Original Article

FREQUENCY OF LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN NORMOTENSIVE ASYMPTOMATIC TYPE II DIABETIC PATIENTS AND ITS RELATIONSHIP WITH DIABETIC CONTROL

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ABSTRACT

OBJECTIVES: The objectives of this study were to determine the frequency of left ventricular diastolic dysfunction (LVDD) in normotensive asymptomatic type II diabetic patients and to compare the frequency of good diabetic control in normotensive asymptomatic type-II diabetic patients with and without LVDD.

MATERIAL AND METHODS:This cross-sectional study was conducted at department of Cardiology, Punjab institute of Cardiology, Lahore from 20/04/2015 to 19/10/2015 (six months). This study involved 200 normotensive asymptomatic type-II diabetic patients. Written informed consent was taken from every patient.

RESULTS: The mean age of the patients was 58.00±11.06 years and there were 104 (52%) male and 96 (48%) female patients in the study group. The mean duration of diabetes was 72.92±18.63 months and the mean BMI of the patients was 29.22±3.46 Kg/m^2. 94 (47%) patients were on oral hypoglycemics while 106 (53%) patients were taking insulin. Family history of DM was present in 82 (41%) patients while rest 118 (59%) patients didn't have a positive family history of DM. Left ventricular diastolic dysfunction was diagnosed in 97 (48.5%) patients while in 103 (51.5%) cases left ventricular function was preserved. 47.5% (n=95) patients had good glycemic control. When compared, the frequency of good glycemic control was significantly higher among patients with preserved left ventricular function (56.3% vs. 38.1%; p=.01) as compared to those with LVDD. When stratified the data to address effect modifiers of LVDD, there was no significant difference of LVDD among various age groups (p=.210), genders (p=.874), and treatment groups (p=.211). However, the frequency of LVDD was significantly higher with increased BMI; 20-25 Kg/m^2 vs. 25-30 Kg/m^2 vs. 30-35 Kg/m^2 (37.5% vs. 40.6% vs. 58.3%; p=.027), increased duration of disease; 48-59 months vs. 60-71 months vs. 72-83 months vs. 84-95 months vs. 96-108 months (28.1% vs. 43.8% vs. 55.6% vs. 61.1% vs. 71.9%; p=.000), and positive family history (57.3% vs. 42.4%; p=.038).

CONCLUSION: The frequency of LVDD was found to be 48.5% in normotensive asymptomatic type-II diabetic patients in local population. Moreover, the frequency of good glycemic control was significantly higher in patients with preserved left ventricular diastolic function as compared to those with LVDD.

KEY WORDS: Type-II Diabetes, Glycemic Control, Left Ventricular Diastolic Dysfunction

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INTRODUCTION

Diabetes is associated with increased incidence of heart failure even after controlling for coronary artery disease and hypertension. Thus, as diabetic cardiomyopathy has become an increasingly recognized entity among clinicians, a better understanding of its pathophysiology is necessary for early diagnosis and the development of treatment strategies for diabetes-associated cardiovascular dysfunction[1]. The 2012 International Diabetes Federation (IDF) confirms that 371 million adults are living with diabetes worldwide, and more than half that number is unaware of disease. Patients with DM are at an increased risk for cardiovascular disease[2].

The incidence of heart failure in diabetic patients 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. The evidence indicates that myocardial damage in diabetic subjects affects diastolic function before the systolic function. The pathogenesis of this left ventricular (LV) dysfunction

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in diabetic subjects is not clearly understood[3,4].

The prevalence and outcomes of this disease in a community-based population have not been defined. Diabetic cardiomyopathy is relatively common in the community with a prevalence of 1.1%. The morbidity and mortality of patients with diabetic cardiomyopathy is high[5]. Among diabetic patients, 16.9% met criteria for diabetic cardiomyopathy and 54.4% had diastolic dysfunction. Diabetes was associated with a 1.9-fold increase in risk of any left ventricular dysfunction, a 1.7-fold increase in risk of diastolic dysfunction, and a 2.2-fold increase in risk of systolic dysfunction[5]. A local study found that among the 40 patients with diabetic cardiomyopathy, 14% had isolated diastolic dysfunction[6]. One international study found that the prevalence of LVDD among normotensive diabetic patients was 39.7%[7].

Different sutdies have been conducted in which authors concluded that LVDD was more impaired in those diabetic patients having poor glycemic control.[8]

OBJECTIVES:

The objectives of this study were

- To determine the frequency of left ventricular diastolic dysfunction in normotensive asymptomatic type II diabetic patients.
- To compare the frequency of good diabetic control in normotensive asymptomatic type-II DM patients with and without LVDD.

OPERATIONAL DEFINITION

1.Type II Diabetes Mellitus: It was defined as blood sugar level >110gm/dl fasting. Patients diagnosed >3 years ago were included.

2.Normotensive Patients: It was defined as if blood pressure is <140/90mmHg.

3.Asymptomatic: Patients with no complaint of chest pain.

4.Glycemic Status: Good glycemic control was defined as HbA1c<8%.

5.Left Ventricular Diastolic Dysfunction: Diastolic dysfunction was defined as mean early diastolic mitral annulus velocity <0.11 m/sec assessed on echocardiography.

MATERIALS AND METHODS:

This cross-sectional study was conducted on 200 patients at Department of Cardiology, Punjab Institute of Cardiology, Lahore from 20.04.2015 to 19.10.2015 (six months).

Inclusion Criteria

Normotensive asymptomatic patients of age 40-80 years of either gender with Type II diabetes mellitus for >3years.

Exclusion Criteria

- Patients with wall motion abnormities, decreased motion of any wall of LV, on echocardiography.
- Patients with CAD, congestive heart failure, valvular heart disease and connective tissue diseases (on clinical evaluation).
- Patients with thyroid dysfunction (TSH>5mg/dl) and renal disease (serum creatinine>1.2mg/ dl).

200 patients who fulfilled the inclusion and exclusion criteria were enrolled from OPD of Department of Cardiology, Punjab Institute of Cardiology, Lahore. Informed consent was taken from each patient. Demographic information (name, age, sex, diabetic level, address and contact) was also noted. Then patients underwent echocardiography by a single operator using Vivid-7 G.E. system. All patients were examined in the left lateral position. To assess the diastolic function two velocities peak early diastolic velocity (Em) and peak late diastolic velocity (Am) at Mitral annulus were determined. Four different sites on the mitral annulus i.e. Lateral, Anterior, Septal and Inferior were selected. For lateral and septal sites apical 4-chamber view and for anterior and inferior sites apical 2-chamber views were utilized. Mean values from above four sites were used to assess global diastolic left ventricular function. LVDD was labeled (as per operational definition). All this information was recorded. 5ml of venous blood was sent for HbA1c level and diabetic control was labeled as per operational definition.

All the collected data was entered into SPSS version10. Numerical variables; age and duration of diabetes were presented by mean ±SD. Categorical variables; gender, good diabetic control and LVDD were presented by frequency and percentage. Chi-Square test was used to compare frequency of good diabetic control in patients with and without LVDD taking $p \leq 0.05$ as significant. Data was stratified for age, gender, BMI and duration of diabetes, treatment taken for diabetes and family history of LVDD to address effect modifiers. Post stratification chi-square has been applied taking $p \leq 0.05$ as significant.

RESULTS:

The age of the patients ranged from 40 years to 80 years with a mean of 58.00±11.06 years. There were 104 (52%) male and 96 (48%) female patients. The duration of diabetes ranged from 48 months (4 years) to 108 months (9 years) with a mean of 72.92±18.63 months. The BMI of the

patients ranged from 23.80 Kg/m^2 to 33.65 Kg/m^2 with a mean of 29.22±3.46 Kg/m^2 (Table-1).

94 (47%) patients were on oral hypoglycemics while 106 (53%) patients were taking insulin. Family history of DM was present in 82 (41%) patients. Left ventricular diastolic dysfunction (LVDD)was diagnosed in 97 (48.5%) patients. 95 (47.5%) patients had good glycemic control (Table-2). When compared, the frequency of good glycemic control was significantly higher among patients with preserved left ventricular function (56.3% vs. 38.1%; p=.01) as compared to those with LVDD (Table-3).

Table-1: Base line Demographic variables

Gender	Male	104(52%)
	Female	96(48%)
	Total	200
Age (Years)		58± 11.062(40-80 Years)
Duration of Diabetes (Months)		72.92±18.63(48-108)
BMI (Kg/m^2)		29.218 ±3.458(23.8-33.65)

Table-2: Frequency Table for Treatment taken, positive family history , LVDD and Glycemic Control

Treatment Taken		Frequency	Percent	Valid Percent	Cumulative Percent
	Oral Hypoglycemics	94	47.0	47.0	47.0
	Insulin	106	53.0	53.0	100.0
	Total	200	100.0	100.0	
Family History					
	Present	82	41.0	41.0	41.0
	Absent	118	59.0	59.0	100.0
	Total	200	100.0	100.0	
LVDD					
	Present	97	48.5	48.5	48.5
	Absent	103	51.5	51.5	100.0
	Total	200	100.0	100.0	
Glycemic Control					
	Good	95	47.5	47.5	47.5
	Poor	105	52.5	52.5	100.0
	Total	200	100.0	100.0	

Table 3: Glycemic Control * Left Ventricular Diastolic Dysfunction Crosstabulation

		Left Ventricular Diastolic Dysfunction		Total	P value
		Present	Absent		
Glycemic Control	Good	37(38.1%)	58(56.3%)	95(47.5%)	0.010
	Poor	60(61.9%)	45(43.7%)	105(52.5%)	
Total		**97(100.0%)**	**103(100.0%)**	**200(100.0%)**	
Age Groups	40-50 Years	27(42.2%)	37(57.8%)	64(100.0%)	0.210
	51-60 Years	32(57.1%)	24(42.9%)	56(100.0%)	
	61-70 Years	22(55.0%)	18(45.0%)	40(100.0%)	
	71-80 Years	16(40.0%)	24(60.0%)	40(100.0%)	
Total		**97(48.5%)**	**103(51.5%)**	**200(100.0%)**	

Table-4: Gender * Left Ventricular Diastolic Dysfunction Crosstabulation

		Left Ventricular Diastolic Dysfunction		Total	P value
		Present	Absent		
Gender	Male	51	53	104	.874
	Female	46	50	96	
Total		97	103	200	

Table-5: Treatment taken * Left Ventricular Diastolic Dysfunction Crosstabulation

		Left Ventricular Diastolic Dysfunction		Total	P value
		Present	Absent		
Treatment taken	Oral Hypoglycemics	50	44	94	.211
	Insulin	47	59	106	
Total		97	103	200	

Table-6: Groups According to BMI * Left Ventricular Diastolic Dysfunction Crosstabulation

		Left Ventricular Diastolic Dysfunction		Total	P value
		Present	Absent		
Groups According to BMI	20-25	15	25	40	.027
	25-30	26	38	64	
	30-35	56	40	96	
Total		97	103	200	

Table -7: Groups According to Duration of Diabetes * Left Ventricular Diastolic Dysfunction Crosstabulation

		Left Ventricular Diastolic Dysfunction		Total	P value
		Present	Absent		
Groups According to Duration of Diabetes	48-59 Months	18	46	64	.000
	60-71 Months	14	18	32	
	72-83 Months	20	16	36	
	84-95 Months	22	14	36	
	96-108 Months	23	9	32	
Total		97	103	200	

Table-8: Family History * Left Ventricular Diastolic Dysfunction Cross-tabulation

		Left Ventricular Diastolic Dysfunction		Total	P value
		Present	Absent		
Family History	Present	47	35	82	.038
	Absent	50	68	118	
Total		97	103	200	

When stratified the data to address effect modifiers of LVDD, there was no significant difference of LVDD among various age groups (p=.210), genders (p=.874), and treatment groups (p=.211) (Table-3,4,5). However, the frequency of LVDD was significantly higher with increased BMI; 20-25 Kg/m^2 vs. 25-30 Kg/m^2 vs. 30-35 Kg/m^2 (37.5% vs.

40.6% vs. 58.3%; p=.027), increased duration of disease; 48-59 months vs. 60-71 months vs. 72-83 months vs. 84-95 months vs. 96-108 months (28.1% vs. 43.8% vs. 55.6% vs. 61.1% vs. 71.9%; p=.000), and positive family history (57.3% vs. 42.4%; p=.038) (Table-6,7,8).

DISCUSSION:

The 2012 International Diabetes Federation confirms that 371 million adults are living with diabetes worldwide, and more than half that number is unaware of disease[2]. Diabetes is associated with increased incidence of heart failure even after controlling for coronary artery disease and hypertension[1]. Studies have reported a high prevalence of pre-clinical diastolic dysfunction among subjects with DM. The evidence indicates that myocardial damage in diabetic subjects affects diastolic function before the systolic function[3,4]. In patients without diabetes several well-studied environmental and physiological factors are now documented for CVD. These include hypercholesterolemia, hypertension, age, cigarette smoking, and obesity. Patients with diabetes are at a considerably higher risk[9] than those without and there are additive effects of other risk factors[10].

Until recently, the contribution of fluctuations and changes in glucose levels to CVD risk was relatively ignored. It's also important to note that many of the CVD risk-prediction tools do not take into account glycemic control or fluctuations in glucose levels. However, recent epidemiological data has confirmed associations between plasma glucose level and CVD risk[11].

Also, in recent years, there has been evidence to suggest that not only hyperglycemia contributes to CVD risk, but also hypoglycemia. As a result, guidelines relating to the therapeutic targets of glucose control have been under revision. Newer therapies targeting hyperglycemia with lower risks of hypoglycemia have also emerged[12].

The existing literature summarizes the frequency of LVDD in type-II diabetics. The frequency of LVDD varies from 41% in India and 71% in Nepal [13,14]. Various factors responsible for this huge variation are selection bias among the studies (age group, hypertensive/normotensive patients, and other co-morbid conditions which can cause LVDD) and population differences. Hameedullah et al. (2009) in Pakistan reported the frequency of LVDD to be 50% in normotensive type-II diabetic local population. But this study has limited sample size of 60 patients only[8].

Left ventricular diastolic dysfunction was diagnosed in 97 (48.5%) patients while in 103 (51.5%) cases left ventricular function was preserved. Our result is in line with that of Hameedullah et al. (2009) who observed the frequency of LVDD to be 50% in normotensive type-II diabetic patients in local population[8].

47.5% (n=95) patients had good glycemic control. When compared, the frequency of good glycemic control was significantly higher among patients with preserved left ventricular function (56.3% vs. 38.1%; p=.01) as compared to those with LVDD. Chaudhary et al. (p=0.0057)[13] and Kumar et al. (p=0.0157)[15] also observed significant difference while Poirier et al. (2001) reported this difference to be insignificant (p>0.05)[16].

When stratified the data to address effect modifiers of LVDD, there was no significant difference of LVDD among various age groups (p=.210), genders (p=.874), and treatment groups (p=.211). Romano et al. in 2010 also reported insignificant difference in terms of age (p=0.355) and gender (p=0.377)[17]. Shrestha et al. in 2009 (p=0.15)[14] and Kumar et al. in 2014 (p=0.088)[15] also observed insignificant difference in term of gender. However, Poirier et al. in 2001 (p=.001)[16], Khalil et al. in 2007 (p=0.032)[18], Shrestha et al. in 2009 (p=0.015)[14], Kumar et al. in 2014 (p=0.0012)[15] and Chaudhary et al. in 2015 (p=0.0012)[13] observed statistically significant difference in terms of age in patients with LVDD and normal ventricular function.

The frequency of LVDD was significantly higher with increased BMI; 20-25 Kg/m^2 vs. 25-30 Kg/m^2 vs. 30-35 Kg/m2 (37.5% vs. 40.6% vs. 58.3%; p=.027). However, Kumar et al. (p=0.0743)[15], Chaudhary et al. (p=0.0702)[13], Poirier et al. (p>0.05)[16], Romano et al. (p=0.691)[17] and Shrestha et al. (p=0.73)[14] didn't observed any significant difference in terms of BMI.

The frequency of LVDD was significantly higher with increased duration of diabetes; 48-59 months vs. 60-71 months vs. 72-83 months vs. 84-95 months vs. 96-108 months (28.1% vs. 43.8% vs. 55.6% vs. 61.1% vs. 71.9%; p=.000). Shrestha et al. (p=0.003)[14] also observed statistically significant difference in terms of duration of disease. While Poirier et al. (p>0.05)[16] and Romano et al. (p=0.225)[17] didn't observe any significant difference.

The frequency of LVDD was significantly higher among patients with positive family history (57.3% vs. 42.4%; p=.038). There was no previously published material considering this parameter.

Thus the frequency of LVDD was found to be 48.5% in normotensive asymptomatic type-II diabetic patients in local population. Furthermore, the frequency of good glycemic control was significantly higher in patients with preserved left ventricular diastolic function (56.3% vs. 38.1%; p=.01) as compared to those with LVDD suggesting a possible association between glycemic control and LVDD.

The strength of our study is that it was conducted on a large sample size of 200 patients. Moreover, the data was stratified to address the effect modifiers. The results of our study if match with some of the existing evidence, conflict with some others too, which still leave the need for further studies with much larger sample size to report something with confidence. In the present study we identified, increased duration of diabetes, BMI and a positive family history as possible attributing factors for LVDD in normotensive asymptomatic type-II diabetic patients. Further case control studies are required to establish the risk associated with these factors.

CONCLUSION:

The frequency of LVDD was found to be 48.5% in normotensive asymptomatic type-II diabetic patients in local population. Moreover, the frequency of good glycemic control was significantly higher in patients with preserved left ventricular diastolic function as compared to those with LVDD.

Author's Contribution

MAR: Conducted the study and wrote the article. MH: Helped in conducting the study and was research coordinator.MITK: Re-analyzed data, reviewed and corrected the article.AH, AN and MA were consultant incharge of the study and gave frequent advice.

REFERENCES

1. Boudina S, Abel ED. Diabetic cardiomyopathy, causes and effects. Rev Endocr Metab Disord. 2010 Mar;11(1):31-9.
2. Aguiree, Florencia, Brown, Alex, Cho, Nam Ho et.al 2013, IDF Diabetes Atlas : sixth edition, International Diabetes Federation, Basel, Switzerland.
3. Patil VC, Shah KB, Vasani JD, Shetty P, Patil HV. Diastolic dysfunction in asymptomatic type 2 diabetes mellitus with normal systolic function. J Cardiovasc Dis Res. 2011 Oct-Dec; 2(4): 213–222.
4. Kazik A, Wilczek K, Polo□ski L. Management of diastolic heart failure. Cardiol J. 2010;17(6):558-65.
5. Dandamudi S, Slusser J, Mahoney DW, Redfield MM, Rodeheffer RJ, Chen HH. The prevalence of diabetic cardiomyopathy: a population-based study in olmsted county, Minnesota. J Card Fail. 2014;20(5):304-9.
6. Muhammad Z, Hashmi A. Frequency of diabetic cardiomyopathy among type-2 diabetics presenting as heart failure. J Coll Physicians Surg Pak. 2013;23(8):538-42.
7. Poulsen MK, Henriksen JE, Dahl J, Johansen A, Gerke O, Vach W, et al. Left ventricular diastolic function in type 2 diabetes mellitus prevalence and association with myocardial and vascular disease. Circ Cardiovasc Imaging. 2010 Jan;3(1):24-31.
8. Hameedullah FM, Bahadar S, Hafizullah M, Najeeb S. Effect of glycaemic status on left ventricular diastolic function in normotensive type 2 diabetic patients. J Ayub Med Coll Abbottabad. 2009;21(3):139-44.
9. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998;339(23):229-34.
10. Gaede P, Vedel P, Larsen N, Jensen GV, Parving HH, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003;348(25):383-93.
11. Seshasai SR, Kaptoge S, Thompson A, Sarwar N, Whincup PH, Mukamal KJ, et al. Diabetes mellitus, fasting glucose, and risk of cause-specific death. N Engl J Med 2011;364(9):829-41.
12. Stephens JW, Ambler G, Vallance P, Betteridge DJ, Humphries SE, Hurel SJ. Cardiovascular risk and diabetes: Are the methods of risk prediction satisfactory? Eur J Cardiovasc Prev Rehabil 2004;11(4):521-8.
13. Chaudhary AK, Aneja GK, Shukla S, Razi SM. Study on diastolic dysfunction in newly diagnosed type 2 diabetes mellitus and its correlation with glycosylated hemoglobin (Hba1c). J Clin Diagn Res 2015;9(8):OC20-2.
14. Shrestha NR, Sharma SK, Karki P, Shrestha NK, Acharya P. Echocardiographic evaluation of diastolic function in asymptomatic type 2 diabetes. JNMA J Nepal Med Assoc. 2009 Jan-Mar;48(173):20-3.

15. Kumar S, Aneja GK, Trivedi A, Atam V, Singh A, Verma N, et al. Glycosylated Hemoglobin (HbA1c) is a reliable predictor of left ventricular hypertrophy (LVH) and left ventricular diastolic dysfunction (LVDD) in newly diagnosed type 2 diabetic patients of western Uttar Pradesh. J Int Sci Res 2014;4(12):1-7.
16. Poirier P, Bogaty P, Garneau C, Marois L, Dumesnil JG. Diastolic dysfunction in normotensive men with well-controlled type 2 diabetes: importance of maneuvers in echocardiographic screening for preclinical diabetic cardiomyopathy. Diabetes Care 2001;24(1):5-10.
17. Romano S, Di Mauro M, Fratini S, Guarracini L, Guarracini F, Poccia G, et al. Early diagnosis of left ventricular diastolic dysfunction in diabetic patients: a possible role for natriuretic peptides. Cardiovasc Diabetol 2010;9:89.
18. Khalil SI, Kamal A, Hashim F, Olaish MA. Study of left ventricular diastolic function in patients with diabetes mellitus. Sudan J Med Sci 2007;2(2):85-90.