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To Study the Diastolic Dysfunction by Echocardiography in young (<40 years) Type -2 Diabetics

Authors
Dr Janki Punekar[1], Dr Amit Anurag Singh[2], Dr Vipin Das P.S.[3]
[1]Associate Professor, Department of Medicine, N.S.C.B. Medical College and Hospital, Jabalpur (M.P.)
[2]Asst. Professor, Department of Medicine, N.S.C.B. Medical College and Hospital, Jabalpur (M.P.)
[3]RMO Medicine, N.S.C.B. Medical College and Hospital, Jabalpur (M.P.)

Abstract
Introduction: *Diabetes Mellitus is a disease with multisystem complications. Heart failure is 2-5 times more common in diabetic patients than in non-diabetic population. Left ventricular diastolic dysfunction (LVDD) represents the first stage of diabetic cardiomyopathy preceding systolic dysfunction of the heart. So it is important to examine the ventricular function in individuals with diabetes mellitus. The detection of LVDD has prognostic importance as early intervention can prevent development of systolic dysfunction and heart failure.*
Aims and Objectives: *To study the prevalence of diastolic dysfunction in young (<40 years) Type - 2 diabetic patients and to correlate the severity of LVDD with duration of diabetes and glycemic control (HbA1C).*
Materials & Methods: *This study was carried out in department of medicine NSCB medical college and hospital ,Jabalpur (M. P) and included 50 cases and 50 controls*
Results: *There is a significant correlation between duration of diabetes and presence of LVDD (Chi square=13.19 and p=0.01).But there is no significant correlation between duration of diabetes and grade of LVDD(Chi square=0.64 and p=0.424). There is significant correlation between HbA1c and presence of LVDD (Chi square=14.14 and p=0.007). But there is no significant correlation between HbA1c and grade of LVDD (Chi square=0.830 and p=0.660)*
Conclusion: *The prevalence of LVDD in Young (<40 years) Type 2 Diabetics is 32%.As the duration of diabetes increases, there is an increase in the prevalence of LVDD (Chi square=13.19 and p=0.01). There is also a higher prevalence of LVDD in those who have higher HbA1c (Chi square=14.14 and p=0.007).It is suggested that all patients of Diabetes Mellitus should be routinely subjected to 2-D color Doppler echocardiographic assessment of cardiac functions. This has important therapeutic implications as early intervention can prevent development of systolic dysfunction and heart failure.*

Introduction

Diabetes Mellitus comprises of a group of common metabolic disorders that share the phenotype of hyperglycemia. Diabetes mellitus is one of the most common diseases in the world. Worldwide, the number of people with diabetes is expected to increase from 285million in 2010 to 438 million in 2030[1,2]. The prevalence of diabetes mellitus is growing in both developed and developing countries.

Cardiovascular disease is the leading cause of death in individuals with diabetes mellitus. Heart failure is 2-5 times more common in diabetic patients than in non-diabetic population. The presence of diabetic cardiomyopathy was first proposed by Rubler et al in 1972 [3] on the basis of post-mortem findings in four diabetic adults who had congestive heart failure in the absence of atherosclerotic, valvular, congenital, hypertensive, or alcoholic heart disease. Several mechanisms for diabetic cardiomyopathy have been proposed which include small and micro vascular disease, metabolic derangements, autonomic dysfunction, interstitial fibrosis and the development of fibrosis caused by the accumulation of a PAS-positive glycoprotein, leading to myocardial hypertrophy and diastolic dysfunction. It appears that Growth hormone is also involved in the pathogenesis of angiopathy in the diabetic patients[4-7]

The term "diastolic dysfunction" refers to changes in ventricular diastolic properties that have an adverse effect on the stroke volume. Left ventricular diastolic dysfunction represent the first stage of diabetic cardiomyopathy preceding changes in systolic function of the heart. The detection of LVDD has prognostic importance as early intervention can prevent development of systolic dysfunction and heart failure.[8,9]

The most useful clinical tool for the assessment of left ventricular diastolic function is Conventional Doppler Echocardiography.

It has been shown that poor control of Diabetes Mellitus leads to early development of micro vascular complications and left ventricular dysfunction initially in the form of left ventricular diastolic dysfunction. Studies are showing correlation between glycemic control and left ventricular diastolic dysfunction with the improvement of cardiac function after adequate treatment. The present study was conducted to determine the prevalence of LVDD in young (<40 years) type 2 diabetics, and to correlate the severity of LVDD with duration of diabetes and glycemic control(HbA1C).

Materials and Methods

This is case control (observational) study. In this study we had taken100 participant (n=50 cases and n=50 controls) using standard sampling procedure .The Participants of the study were the one who attended Diabetic and Medicine OPD in Netaji Subhash Chandra Bose Medical college Jabalpur in period of march 2016 to August 2017. Informed consent was obtained from the subjects and the Hospital ethical committee, approved the study

Inclusion Criteria

Case

- Age < 40 Years male & female.
- Known and established cases of diabetic mellitus type 2

Control

Healthy individual < 40 Years having normal blood sugar.

Exclusion Criteria

- Subjects with evidence of coronary artery disease - CAD [excluded by history of angina, chest pain, Electrocardiogram (ECG) changes and abnormal Treadmill test (TMT) results.
- Subjects with evidence of valvular heart disease.
- Hypertensive patients, patients on antihypertensive agents, patients with evidence of left ventricular hypertrophy on echocardiography
- Subjects with poor transthoracic echo window
- Other causes leading to diastolic dysfunc-tion like hypothyroidism and obesity

Complete history and full physical examination was done on every patient included in the study.

After a 12-hour fast, a venous blood sample was collected and sent to the biochemistry laboratory for estimation of the following:

a. All routine lab parameters

b. Blood glucose on admission: FBS, PPBS

c. Renal function tests, including electrolytes.

d. Glycosylated hemoglobin (HbA1c)

e. Fasting Lipid profile

f. ECG
g. urine routine and microscopy study
h. Fundoscopy
i. Echocardiography was done in each patient and 3-4 cardiac cycles were analyzed to get best phase for better outcome of results.

Echocardiography

Echocardiograms were recorded with a commercially available ultrasound system. All recordings and measurements were obtained according to the recommendations of the American Society of Echocardiography[10]. Echocardiography was performed at midday to avoid the influence of circadian rhythm on left ventricular diastolic function. Cardiac anatomy was visualised in the apical four chamber view and a Doppler sample volume was positioned within inflow area of the left ventricle just below the mitral valve annulus (near the mitral valve tips and parallel to the presumed axis of blood flow). In order to minimize potential effects of transducer angulations, Doppler sampling volume was aligned in different planes until maximum diastolic flow velocities were recorded till optimal spectral pattern was obtained. From the transmitral recording, following measurements were carried out.

1. Peak E velocity in m/sec - peak early transmitral filling velocity during early diastole (normal: 0.5-0.8).
2. Peak A velocity in m/sec – peak transmitral atrial filling velocity during late diastole (normal: 0.3-0.5).
3. Ratio of peak E to peak A (E/A) (normal: 1-2).
4.Left Atria size

The definitions published by Canadian consensus on diastolic dysfunction by ECHO were used to classify diastolic dysfunction as normal, impaired relaxation, pseudonormal or restrictive pattern.

Classification of LVDD

Grade 1: Delayed relaxation time i.e. E/A <1
Grade 2: Pseudo normalisation
Grade 3: Reversible restrictive pattern
Grade 4: Irreversible restrictive pattern

Statistical Analysis

The data were analysed using SPSS 20. Appropriate univariate and bivariate Statistical analysis were carried out using the Student's t test for the continuous variable (Age) and two-tailed Fisher exact test or chi-square (c2) test for categorical variables. To measure the linear dependence between two random variables Pearson's correlation coefficient was used. All means are expressed as mean ± standard deviation. The critical levels of significance of the results were considered at 0.05 levels i.e. $P < 0.05$ was considered significant

Diagnostic criteria [11]

• **Diabetes mellitus** (DM): FPG:126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.

OR

2-h PG:200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.

OR

HbA1c: 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.

OR

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose >200 mg/dL (11.1 mmol/L)

- **Diastolic dysfunction**: LV diastolic dysfunction was considered to be present if any of the following findings were seen:
  • E/A ratio < 1 or > 2
  • Increased Left Atrium size

Results

The mean age of patients in our study under case group was 35.12± 3.28 years and in control group was 34.04 ± 4.01years. The mean duration of diabetes in cases were 2.92±2.02 years. In the present study the overall prevalence of LVDD in young (<40 years) diabetic patients were 32%.Out

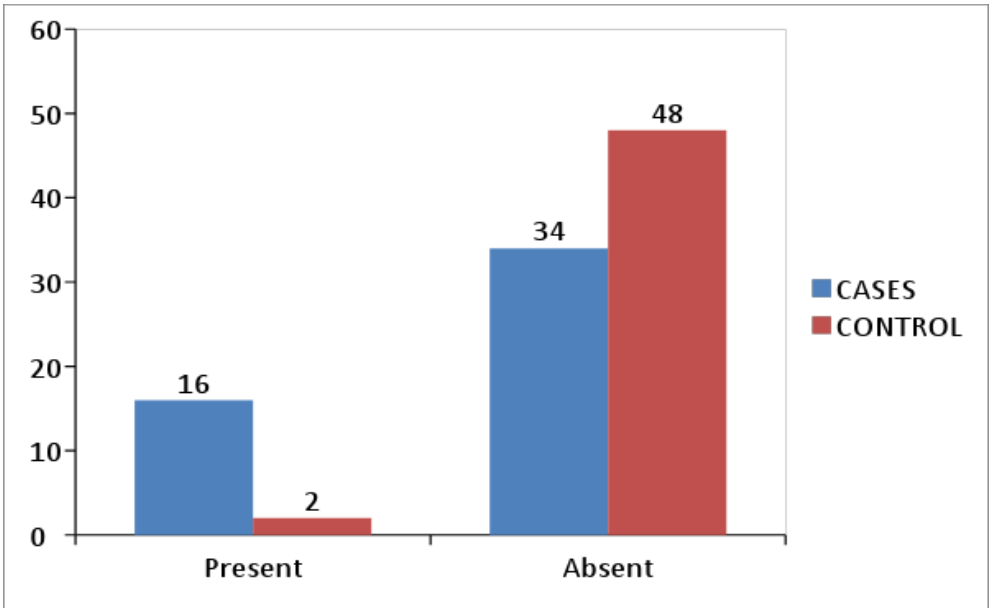
of 50 cases 16(32%) had diastolic dysfunction. Out of 16 cases with left ventricular diastolic dysfunction, 15(93.75%) had grade I (impaired relaxation) diastolic dysfunction and 1(6.25%) had grade 2 diastolic dysfunction. None of the patients had grade 3 or grade 4diastolic dysfunction.

Out of 50 cases 4 had duration of diabetes < 6 Months. None of them had LVDD.31 cases had duration of diabetes 6 Months - 3 Years .6 (19.35%) of them had LVDD. Those 6 had grade 1 LVDD. 15 had duration of diabetes >3 years.10 (66.66 %) of them had LVDD.9 (60 %) of them had grade 1 LVDD and 1 (6.67%) had grade 2 LVDD. There is a significant correlation between duration of diabetes and presence of LVDD(Chi square=13.19 and p=0.01).But there is no significant correlation between duration of diabetes and grade of LVDD (Chi square=0.64 and p=0.424).Out of 50 cases 5 had HbA1C of <6.5%.Out of which 1(20%) had LVDD and it was grade 1 LVDD.38 cases had HbA1c of 6.5-8.5%.Out of which 9(23.68%) had LVDD.8 of them had grade 1 LVDD and 1 had grade 2 LVDD.7 cases had HbA1c of >8.5%.out of which 6(85.71%) had LVDD. All of them were grade 1 LVDD There is correlation between HbA1c and presence of LVDD (Chi square=14.14 and p=0.007) but there is no significant correlation between HbA1c and grade of LVDD (Chi square=0.830 and p=0.660).

Distribution of Diastolic Dysfunction in Cases and Controls

	Present	Absent	Total
CASES	16 (32%)	34	50
CONTROL	2 (4%)	48	50

Chi square=13.27; p=<0.0001



Correlation between Duration of Diabetes and Grade of Diastolic Dysfunction

Grade of Diastolic Dysfunction	Diastolic Dysfunction							
	No diastolic dysfunction		Grade 1 diastolic dysfunction		Grade 2 diastolic dysfunction		Grade 3 and grade 4 diastolic dysfunction	
Duration of diabetes	No.	%	No.	%	No.	%	No.	%
< 6 months	4	100 %	0	0 %	0	0 %	0	0 %
6 months -3 years	25	80.65%	6*	19.35 %	0*	0 %	0	0 %
>3 years	5	33.33 %	9*	60 %	1*	6.67 %	0	0 %

Chi square =13.19; df= 4, p=0.01
Chi square test*= 0.64 df=1 p value= 0.424

Correlation between HbA1c and Grade of Diastolic Dysfunction

GRADE OF DIASTOLIC DYSFUNCTION	DIASTOLIC DYSFUNCTION							
	No diastolic dysfunction		Grade 1 diastolic dysfunction		Grade 2 diastolic dysfunction		Grade 3 and grade 4 diastolic dysfunction	
HbA1c	No.	%	No.	%	No.	%	No.	%
Upto 6.5 %	4	80 %	1*	20 %	0*	0 %	0	0 %
6.5-8.5 %	29	76.3 %	8*	21.05 %	1*	2.63 %	0	0 %
>8.5 %	1	14.29 %	6*	85.71 %	0*	0 %	0	0 %

Chi square=14.14:df= 4, p=0.007
Chi square*=0.830, df= 2, p =0.660

Discussion

In the present study the overall prevalence of LVDD in young (<40 years) diabetic patients were 32%.Out of 50 cases 16 had diastolic dysfunction. Out of 50 controls 2 had diastolic dysfunction. Out of the 2 controls with LVDD 1 had BMI of more than 30kg/m2. Significantly (p=<0.0001) higher prevalence of diastolic dysfunction was present in cases compared to controls.

The study by Zarich et al [7] showed a prevalence of 30% diastolic dysfunction in daibetics. The study conducted by N senthil, [12] showed a prevalence of 30% diastolic dysfunction in young(<40 years) diabetics. Sohail et al [13] in their study of 212 diabetic population found that 30.76% patients with Type II DM had diastolic dysfunction. The study conducted by Abhay kumar choudhari [14] revealed a prevalence of 41% LVDD in type 2 diabetes mellitus. The study by Patil et al [16] revealed the prevalence of diastolic dysfunction in asymptomatic type 2 diabetics as high as 54.33% (higher prevalence could be attributed to the duration of diabetes in these patients which were mostly more than 5 years in their study).

Out of 50 cases 4 had duration of diabetes < 6 Months. None of them had LVDD.31 cases had duration of diabetes 6 Months - 3 Years .6 (19.35%) of them had LVDD. Those 6 had grade 1 LVDD. 15 had duration of diabetes >3 years.10 (66.66 %) of them had LVDD.9 (60 %) of them had grade 1 LVDD and 1 (6.67%) had grade 2 LVDD. There is a significant correlation between duration of diabetes and presence of LVDD (Chi square=13.19 and p=0.01). This is comparable with the study conducted by Patil et al [9] (p<0.05),(60) and Panda p [15].But there is no significant correlation between duration of diabetes and grade of LVDD(Chi square=0.64 and p=0.424).

Out of 50 cases 5 had HbA1C of <6.5%.Out of which 1(20%) had LVDD and it was grade 1 LVDD.38 cases had HbA1c of 6.5-8.5%.out of which 9(23.68%) had LVDD.8 of them had grade 1 LVDD and 1 had grade2 LVDD.7 cases had HbA1c of >8.5%.out of which 6(85.71%) had LVDD. All of them were grade 1 LVDD There is correlation between HbA1c and presence of LVDD(Chi square=14.14 and p=0.007) but there is no significant correlation between HbA1c and grade of LVDD(Chi square=0.830 and p=0.660)

In a study conducted by Abhay kumar choudhari [14] showed a strong correlation between LVDD and HbA1c (p=0.0057). Study conducted by Patil et al[9] showed a strong correlation between LVDD and HbA1c. The study by Fiorina[16] revealed that glycaemic levels had an impact on diastolic dysfunction. Study by Hiramatsu et al [17] concluded that a short term glycaemic control resulted in a decrease in diastolic dysfunction. Studies done by N Senthil [13] Beljic et al [18] and Gough et al [19] found that there was no positive correlation with diastolic dysfunction and HbA1C levels assessed with pulsed wave Doppler.

Conclusion

The prevalence of LVDD in Young (<40 years) Type 2 Diabetics is 32%.As the duration of diabetes increases, there is an increase in the prevalence of LVDD (Chi square=13.19 and

p=0.01). There is also a higher prevalence of LVDD in those who have higher HbA1c (Chi square=14.14 and p=0.007).All patients of Diabetes Mellitus should be subjected to 2-D color Doppler echocardiographic assessment of cardiac functions. This has important therapeutic implications as early intervention can prevent development of systolic dysfunction and heart failure.

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