, prevalence of diastolic dysfunction were found to be increases (Table 1)

Table 1: Duration of diabetes and its correlation with diastolic dysfunction

Duration in years	No of patients	Diastolic Present	Dysfunction Absent
0-5	35	18	17
6-10	22	13	9
11-15	14	12	2
>15	4	4	0
Total	75	47	28

With the rise in HbA1c levels there were a statistically significant gradually increased in the prevalence of diastolic dysfunction (Table 2).

Table 2: Correlation of diastolic dysfunction with HBA1C level

HBA1C level	6.4- 7%	7.1- 8%	8.1- 10%	>10%
Diastolic dysfunction				
Present	6	8	24	9
Absent	17	5	5	1
No. of cases	23	13	29	10

To detect diastolic dysfunction among participated patient'sE/A ratio < 1 were considered. 0.74±0.12 were the mean E/A ratio among the patient who had diastolic dysfunction and without diastolic dysfunction it was 1.34±0.19 (Table 3). In female and males left atrial size was compared in this study and found to be significantly increased in both the sex who had diastolic dysfunction. Mean HbA1c of 8.93±1.6 % were found in patient with diastolic dysfunction. with diastolic dysfunction average age for patients of patients were 57.29±14.3.

Table 3: Comparison of study parameters among the prevalence of diastolic dysfunction

Parameters	Present	Absent
Age(yrs)	57.29±14.3	49.3±11.2
Duration (yrs)	9.13±6.98	4.38±3.22
HbA1C	8.93±1.6	6.81±1.1
E(m/sec)	0.64±0.15	0.80±0.14
A(m/sec)	0.78±0.16	0.62±0.15
E/A	0.74±0.12	1.34±0.19

Discussion

Cardiovascular complications, including diabetic cardiomyopathy, are the major cause of fatalities in diabetes. Diabetic cardiomyopathy is a distinct entity independent of coronary artery disease and commonly prevalent in the diabetic population [10]. Pathophysiology of diabetic cardiomyopathy include, for example, microangiopathy, endothelial dysfunction, cardiac fibrosis, and disruption of the intracellular Ca^{2+} transport, all triggered by the diabetic milieu. Additionally, inflammation with increased numbers of immune competent cells in the cardiac tissue plays a pivotal role in the pathophysiology of diabetic cardiomyopathy, as we were able to demonstrate recently in an experimental model of diabetes.Diabetes is a metabolic syndrome that manifests a low grade of systemic inflammation, leads to an increase in all-cause mortality and contributes to the development of number of cardiovascular complications [11]. Cardiovascular diseases remain the leading cause of deaths in the United States and in many countries globally, including coronary heart disease, stroke, high blood pressure, and arterial diseases [10]. Notably, death rates among adults with both heart disease and diabetes mellitus are 2–4 times higher than those with heart disease alone, and the mortality rate of patients with heart

disease >65 years of age is ~68% in conjunction with diabetes [10]. Clearly diabetes very negatively impacts the progression and outcome of heart disease, thus understanding the interplay between the two is an important endeavor for advancing treatment strategies of patients with diabetic cardiomyopathy (DCM). The mechanisms contributing to diabetic cardiac dysfunction are complex and involve a number of molecular phenotypes including insulin resistance, oxidative/nitrative stress [12, 13], activation of mitogen-activated protein kinase (MAPK) [14, 15], pro-inflammatory, poly (adenosine diphosphate [ADP]-ribose) polymerase (PARP)[16],, transcription factors [17] as well as changes in the composition of extracellular matrix [18] and inactivation of pro-survival pathways [19], eventually leading to cell death [10], , which have been reviewed elsewhere [21].In individuals with diabetes, left ventricular diastolic dysfunction is the important for early examination of ventricular function as it represents the first stage of diabetic cardio myopathy following systolic dysfunction. Diastolic dysfunction in diabetic patients with normal systolic ventricular function was firstly founded by Schannwell C M et al in 1999, who also concluded it as an early marker of a Diabetic cardiomyopathy [22]. Several studies have already done which confirms that in uncontrolled T2DM subjects elevated blood glucose level is the main cause of various cardiovascular diseases [23-25].

Conclusion

Diastolic function affects before systolic function in patients with diabetes because of myocardial damage during the process. In diabetic patients with diastolic dysfunction, E/A ratio is significantly altered. Before actual clinical manifestation appears early detection of myocardial injury and diagnosing diastolic dysfunction can retard the progression of further myocardial injury. By Doppler Echocardiography, in 2001 Paul Poirier et al studied 40 diabetic patients without clinical evidence of cardiac disease and concluded like in this observation that diastolic function in diabetic patients were impaired even though found normal systolic function.

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