ISSN: 0976-3031

Available Online at http://www.recentscientific.com

International Journal of Recent Scientific Research
Vol. 7, Issue, 10, pp. 13839-13843, October, 2016

International Journal of Recent Scientific Research

Research Article

GLYCOSYLATED HEMOGLOBIN AND LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

Sastry K.B.R., Sunil Kumar., Mujeeb Afzal., Anuradha P and Priyadarshini P

Department of Medicine Gandhi Medical College, Secunderabad, Telangana, India

ARTICLE INFO

Article History:

Received 06th July, 2015
Received in revised form 14th August, 2016
Accepted 23rd September, 2016
Published online 28th October, 2016

Key Words:

Glycosylated hemoglobin (HbA1c); Diastolic dysfunction; Diabetes Mellitus.

ABSTRACT

Introduction: There is a substantial increase in the coincidence of diabetes mellitus and cardiomyopathy. The cardiomyopathy may occur in patients who have no evidence of large vessel disease or abnormalities.

Aims: The present study was undertaken to assess the prevalence of diastolic dysfunction in patients with type 2 diabetes and to assess the correlation of diastolic dysfunction and HbA1c% levels

Materials and Methods: A total of 100 diabetic patients with minimum 5 years duration of diabetes were selected from Gandhi Hospital attached to Gandhi Medical College Secunderabad between June 2014 and June 2015 and were scrutinized for Doppler echo cardiography and HbA1c levels.

Results: Diastolic dysfunction of left ventricle was observed in 59 patients out of 100, of which 47 (79.66%) patients had HbA1c% of > 7. 8 (13.5%) patients belong to HbA1c% group of 6.1-7 and 4(6.7%) patients belong to HbA1c% of <6.

Conclusion: Our findings indicate that myocardial damage in patients with diabetes affects diastolic function before systolic function.Even young patients with diabetics with normal systolic ventricular function have diastolic dysfunction, which serves as a marker of a diabetic cardiomyopathy. Diastolic impairment seems not to correlate with disease duration. HbA1c% can be a very good indicator of long term prognosis. Strong correlation exist between diastolic dysfunction and HbA1c%.

INTRODUCTION

Diabetes mellitus is a complex metabolic disease characterized by a primary defect in carbohydrate metabolism associated with protein and fat metabolism and modulated by genetic, HLA and environmental factors resulting in micro and macroangiopathy. It often runs in families. It is associated with decrease in insulin production or utilization, resulting in body's inability to utilize nutrients appropriately. Various genetic and environmental factors influence the aetiology and prognosis of diabetes. Important differences in the types and frequency of diabetes and its complications have been reported between countries as well as ethnic and cultural groups.

Indians are genetically more susceptible to diabetes compared to other races. Indians settled abroad also show increased prevalence to diabetes indicating that environmental factors also play a role in incidence of diabetes.

India will have the largest number of diabetic subjects in the world by 2025 and one out of 5 diabetic subject in the world will be an Indian. India is going to be the "Diabetic capital of the world".

Diabetic cardiomyopathy was brought to notice by Rubier in 1972. In 1974, Framingham study showed that heart failure was more common in diabetes due to diabetic cardiomyopathy. Subclinical abnormalities of left ventricular function are recognized in both type 1 and type 2 diabetics. Shapiro *et al* found that asymptomatic diabetic subjects had impaired left ventricular relaxation on digitalized M-mode echocardiography as compared with non-diabetic controls. Studies using Doppler echocardiography have confirmed the findings of abnormal diastolic function as an early indicator of cardiomyopathy in asymptomatic patients.[1]

This study was undertaken to evaluate LV diastolic function in diabetics and to assess the correlation of diastolic dysfunction and HbA1c levels.

MATERIALS AND METHODS

Source of data

A total of 100 diabetic patients with minimum 5 years duration of diabetes were selected from Gandhi hospital, Secunderabad attached to Gandhi medical college Secunderabad between Jan 2014 to Jan 2015.

**Corresponding author: Sastry K.B.R*
Department of Medicine Gandhi Medical College, Secunderabad, Telangana, India

Method of collection

Patients with minimum history of 5 years of type 2 diabetes in Gandhi hospital were scrutinized for Doppler Echocardiography and HbA1c levels.

Inclusion criteria

- Age group 30-55yrs independent of sex.
- Patient's with history of type 2 diabetes for a minimum period of 5 yrs duration.

Exclusion criteria

- Patients with systemic hypertension.
- Patients with thyroid disease.
- Patients with coronary heart disease.
- Patient with peripheral vascular disease.
- Patients with age above 55 years.

Study design: It is an observational study of patients with type 2 diabetes with minimum of 5 years duration of disease was evaluated for Doppler echocardiography and HbA1c levels.

In Doppler study the following values were studied.

- E-Peak velocity of early mitral flow (E-Cms-1)
- A-Peak velocity of late mitral flow (A-Cms-1)
- E/A. ratio
- VTIM-Velocity time integral of the entire mitral curve (VTIM- cms-1)
- VTIA-Velocity time integral of the atrial curve (VTIA-cms-1)
- VTIA / VITM ratio
- PHT-Pressure half - time (PHT - ms)
- IRT-Isovolumic relaxation time (IRT - ms)
- EF%-Ejection fraction

Investigations

- Echo cardiogram
- HbA1c%
- FBS
- PPBS

Immunoturbidometric method was used for estimating HbA1c

Statistical test applied

Chi – square test and Student's unpaired test were applied.

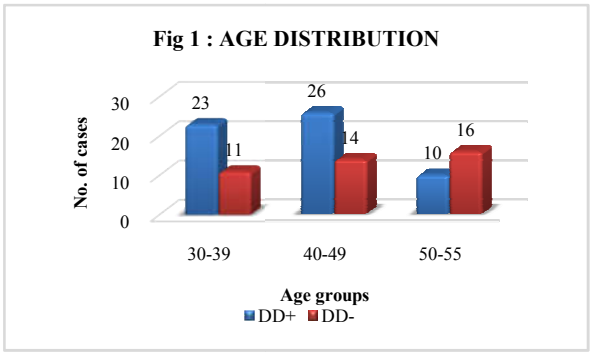
RESULTS

Age

In the present study 34 patients belong to age group of 30-39, out of which 23 were positive for diastolic dysfunction and 11 were negative.

40 patients belong to 40-49 age group, out of which 26 were diastolic dysfunction positive and 14 were negative whereas 26 patients belong to 50-55 age group, out of which 10 were diastolic dysfunction positive and 16 were negative.

Mean age in diastolic dysfunction positive group is 42.8 years and standard deviation of 6.6 while the Mean age in diastolic dysfunction negative group is 45.7 years and standard deviation of 7.3. The Mean difference is 2.96, t value is 2.21 and P value 0.04(S)

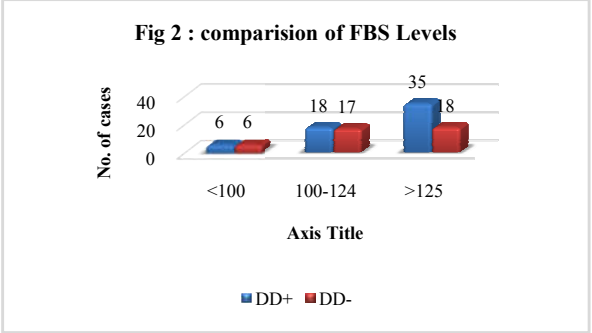


Sex

In this study 62 were males out of which 40 were positive for diastolic dysfunction and 22 were negative whereas 38 patients were female out of which 19 were positive for diastolic dysfunction and 19 were negative. Chi-square test is 2.05 and P value is 0.15(NS).

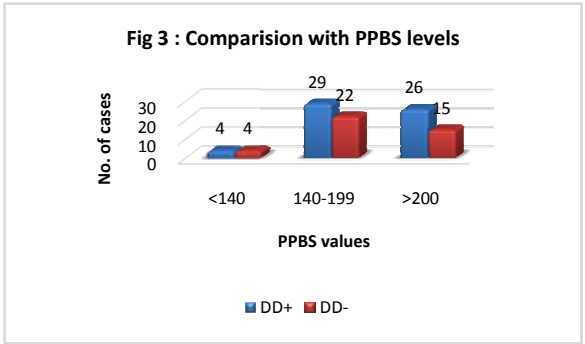
FBS

In the present study 12 patients belong to FBS values of <100 out of which 6 were positive for diastolic dysfunction and 6 were negative. 35 patients belong to FBS range of 100-125 out of which 18 were positive for diastolic dysfunction and 17 were negative. 53 patients belong to FBS range of >125 out of which 35 were positive for diastolic dysfunction and 18 were negative. Chi square test is 2.31 and P value is 0.31(NS)



PLBS

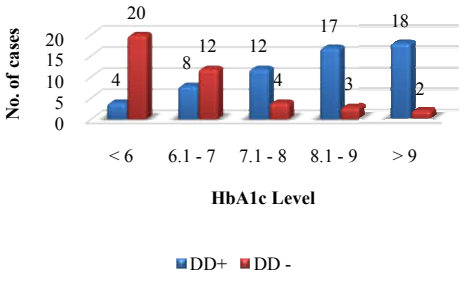
In the present study 8 patients belong to group with PPBS <140 out of which 4 were positive for diastolic dysfunction and 4 were negative. 51 patients belong to PPBS range of 140-199 out of which 29 were positive for diastolic dysfunction and 22 were negative. 41 patients belong to PPBS range of >200 out of which 26 were positive for diastolic dysfunction and 15 were negative. Chi- square test is 0.69 and P value is 0.70(NS).



HbA1c

In the present study, 24 patients belong to group with HbA1c% <6 out of which 4 were positive for diastolic dysfunction and 20 were negative. 20 patients belong to HbA1c% range of 6.1-7 out of which 8 were positive for diastolic dysfunction and 12 were negative. 16 patients belong to HbA1c range of 7.1 - 8 out of which 12 were positive diastolic dysfunction and 4 were negative. 20 patients belong to HbA1c% range of 8.1- 9 out of which 17 were positive for diastolic dysfunction and 3 were negative. 20 patients belong to HbA1c% range of > 9 out of which 18 were positive for diastolic dysfunction and 2 were negative. Chi-square test is 35.99 and P value is < 0.00001(HS).

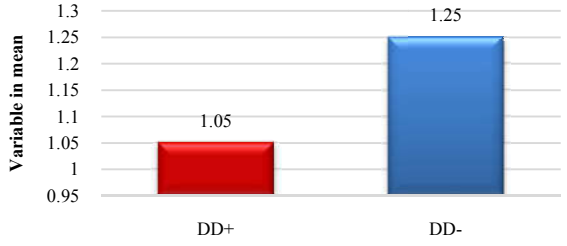
Fig 4 : Comparision with HbA1c% Levels



E/A ratio

E/A were 1.05 and 1.25 in diastolic dysfunction positive and negative patients. E/A ratio was significantly reduced in patients with diastolic dysfunction (p 0.002).

Fig 5 : E/A ratio in Diastolic dysfunction positive and negative patients



VTIM/VTIA

VTIM/VTIA were 0.59 and 0.41 in diastolic dysfunction positive and negative patients. VTIM/ VTIA was not significantly reduced in patients with diastolic dysfunction (p=0.13).

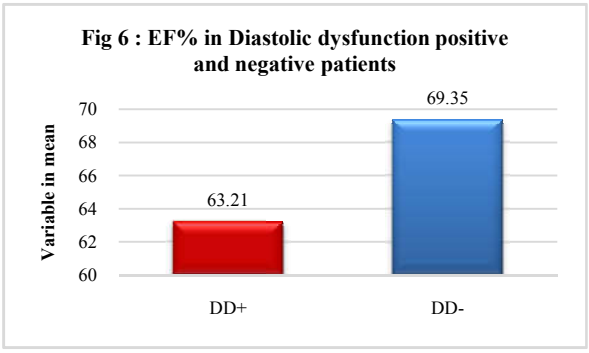
PHT

Pressure half time were 58.74 and 54.14 in diastolic dysfunction positive and negative patients. PTH was significantly increased in patients with diastolic dysfunction (p=0.02).

Ejection fraction

Ejection fraction percentages were 63.21 and 69.35 in diastolic dysfunction positive and negative patients. EF was significantly reduced in patients with diastolic dysfunction (p=0.0005).

Fig 6 : EF% in Diastolic dysfunction positive and negative patients



DISCUSSION

Together with diabetic nephropathy, retinopathy, and neuropathy, a specific heart disease due to diabetes, termed diabetic cardiomyopathy has been suggested. The pathogenesis of diabetic cardiomyopathy is unsettled whereas proposed mechanisms include small vessel disease and metabolic alteration of the diabetic myocardium.

Diastolic dysfunction may be the earliest marker of a diabetes induced heart muscle disease which leads to the progressive development of cardiac failure.

In recent years physicians have become increasingly aware that symptoms of congestive heart failure may occur in diabetic patients who have normal systolic function. The importance of altered diastolic properties in the genesis of symptoms of heart failure in these patients has been recognized by clinicians and physiologists.[2]

Myocardial damage in patients with diabetes affects diastolic function before systolic function.[3] Apart from Diabetes, ischemic heart disease, systemic hypertension, thyroid diseases, cardiomyopathy, valvular heart diseases also cause LV diastolic dysfunction.

In our present study the patients with above conditions which affect LV diastolic function were avoided. Patients with systolic dysfunction also were avoided. It was found out that 59% of patients in our study group comprising of 100 patients had significant LV diastolic dysfunction.

The mean peak velocity of early mitral flow (E) value was 69.45. The mean peak velocity of late mitral flow (A) value 67.06, pressure half time (PHT) was 58.74, Isovolumic relaxation time (IRT) was 83.93, E/A ratio was 1.05, and left ventricular ejection fraction (EF%) was 63.21%. There was significant correlation between diastolic dysfunction and HbA1c (P<0.001).

No significant difference in incidence of diastolic dysfunction was observed in males and females.

None of these patients had clinical symptoms suggestive of cardiac disease. ECG, clinical examination as well as x-ray chest were normal. No patient had clinical features of cardiac failure.

To explain the patho-physiological basis of this left ventricular impaired relaxation, the concept that diabetes per se might cause a stand-alone cardiomyopathy should be accepted[4]. Diabetic cardiomyopathy has been defined as the presence of myocardial abnormalities in the absence of coronary artery

disease, hypertension or other significant etiology[5]. In a very recent report, Anderson and coworkers[6] compared two cohorts of 31 patients having EF > 35%, without significant coronary artery disease (CAD), prior myocardial infarction, cardiac pacemaker, atrial fibrillation, or significant valve disease, one diabetic and the other one controls, matching the two groups on age, gender and presence of hypertension. The Authors concluded that in this set of patients diabetes is anyway associated with global diastolic dysfunction. This finding is in accordance with the hypotheses of increased myocardial stiffness, increased resting myocyte tension and deposition of advanced glycated end products associated with diabetic cardiomyopathy; In fact, intracellular hyperglycemia is at basis of formation of advanced-glycated end products (AGEs) as collagen, elastin and other connective tissue proteins[7] which produce myocardial fibrosis resulting in diastolic dysfunction.
This study revealed that, echo Doppler can detect diastolic dysfunction in diabetic subjects much before clinical symptoms appear. If left untreated, diastolic dysfunction can progress to clinically significant heart failure.

Therefore by early detection of diastolic dysfunction we can start early treatment for the same and can either retard or arrest the progression of LV diastolic dysfunction.

This study findings demonstrate that pre-clinical diastolic dysfunction is common in patients with DM. Pre-clinical diastolic dysfunction has been broadly defined as diastolic dysfunction in patients with normal systolic function, and no symptoms of heart failure (HF). Present study reveals high burden of diastolic dysfunction in cohort of type 2 DM population. Total 59 (59%) type 2 Diabetic had diastolic dysfunction. Subjects with HBA1c > 7% had more prevalence of diastolic dysfunction than subjects with HBA1c < 7% ('P' < 0.02). Diastolic dysfunction was significantly high in patient with age > 45 years compared to age < 45 years ('P' < 0.05).

We compared our results with various studies. Soldatos *et al*.[8] in their case control study of 55 individuals with type -2 DM found that Diastolic dysfunction, present in a significant proportion of population with Type 2 DM. Similarly, in the present study, 59% of subjects had diastolic dysfunction (P < 0.001).

In 2014 Sanjeev Kumar *et al*.[9] demonstrated a very significant positive correlation between level of glycosylated hemoglobin (HbA1C) and frequency of Left ventricular hypertrophy and Left Ventricular Diastolic dysfunction in the newly diagnosed cases of type 2 diabetes mellitus.

In 2011 Patil VC *et al*.[10] showed the prevalence of 54.33 among asymptomatic type 2 Diabetic patients with Good LV function. There was a significant correlation of LV diastolic dysfunction with the duration of diabetes, glycated HbA1c levels, obesity indices (WC and WHR), retinopathy, autonomic neuropathy and hypertriglyceridemia, as determined by multivariate analysis.

Van Heerebeek *et al*.[11] in their study of 36 type -2 DM patients stated that, the cardiomyocyte resting tension is more important when LVEF is normal. Excessive diastolic left ventricular stiffness is an important contributor to heart failure in subjects with DM. Diabetes is presumed to increase stiffness through myocardial deposition of collagen and advanced glycation end products. Similarly, in the present study, 59% of subjects from the case group had diastolic dysfunction with normal LVEF.
In 2010 R. Stahrenberg[12] *et al* found HbA1c correlated with early diastolic mitral inflow velocity (E): early diastolic tissue Doppler velocity at mitral annulus (e′) ratio (E:e′) (r=0.20, p<0.001). HbA1c was significantly associated with E:e′ on multivariate analysis.

Table 1 Comparison of Prevalance of Diastolic Dysfunction

	Prevalence of Diastolic Dysfunction
Present study	59%
Patil VC *et al*.	54.33%
Sohail *et al*.	30.76%
Exiara *et al*.	63.2%
Aaron *et al*.	23%
Boyer *et al*.	75%
Dawson *et al*.	74%

From the above discussion and comparison of present study findings with various studies, we found that there was high prevalence of diastolic dysfunction in subjects with asymptomatic type 2 DM, and it was correlated with age and HbA1c levels. Future studies should be conducted to test the hypothesis that screening and aggressive management of diabetic patients with pre-clinical diastolic dysfunction may delay the progression to heart failure.

Limitations of the Study

Measurement of mitral inflow velocities are dependent on sample volume location which moves during cardiac cycles and respiration. The different mitral flow velocity indices are dependent on many factors such as left ventricular relaxation, left atrial pressure and left ventricular passive distensibility, that cannot be ascertained without sophisticated catheterization.

CONCLUSION

Our findings indicate that myocardial damage in patients with diabetes affects diastolic function before systolic function. HbA1c can be a very good indicator of long term prognosis. Diabetic cardiomyopathy is characterized by an early diastolic dysfunction and a later systolic dysfunction. Impaired diastolic function was not affected by sex or type of diabetes. Even young patients with diabetics with normal systolic ventricular function have diastolic dysfunction, which serves as a marker of a diabetic cardiomyopathy. Diastolic impairment seems not to correlate with disease duration.

E/A ratio and isovolumic relaxation time are significantly altered in diabetic patients.

References

1. Yudkin, John S. "Vascular events and diabetes: Acute myocardial infarction and stroke", Ch. 64 in International Textbook of Diabetes Mellitus, Albertti K.G.M.M., Zimmet P., Defronzo R.A., England: John Wiley and Sons Ltd., Ed 2, 1997, 1827pp.
2. Gaasch William H and Martin M. Le Winter. "Left ventricular diastolic dysfunction and heart failure, Philadelphia, Lee and Febriger, 1993, 498pp.
3. Raev D.C. *et al*. 1994. "Which left ventricular function is impaired earlier in the evaluation of diabetic

cardiomyopathy. An echocardiographic study of young type -1 diabetic patients". Diabetes care, 17; 633-639.
4. Saunders J, Mathewkutty S, Drazner MH, McGuire DK: Cardiomyopathy in type 2 diabetes: update on pathophysiological mechanisms. Herz 2008, 33:184-90. 2.
5. Aneja A, Tang WH, Bansilal S, Garcia MJ, Farkouh ME: Diabetic cardiomyopathy: insights into pathogenesis, diagnostic challenges, and therapeutic options. Am J Med 2008, 121:748-757.
6. Andersson C, Gislason GH, Weeke P, Hoffmann S, Hansen PR, Torp-Pedersen C, Søgaard P**: Diabetes is associated with impaired myocardial performance in patients without significant coronary artery disease.***CardiovascDiabetol* 2010, **9:**3.
7. Eckel RH, Wassef M, Chait A, *et al*.: Prevention Conference VI: Diabetes and cardiovascular disease: Writing Group II: Pathogenesis of atherosclerosis in diabetes. Circulation 2002, 105:e138-43.
8. Soldatos G, Jandeleit-Dahm K, Thomson H, Formosa M, D'orsa K, Calkin AC, *et al*. Large artery biomechanics and diastolic dysfunctionin patients with Type 2 diabetes. Diabet Med 2011;28:54-60.
9. Sanjeev Kumar, GK Aneja, Arvind Trivedi *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. Intern J of Sci and Res Pub, Vol 4, I 12, Dec 2014.
10. Patil VC, Patil HV, Shah KB, Vasani JD, Shetty P. Diastolic dysfunction in asymptomatic type 2 diabetes mellitus with normal systolic function. J Cardiovasc Dis Res 2011;2:213-22.
11. Van Heerebeek L, Hamdani N, Handoko ML, Falcao-Pires I, Musters RJ, Kupreishvili K, *et al*. Diastolic stiffness of the failing diabetic heart: Importance of fibrosis, advanced glycation end products, and myocyte resting tension. Circulation 2008;1;117:43-51.
12. R. Stahrenberg, F. Edelmann, M. Mende *et al*. Association of glucose metabolism with diastolic function along the diabetic continuum, Diabetologia (2010) 53:1331–1340

****

How to cite this article:

Sastry K.B.R *et al*.2016, Glycosylated Hemoglobin And Left Ventricular Diastolic Dysfunction In Patients With Type 2 Diabetes Mellitus. *Int J Recent Sci Res.* 7(10), pp. 13839-13843.