Prevalence of Diastolic Dysfunction in Type 2 Diabetes Mellitus

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ABSTRACT

Background

Diastolic dysfunction is an inability of the ventricle to fill to a normal end-diastolic volume, both during exercise as well as at rest. Diabetes mellitus increases the risk of heart failure even in the absence of other co-morbidities.

Objective

To find the prevalence of diastolic dysfunction in patients with type 2 diabetes mellitus and its association with age, gender, duration, glycosylated hemoglobin levels, dyslipidemia, tobacco smoking and alcohol consumption.

Method

Ninety patients with type 2 diabetes mellitus of both genders, aged 30 to 60 years, were included in this study. Doppler echocardiography was performed to evaluate diastolic dysfunction.

Result

The mean age of the study population was 46.21 ± 9.20 yrs. The overall prevalence of diastolic dysfunction in the study population was 47.8%. The prevalence of diastolic dysfunction increases with age: 23.1% in patients of age 30 – 39 yrs to 65.8% in patients of age 50 – 60 yrs (adjusted OR 0.16, 95% CI 0.04 - 0.64, P = 0.010) and with the duration of diabetes: 32.8% in patients with diabetes for <5 yrs to 75% in patients with diabetes for >10 yrs (adjusted OR 0.31, 95% CI 0.08 - 1.00, P = 0.05). There was no significant association between diastolic dysfunction and dyslipidaemia, BMI, tobacco smoking, alcohol consumption, HbA1c and gender.

Conclusion

Prevalence of diastolic dysfunction in type 2 diabetes mellitus was 47.8% in our study. A rising trend of prevalence of diastolic dysfunction with the duration of diabetes and increasing age of patients was observed.

KEY WORDS

Diastolic dysfunction, Prevalence, Type 2 diabetes mellitus

INTRODUCTION

Diastolic dysfunction (DD) has been broadly defined as left ventricular diastolic dysfunction (LVDD) indicating a functional abnormality of diastolic relaxation, elasticity or distensibility of the left ventricle (LV), regardless of whether the left ventricle ejection fraction (LVEF) is normal or abnormal and whether the patient is symptomatic or not.[1-3] Asymptomatic DD defined as subjects with LVDD, without signs or symptoms of heart failure (HF), and with normal systolic function. When asymptomatic DD progresses to symptomatic heart failure called diastolic heart failure or HF with preserved ejection fraction.

In diabetes mellitus, DD results from abnormal myocardial active relaxation and an increase in passive stiffness due to metabolic derangements, microvascular disease, autonomic dysfunction and structural remodeling.[4,5] However, the exact pathogenesis of diabetic cardiomyopathy is still unclear. Diabetes mellitus increases the risk of heart failure even in the absence of coronary artery disease, hypertension, or other co-morbidities.[6,7]

The LVDD represents the earliest pre-clinical manifestation of diabetic cardiomyopathy, preceding the systolic dysfunction and being able to evolve to symptomatic heart failure.[8] Diastolic dysfunction is the dominant cause of the heart failure in patients having diastolic heart failure.[9,10] Prevalence of LVDD in T2DM varies from 47% to 71% in different studies.[9-13] There is significant uncertainty about whether a correlation exists between glycemic control and LVDD with studies showing mixed results.[14,15]

This study was done to know the burden of LVDD in patients with type 2 diabetes and its association with the duration of diabetes, age, gender, obesity, smoking, alcohol consumption, HbA1c and dyslipidaemia.

METHODS

This is a hospital-based cross sectional study carried out at Kathmandu Medical College Teaching Hospital, and Temple of Healing Clinic, Nepal. These two centers were chosen to improve sample size. A total of 90 participants with type 2 diabetes mellitus of both genders and between the age of ≥30 and ≤60 years, presenting to Kathmandu Medical College Teaching Hospital and Temple of Healing Clinic from September 2014 to March 2015 were enrolled in the study after taking consent. American Diabetes Association (ADA) guidelines 2013 for the diagnosis of diabetes mellitus was followed.[16] The criteria for the diagnosis of diabetes mellitus was fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) or 2 hrs plasma glucose of ≥ 11.1 mmol/l (200 mg/dl) after 75g oral glucose load or HbA1c ≥ 6.5%. Patients having Type 1 DM, HTN, Hypothyroidism, Hypertrophic obstructive cardiomyopathy (HOCM), Restrictive cardiomyopathy (RCM), Valvular heart disease (VHD), Chronic renal disease (CKD), Coronary artery disease (CAD), Hyperthyroidism or Hypothyroidism, and those not willing to participate were excluded from the study.

Detailed history and careful clinical examination were carried out. Weight in kilogram, height in centimeter, body mass index in kg/m^2, and blood pressure in mmHg were recorded. Routine and specific investigations- Complete Blood Count (CBC), Blood urea, Serum creatinine, fasting blood sugar (FBS), post prandial blood sugar (PPBS), glycated haemoglobin (HbA1c), Total Cholesterol (TC), High Density Lipoprotein Cholesterol, (HDL-c), Low Density Lipoprotein Cholesterol (LDL-c), Triglyceride (TG), thyroid Stimulating Hormone (TSH) and Electrocardiogram (ECG) were done. Echocardiography was performed by the same cardiologist and the findings were recorded. LV diastolic dysfunction was considered to be present if any of the following echocardiographic findings were seen.[17,18]

Mitral E/A ratio < 1or >2,

DT <150 or >220 ms,

IVRT <60 or >100 ms

Dyslipidemia was defined as low-density lipoprotein level ≥130 mg/dl or high-density lipoprotein level <40 mg/dl in male and <50 mg/dl in female, or triglyceride level ≥150 mg/dl or total cholesterol ≥200 mg/dl or treatment with antihyperlipidemic agents.[19] Body mass index (BMI) <18.5 Kg/m^2, 18.5 – 22.9 Kg/m^2, 23 – 24.9 Kg/m^2 and ≥25 Kg/m^2 were defined as underweight, normal, overweight and obese respectively in accordance to WHO Expert Consultation for appropriate body-mass index in Asian population.[20] Coronary artery disease was ruled out by clinical history of angina, chest pain, ECG changes, and ECHO changes.

IBM-SPSS version 20 was used for data entry. Variables were categorized. The study population were divided into two groups, one with diastolic dysfunction and another without diastolic dysfunction. Descriptive statistics were used to identify diastolic dysfunction prevalence, mean, and standard deviation. Comparison of baseline characteristics between diabetic patients with normal diastolic function and those with diastolic dysfunction was done using student's t tests and Chi square (χ^2) tests for quantitative (means) and qualitative (frequencies) data respectively. Binary logistic regression (simple and multivariate) analysis was used to evaluate association between diastolic dysfunction and candidate's baseline characters, calculating odd ratios (ORs) and adjusted ORs with 95% confidence interval (CI) respectively. Statistical significance was set at $P < 0.05$ for all tests.

RESULTS

Ninety patients with type 2 diabetes mellitus (51 male and 39 female) were studied. The mean age of study population was 46.21 ± 9.20 yrs. The overall prevalence of diastolic dysfunction in the study population was 47.8%,

male (34.44%), female (13.33%). Patients with diastolic dysfunction were older (p = 0.001), and had diabetes for longer duration (p=0.015) than patients without diastolic dysfunction as shown in table-1.

A rise in prevalence of diastolic dysfunction with increasing age was observed from 23.1% in patients of age 30-39 years to 65.8% in patients of age 50- 60 years (adjusted OR 0.16, 95% CI 0.04-0.64, p= 0.010). Similarly, the prevalence of diastolic dysfunction increased with the duration of diabetes, from 32.8% in patients with diabetes for <5 yrs to 75% in patients with diabetes for 10 yrs (adjusted OR 0.31, 95% CI 0.08 - 1.00, p= 0.05). Hence age of patients and duration of diabetes were risk factors for diastolic dysfunction as revealed by logistic regression analysis in table 2. There was no significant association between diastolic dysfunction and dyslipidaemia, BMI, tobacco smoking, chewing tobacco, alcohol, HbA1c and gender.

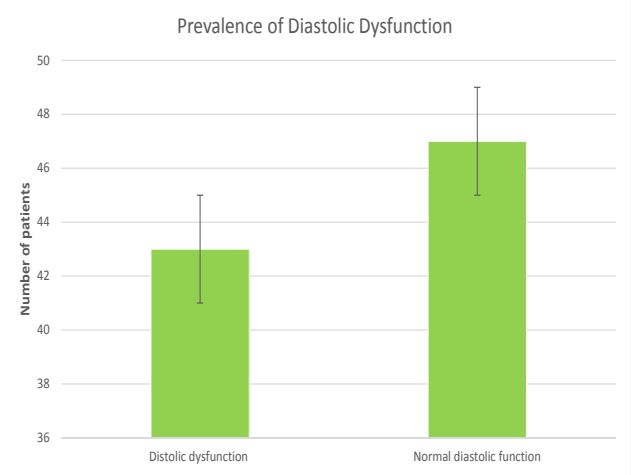

Figure 1. Bar diagram showing prevalence of diastolic dysfunction

Table 1. Baseline demographic and laboratory characteristics of the study participants with normal diastolic function and those with diastolic dysfunction.

Variables		Total	LVDD present (n=43)	LVDD absent (n =47)	p–value
Age(year)	Mean ±SD	46.21± 9.20	50.23± 8.52	42.53± 8.29	<0.001$^{\Psi}$
Gender					
Male	Number (%)	59(65.5)	31(52.5)	28(47.5)	0.296*
Female		31(34.5)	12(38.7)	19(61.3)	0.093$^{\Psi}$
BMI (Kg/m^2)	Mean ±SD	24.81± 4.16	24.04± 3.40	25.51± 4.68	0.848$^{\Psi}$
Waist/Hip ratio	Mean ±SD	0.96± 0.90	0.96± 0.06	0.95± 0.11	0.477$^{\Psi}$
Body Surface Area (m^2)	Mean ±SD		1.64 ± 0.15	1.67 ± 0.21	
Education					
Illiterate	Number (%)	18(20)	9(50)	9(50)	0.142*
School		46(51.11)	17(37)	29(63)	
Undergraduate		15(16.67)	10(66.7)	5(33.3)	
Graduate and above		11(12.22)	7(63.3)	4(36.4)	
Tobacco					
Nonsmoker	Number (%)	69(76.67)	30(43.5)	39(56.5)	0.139*
Smoker		21(23.33)	13(61.9)	8(38.1)	
Alcohol					
Non consumer	Number (%)		35(46.7)	40(53.3)	0.637*
Consumer			8(53.3)	7(46.7)	
Duration of Diabetes (yrs.)	Mean ±SD	3.96± 4.15	5.19± 4.33	3.05± 3.81	0.015$^{\Psi}$
Total Cholesterol (mg/dl)	Mean ±SD	180.56± 48.31	188.11± 58.45	173.65± 35.98	0.157$^{\Psi}$
HDL Cholesterol (mg/dl)	Mean ±SD	41.46± 5.82	41.23± 5.29	41.68± 6.32	0.718$^{\Psi}$
LDL cholesterol (mg/dl)	Mean ±SD	99.10± 42.00	101.37± 48.65	97.08± 35.26	0.631$^{\Psi}$
Triglyceride (mg/dl)	Mean ±SD	187.27± 109.87	195.04± 93.22	180.17± 123.75	0.524$^{\Psi}$
HbA1C (%)	Mean± SD	9.08± 2.46	8.86± 2.41	9.29± 2.50	0.406$^{\Psi}$
LA volume (ml)	Mean ±SD	23.65± 5.93	22.99± 5.73	24.26± 6.12	0.312$^{\Psi}$

*chi Square test, $^{\Psi}$t–test

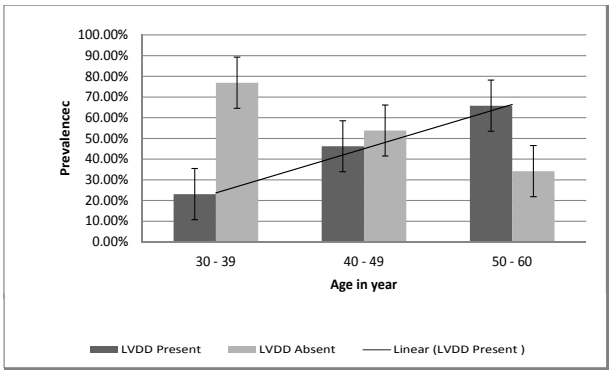

Figure 2. Prevalence of LVDD according to the age of patients.

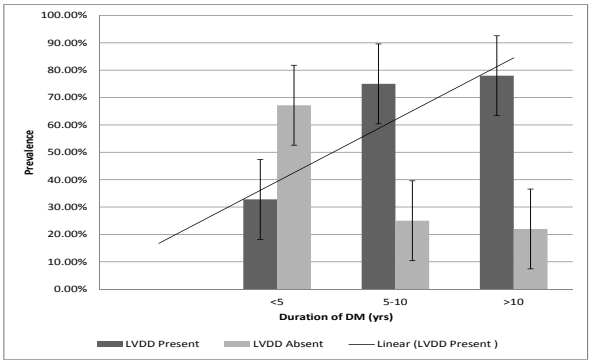

Figure 3. Prevalence of LVDD according to duration of Diabetes.

Table 2. Associations with diastolic dysfunction (Binary logistic regression analysis)

Variables	LVDD present (N/%)	Bivariate analysis		Multivariate analysis	
		Odd ratio (95% CI)	p-value	Adjusted Odd ratio (95% CI)	p-value
Age					
30-39	6(23.1)	Ref.			
40-49	12(46.2)	2.24(.81-6.23)	0.121	0.27(0.69-1.10)	0.067
50-60	25(65.8)	6.41(2.07-19.88)	0.001	0.16(0.04-0.64)	0.010
Gender					
Male	31(52.5)	Ref.			
Female	12(38.7)	1.75(0.72-4.24)	0.214	1.62(0.45-5.80)	0.454
Tobacco					
Nonsmoker	30(43.5)	Ref.			
Smoker	13(61.9)	0.47(0.17-1.28)	0.143	0.48(0.12-1.95)	0.307
Tobacco					
Non chewer	33(50.8)	Ref.			
Chewer	10(40.0)	1.55(0.60-3.94)	0.360	1.81(0.49-6.68)	0.375
Alcohol					
Non consumer	35(46.7)	Ref.			
Consumer	8(53.3)	0.76(0.25-2.30)	0.638	0.51(0.12-2.19)	0.363
BMI (Kg/m²)					
<25	28(51.9)	Ref.			
≥25	15(41.7)	1.51(0.64–3.53)	0.344	1.67(0.53-5.28)	0.385
HbA1c (%)					
≤7	12(48.0)	Ref.			
>7	31(47.7)	1.01(0.40-2.54)	0.979	0.74(0.20-2.71)	0.645
T. Cholesterol (mg/dl)					
<200	31(45.6)	Ref.			
≥200	12(54.5)	1.43(0.54-2.76)	0.466	0.24(0.04-1.38)	0.111
TG (mg/dl)					
<150	10(30.3)	Ref.			
≥150	33(57.9)	3.16(1.27–7.85)	0.013	0.45(0.14-1.45)	0.180
LDL-c (mg/dl)					
<130	39(50.0)	Ref.			
≥130	4(33.3)	0.50(0.14-1.80)	0.288	4.06(.49-33.56)	0.194
HDL-c					
<40	15(41.7)	Ref.			
≥40	28(51.9)	0.66(0.28–1.55)	0.34	0.97(0.31-3.08)	0.964
Duration of DM (Years)					
<5	19(32.8)	Ref			
5-10	18(75.0)	0.40 (0.08-1.80)	0.232	0.984 (0.17-5.80)	0.986
>10	6(78.0)	2.27 (0.61-8.43)	0.006	0.31 (0.08-1.00)	0.05

Ref. stands for referent

DISCUSSION

There is a greater risk of cardiovascular morbidity and mortality, particularly congestive cardiac failure, in diabetic subjects independent of coronary artery disease and hypertension as compared with those without diabetes as shown by Epidemiological data.[21,22] The prevalence of diastolic dysfunction in diabetic patients is 54.33% as compared to 11% in healthy population.[11] Several studies in patients with DM have identified diastolic dysfunction as the earliest functional alteration in the course of diabetic cardiomyopathy.[22-25]

In our study, the prevalence of diastolic dysfunction was 47.8% (mean age 50.23 ± 8.52) which is consistent with a study by Ernande et al. which reported 47% (mean age 46.21 ± 9.20 yrs) in France.[26] Similarly, a study by Patil VC et al. done in India has shown LVDD of 54.33% in patients with T2DM (mean age 50.0 ± 9.5yrs).[12] However, Exiara et al. in Greece in 2010 demonstrated 63.2% prevalence of diastolic dysfunction in well controlled T2DM (HbA1c<6.5) patients (mean age of 44 ± 8.2 yrs.[11] According to Shrestha et al. 71% of asymptomatic T2DM patients (mean age 52.3 ± 9.9 yrs) had diastolic dysfunction.[13]

In multiple studies, logistic regression analysis has shown the age and duration of diabetes mellitus to be statistically significant risk factors for diastolic dysfunction.[11,12,27] Also in our study, longer duration of diabetes and older age were found statistically significant risk factors for diastolic dysfunction. There was no statistically significant difference of diastolic dysfunction in male and female. However in the study of Exiara et al. and Shrestha et al. diastolic dysfunction is more prevalent in female.[11,13]

In our study, no significant association between diastolic dysfunction and dyslipidaemia, BMI, tobacco smoking, chewing tobacco, alcohol, HbA1c and gender was found. However, studies have conflicting results for these risk factors with prevalence of diastolic dysfunction.

Severity of diastolic dysfunction was not graded by ECHO in our study. Diastolic dysfunction in normal healthy age and gender matched subjects would have been desirable.

CONCLUSION

Prevalence of diastolic dysfunction in type 2 diabetes mellitus was 47.8% in our study and its prevalence increased with duration of diabetes and increasing age. There was no association between prevalence of diastolic dysfunction in patient with type 2 diabetes mellitus and age, gender, duration, glycosylated hemoglobin levels, dyslipidemia, tobacco smoking and alcohol consumption in our study.

REFERENCES

1. Zile MR, Brutsaert DL. New concepts in diastolic dysfunction and diastolic heart failure: Part I: diagnosis, prognosis, and measurements of diastolic function. *Circulation.* 2002;105(11):1387-93.
2. Aurigemma GP, Gaasch WH. Clinical practice. Diastolic heart failure. *The New England journal of medicine.* 2004;351(11):1097-105.
3. Paulus WJ, Tschope C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers FE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *European heart journal.* 2007;28(20):2539-50.
4. Von Bibra H, St John Sutton M. Diastolic dysfunction in diabetes and the metabolic syndrome: promising potential for diagnosis and prognosis. *Diabetologia.* 2010;53(6):1033-45.
5. From AM, Scott CG, Chen HH. Changes in diastolic dysfunction in diabetes mellitus over time. *Am J Cardiol.* 2009;103:1463–6.
6. Kosmala W, Colonna P, Przewlocka-Kosmala M, Mazurek W. Right ventricular dysfunction in asymptomatic diabetic patients. *Diabetes care.* 2004;27(11):2736-8.
7. Parsaee M, Bahmanziari P, Ardeshiri M, Esmaeilzadeh M. Obvious or Subclinical Right Ventricular Dysfunction in Diabetes Mellitus (Type II): An Echocardiographic Tissue Deformation Study. *The journal of Tehran Heart Center.* 2012;7(4):177-81.
8. Freire CM, Moura AL, Barbosa Mde M, Machado LJ, Nogueira AI, Ribeiro-Oliveira Jr A. Left ventricle diastolic dysfunction in diabetes: an update. *Arq Bras Endocrinol Metabol.* 2007 Mar;51(2):168-75.
9. Zile MR, Gaasch WH, Carroll JD, Feldman MD, Aurigemma GP, Schaer GL, et al. Heart failure with a normal ejection fraction: is measurement of diastolic function necessary to make the diagnosis of diastolic heart failure? *Circulation.* 2001;104(7):779-82.
10. Zile MR, Baicu CF, Gaasch WH. Diastolic heart failure--abnormalities in active relaxation and passive stiffness of the left ventricle. *The New England journal of medicine.* 2004;350(19):1953-9.
11. Exiara T KA, Papazoglou L, Kouroupi M, Kalpaka A, Mporgi L, et al. Left ventricular diastolic dysfunction in diabetes mellitus Type 2. *J Hypertens.* 2010;28:e294.
12. Patil VC, Patil HV, Shah KB, Vasani JD, Shetty P. Diastolic dysfunction in asymptomatic type 2 diabetes mellitus with normal systolic function. *Journal of cardiovascular disease research.* 2011;2(4):213-22.
13. Shrestha NR, Sharma SK, Karki P, Shrestha NK, Acharya P. Echocardiographic evaluation of diastolic function in asymptomatic type 2 diabetes. *JNMA; journal of the Nepal Medical Association*. 2009;48(173):20-3.
14. Hiramatsu K, Ohara N, Shigematsu S, Aizawa T, Ishihara F, Niwa A, et al. Leftventricular filling abnormalities in noninsulin-dependent diabetes mellitus andimprovement by a short-term glycemiccontrol. *Am J Cardiol.* 1992;70:1185–9.
15. Gough SC, Smyllie J, Barker M, Berkin KE,Rice PJ, Grant PJ. Diastolic dysfunction is notrelated to changes in glycaemic control over 6 months in type 2 (non-insulin dependent)diabetes mellitus: a cross-sectional study. *ActaDiabetol.* 1995;32:110–5.
16. American Diabetes A. Standards of Medical Care in Diabetes -2013. *Diabetic care.* 2013;36(Suppl 1):S11-S66.
17. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Dopplercatheterization study. *Circulation.* 2000;102(15):1788-94.
18. OH JK SJ, Tajik AJ. Assessment of diastolic dysfunction and diastolic heart failure. 3rd ed. New Dehli: Wolters Kluwer; 2006.
19. National Cholesterol Education Program Detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III) *Circulation*. 2002;106:3143–21.
20. WHO Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet.* 2004 Jan 10;363(9403):157-63.
21. Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure: the Framingham study. *The American journal of cardiology.* 1974;34(1):29-34.
22. Boudina S, Abel ED. Diabetic cardiomyopathy revisited. *Circulation.* 2007;115(25):3213-23.
23. 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.
24. From AM, Scott CG, Chen HH. The development of heart failure in patients with diabetes mellitus and pre-clinical diastolic dysfunction a population-based study. *Journal of the American College of Cardiology.* 2010;55(4):300-5.
25. Galderisi M. Diastolic dysfunction and diabetic cardiomyopathy: evaluation by Doppler echocardiography. *Journal of the American College of Cardiology.* 2006;48(8):1548-51.
26. Ernande L, Bergerot C, Rietzschel ER, De Buyzere ML, Thibault H, Pignonblanc PG et al. Diastolic dysfunction in patients with type 2 diabetes mellitus: is it really the first marker of diabetic cardiomyopathy? *Journal of the American Society of Echocardiography: official publication of the American Society of Echocardiography.* 2011;24(11):1268-75.e1.
27. Khalil SI KA, Hashim F, Olaish MA. Study of Left Ventricular Diastolic Function in Patients with Diabetes Mellitus. *Sudan Journal of Medical Sciences.* 2007;2:85-90.