Original Research Article

Correlation of glycated hemoglobin and diastolic dysfunction in type 2 diabetes mellitus patients in a tertiary care centre

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Abstract

Background: 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. The early and commonest hemodynamic derangement of diabetic cardiomyopathy is left ventricular diastolic dysfunction. So, 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 Malla Reddy Hospital, Suraram from August 2020 to June 2022. Patients with minimum history of 5 years of type 2 diabetes were scrutinized for Doppler echo cardiography and HbA1c levels.

Results: Diastolic dysfunction of left ventricle was observed in 58 patients out of 100, of which 54 (93.1%) patients had HbA1c% of > 6.4. 2 (3.4%) patients belong to HbA1c% group of 5.7-6.4. and 2(3.4%) patients belong to HbA1c% of < 5.

Conclusion: Our findings indicate that myocardial damage in patients with diabetes affects diastolic function before systolic function. 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. HbA1c% can be a very good indicator of long term prognosis. Strong corelation exists between diastolic dysfunction and HbA1c.

Key words

Glycated hemoglobin, Diastolic dysfunction, Type 2 diabetes mellitus.

Introduction

Diabetes is a disease known to mankind for the past 2500 years. The term diabetes which in Greek, means "to run through" or 'Siphon', was first coined by Aratoeus of Cappadocia in 2nd century AD as a generic description for conditions causing increased urine output [1].

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 etiology 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.

Diabetes is a disease of antiquity. The world health organization estimates that the disease burden of diabetes mellitus the world over would be more than 500 million in 21st century. Diabetes was formerly considered a disease of affluent. It has now become apparent that increase in diabetes is due to demographic changes, cultural transition and population ageing, urbanization, increased consumption of refined foods, westernization, sedentary habits and over nutrition. Diabetes has become a leading cause of premature death, disability and high health care costs. It is a silent killer disease.

Diabetes in Indian Prospective

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 subjects in the world will be an Indian. India is going to be the "Diabetic capital of the world".

Diabetes and Heart

Robinowitch (1934) was the first to notice increased incidence of IHD, in diabetes which was confirmed by autopsy series by Clawson and Bell (1948). Ditzel and Rooth first used the term microangiopathy in 1955. 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. DCCT trail is one of the largest prospective study in the field of diabetes showed diabetics are 5 times more prone for acute myocardial infarction and death. HOPE study findings are also suggestive of the same. 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 [2].

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 Malla Reddy Hospital from August 2020 to June 2022.

Method of collection

Patients with minimum history of 5 years of type 2 diabetes in Malla Reddy Hospital were scrutinized for Doppler echo cardiography and HbA1c levels.

Inclusion criteria

- Age group 30-55 years 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.
- Patient with peripheral vascular disease.
- Patients with age above 55 years.

Study design

It was 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 following values was 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 of estimating HbA1c Method

Total hemoglobin and HbA1c concentrations were determined after hemolysis of the anticoagulated whole blood specimen. Total Hb was measured colorimetrically. HbA1c was determined immunoturbidimetrically. The ratio of both concentrations yields the final percent HbA1c results.

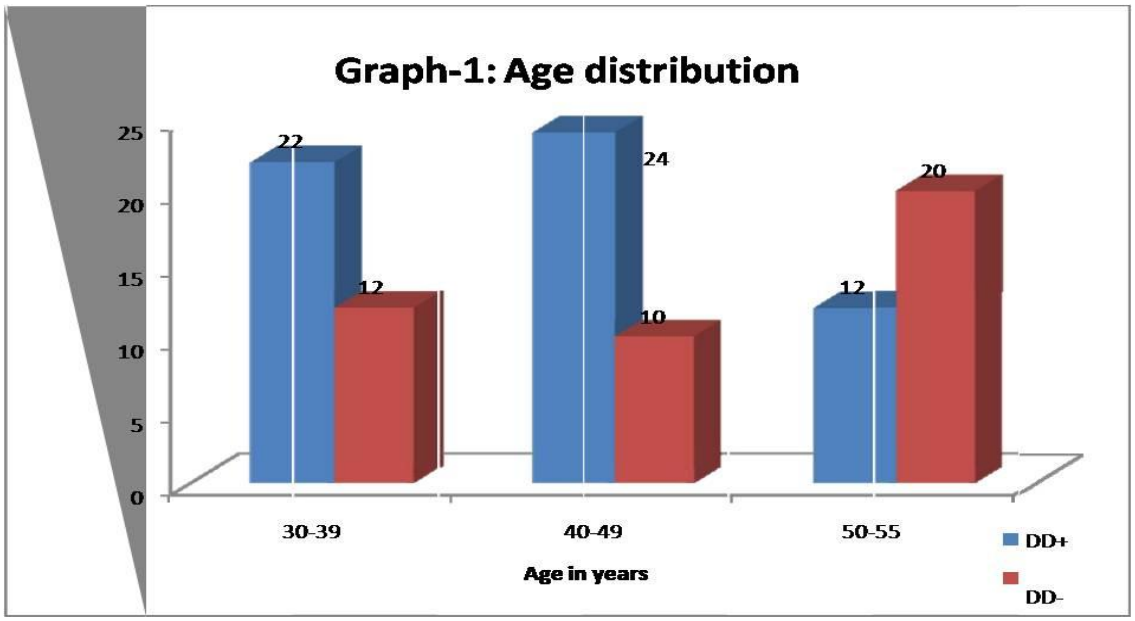
Results

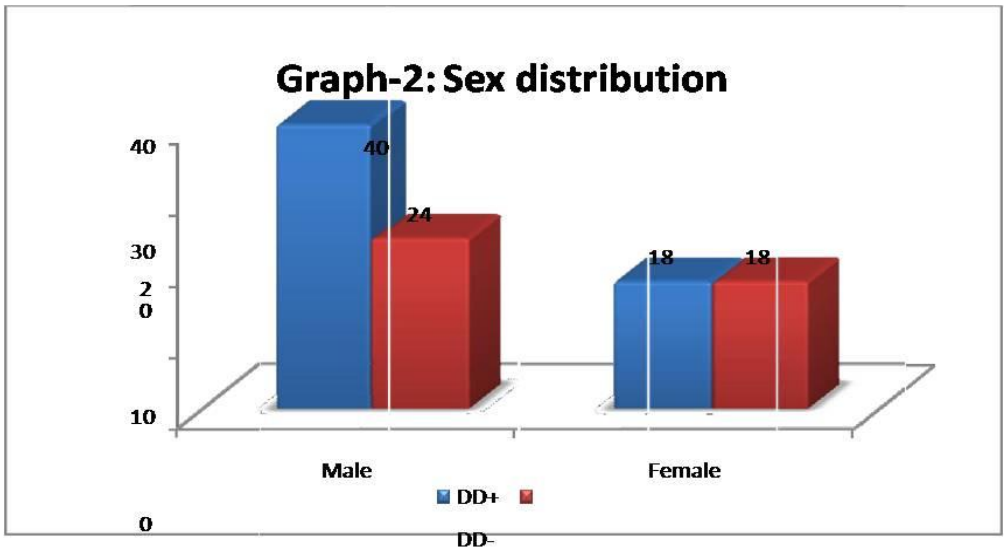
In the present study, 34 patients belonged to age group of 30-39 years, out of which 22 were positive for diastolic dysfunction and 12 were negative. 34 patients belong to 40-49 years age group, out of which 24 were diastolic dysfunction positive and 10 were negative. 32 patients belonged to 50-55 years age group, out of which 12 were diastolic dysfunction positive and 20 were negative (**Graph – 1**).

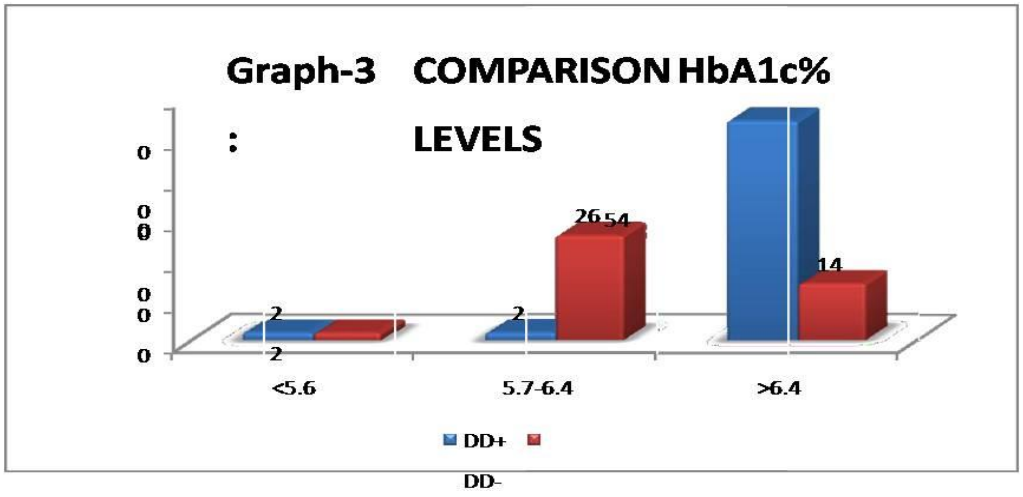
In the present study, 64 were males out of which 40 were positive for diastolic dysfunction and 24 were negative. 36 patients were female out of which 18 were positive for diastolic dysfunction and 18 were negative. Chi-square test was 1.48 and P value was 0.22 (NS) as per **Graph – 2**.

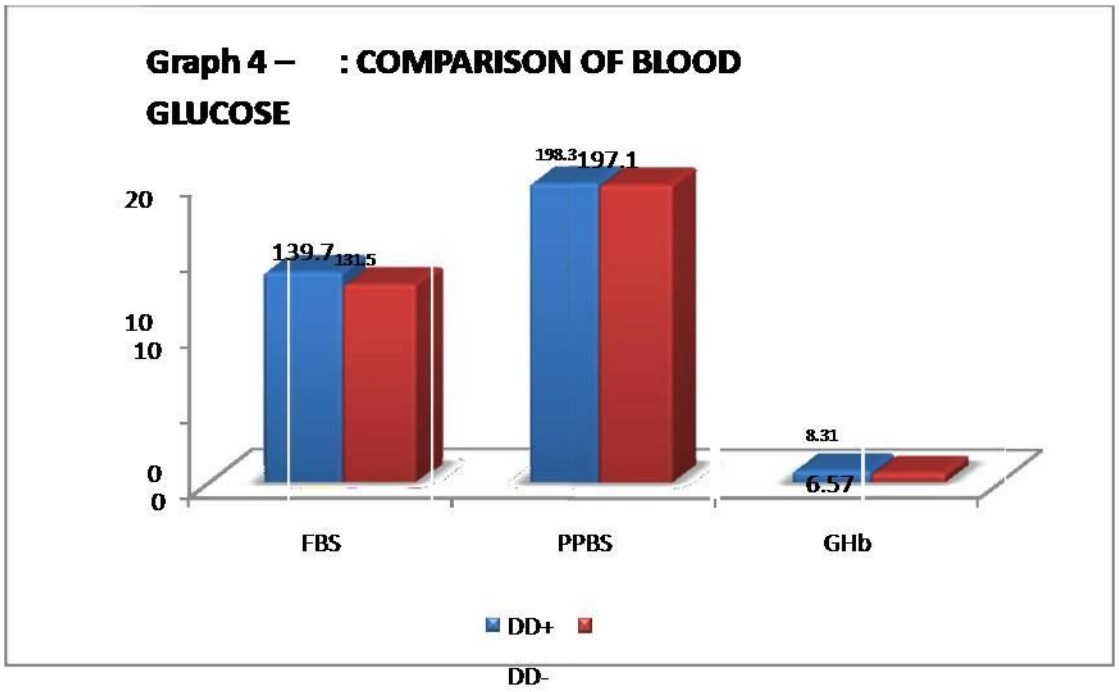
In the present study, 4 patients belong to group with HbA1c% <5.6 out of which 2 were positive for diastolic dysfunction and 2 were negative. 28 patients belonged to HbA1c% range of 5.7-6.4 out of which 2 were positive for diastolic dysfunction and 26 were negative. 68 patients belonged to HbA1c range of >6.4 out of which 54 were positive diastolic dysfunction and 14 were negative. Chi-square test was 42.63 and P value was <0.001 (HS) as per **Graph – 3**.

Comparison of blood glucose was as per **Graph – 4.**


Graph-1: Age distribution
25
20
15
10
5
0
22
12
24
10
12
20
30-39
40-49
50-55
Age in years
DD+
DD-

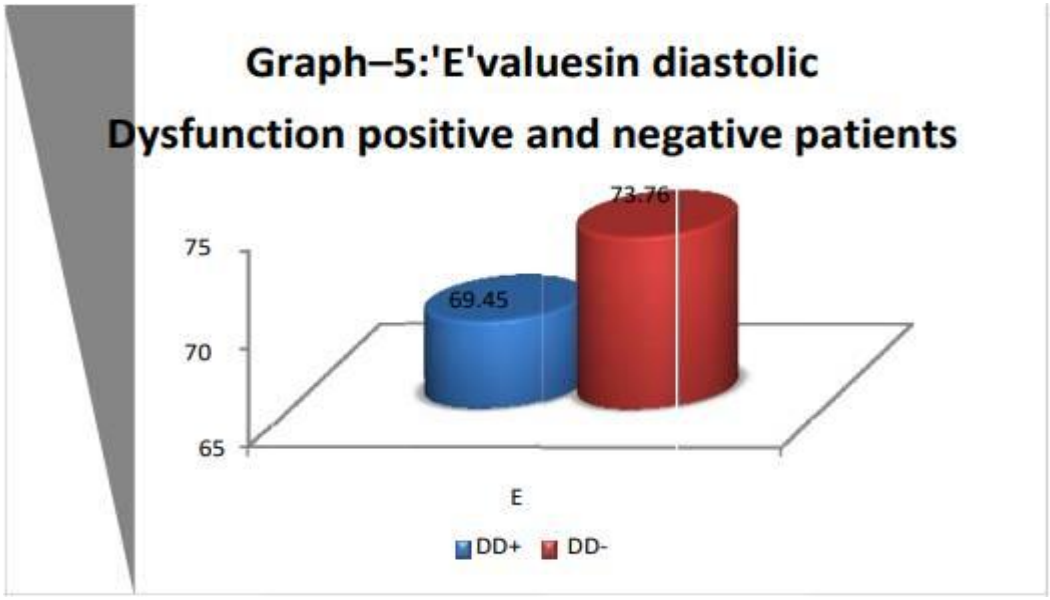

Graph-2: Sex distribution
40
30
2
0
10
0
40
24
18
18
Male
Female
DD+
DD-


Graph-3 COMPARISON HbA1c%
: LEVELS
0
0
0
0
0
0
2
2
26
54
2
14
<5.6
5.7-6.4
>6.4
DD+
DD-



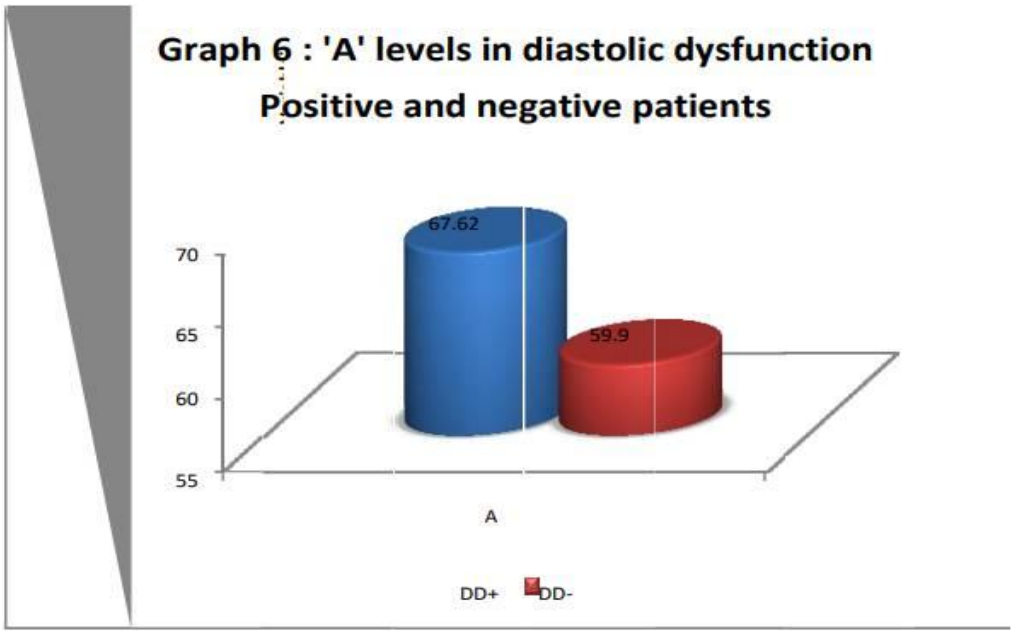
Peak mitral velocity {e} of patients with diastolic dysfunction were 69.65 and 73.76 in negative patients. There was a significant reduction of 'E' value compared to patients without diastolic dysfunction (p=0.01) as per **Graph – 5.**

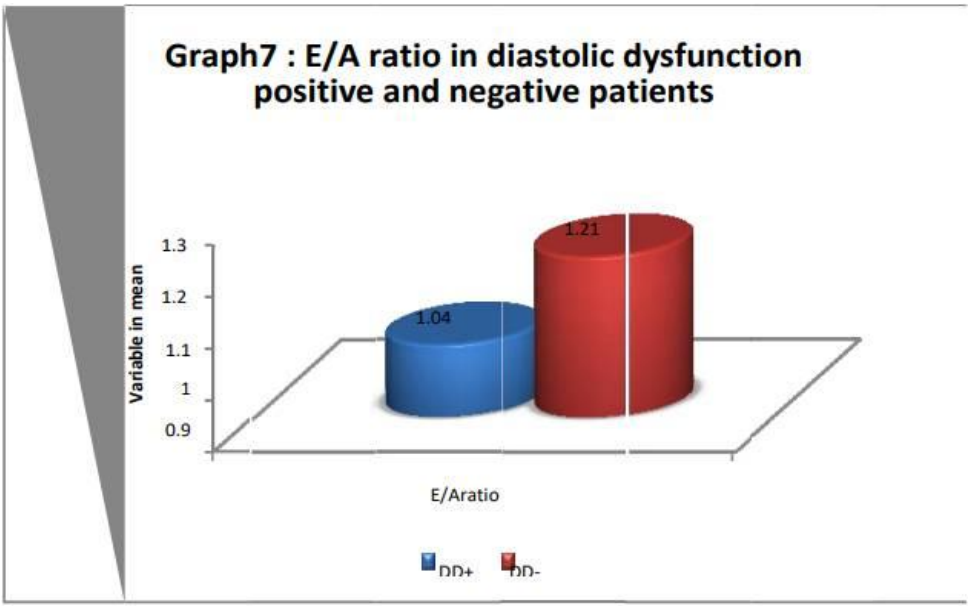
Peak velocity late mitral flow (A) in patients with diastolic dysfunction were 67.62 and 59.90 in negative patients. There was a significant increase in 'A' value compared to patients without diastolic dysfunction (p=0.001) as per **Graph – 6.**

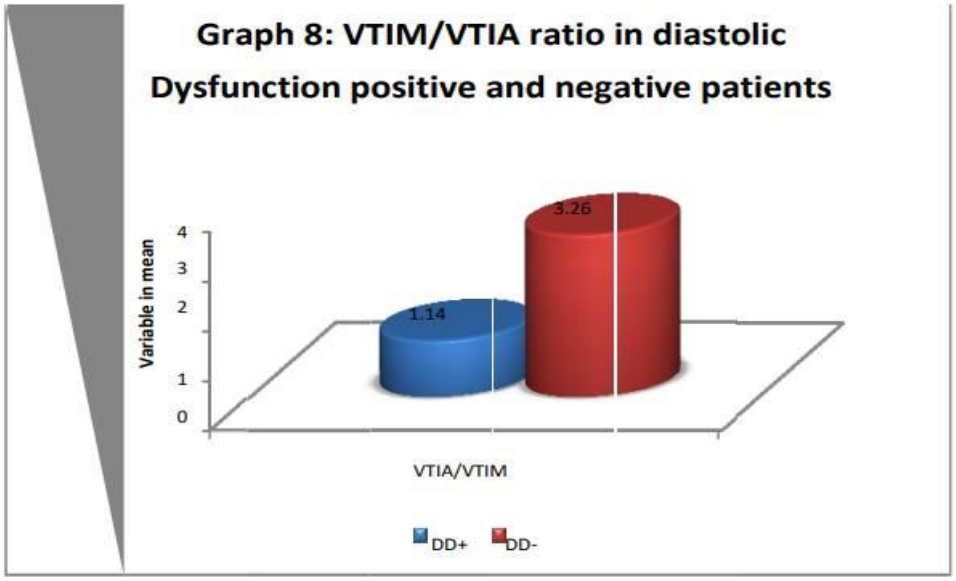


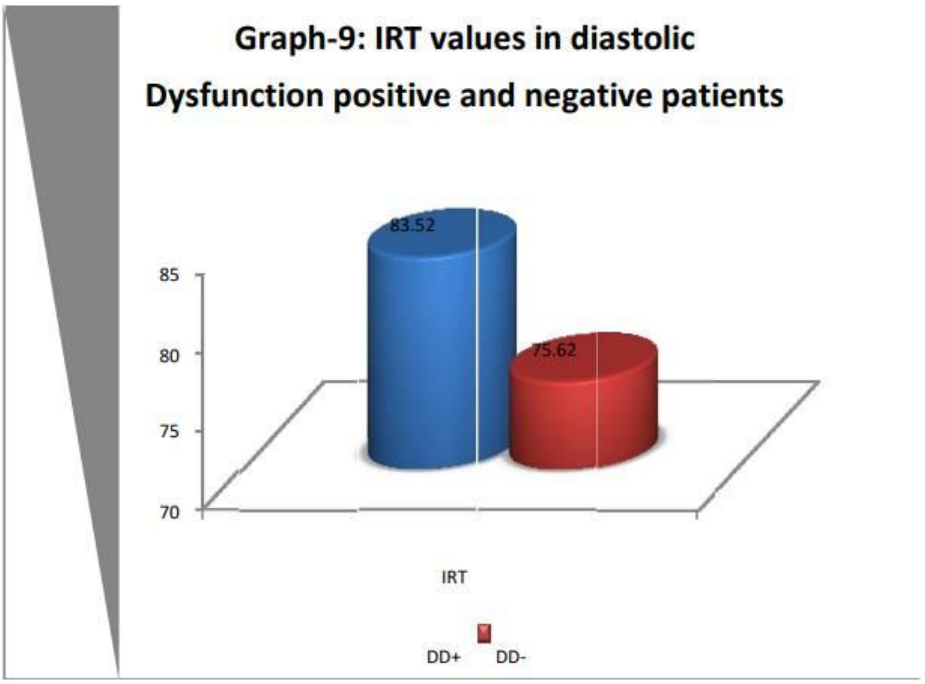
E/A were 1.04 and 1.21 in diastolic dysfunction positive and negative patients. E/A ratio was significantly reduced in patients with diastolic dysfunction (p <0.001) as per **Graph – 7.**

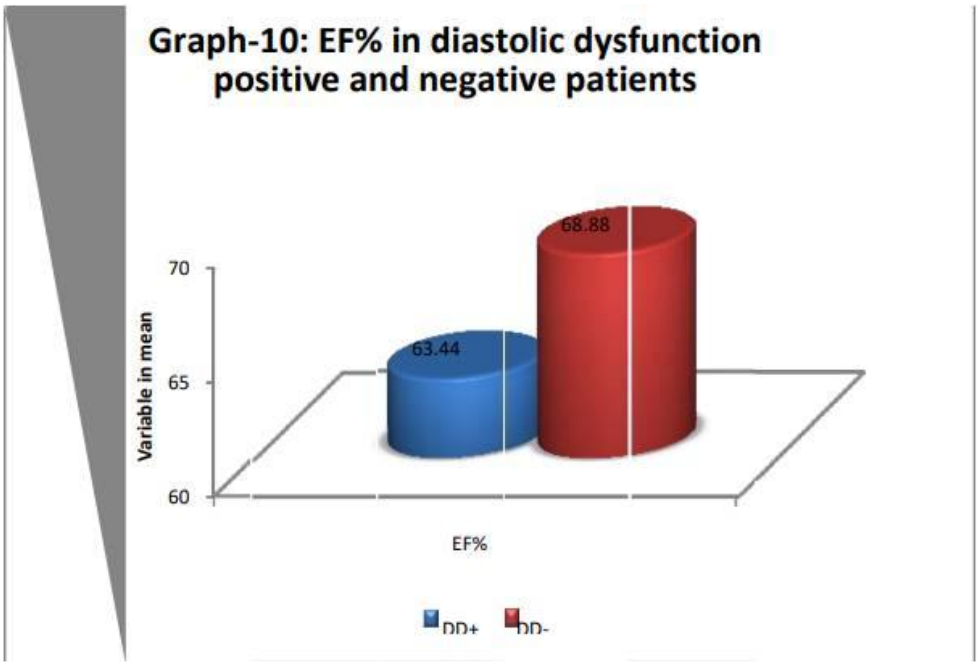
VTIM/VTIA were 1.14 and 0.41 in diastolic dysfunction positive and negative patients. VTIM/ VTIA was not significantly reduced in patients with diastolic dysfunction (p=0.08) as per **Graph – 8.**


Graph 6 : 'A' levels in diastolic dysfunction
Positive and negative patients
67.62
59.9
70
65
60
55
A
DD+
DD-


Graph7 : E/A ratio in diastolic dysfunction
positive and negative patients
Variable in mean
1.3
1.2
1.1
1
0.9
1.04
1.21
E/Aratio
DD+
DD-


Graph 8: VTIM/VTIA ratio in diastolic
Dysfunction positive and negative patients
Variable in mean
4
3
2
1
0
1.14
3.26
VTIA/VTIM
DD+
DD-





Isovolumic relaxation time were 83.52 and 75.62 in diastolic dysfunction positive and negative patients. IRT was significantly increased in patients with diastolic dysfunction (p=0.001) as per **Graph – 9.**

Ejection fraction percentages were 63.44 and 68.88 in diastolic dysfunction positive and negative patients. EF was significantly reduced in patients with diastolic dysfunction (p=0.001) as per **Graph – 10.**

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 where as 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 [3].

Myocardial damage in patients with diabetes affects diastolic function before systolic function [4]. 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 58% 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 69.44. The mean peak velocity of late mitral flow (A) value 67.62, pressure half time (PHT) was 58.79, Isovolumic relaxation time (IRT) was 83.51, E/A ratio was 1.04, and left ventricular ejection fraction (EF%) was 63.43. T

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.

Our present 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.

Markuszewski L., et al. [5] studied 57 subjects (35 men and 22 women) with DM2, without coronary stenosis in coronarography, with normal and elevated HbA1c levels. The subjects were divided into two groups depending on HbA1c level: with HbA1c< or = 6.1% and HbA1c >6.1%. Parameters of left ventricular diastolic function were assessed in echocardiography according to criterions of European Society of Cardiology. Diastolic dysfunction was observed in 43% of patients with HbA1c >6.1% comparing to 4.5% of patients in the group with HbA1c <or= 6.1%. In the group with HbA1c >6.1% in 38% of the patients abnormal relaxation in early filling phase and in 5% abnormal isovolumetric relaxation were noted.

In 1999 Hoit B.D., et al. studied cardiac dysfunction by echocardiography in streptozotocin induced diabetic rats and concluded that diabetic rats showed bradycardia before contractile dysfunction. Overt and Covert contractile dysfunction unmasked by isoproterenol begins at 5 week of diabetes. The Overt LV systolic and diastolic dysfunctions are fully manifested after 6 weeks of diabetes [6].

The exact mechanism of diastolic dysfunction is still questionable, and several mechanisms have been proposed including small and microvascular disease, autonomic dysfunction, metabolic derangements, and interstitial fibrosis. However, the weight of evidence leans towards the development of fibrosis, possibly caused by the accumulation of a peroxidase acid Schiff (PAS) positive glycoprotein, leading to myocardial hypertrophy and diastolic dysfunction [7].

In 1996, Di Bonito, et al. demonstrated that an impairment of left ventricular diastolic function occurs early in the natural history of NIDDM and this abnormality is unlikely to be related to clinical evidence of microangiopathic complication [8].

Fiorini G, et al. in 1995 evaluated LV diastolic function in 30 type 2 diabetic patients without coronary artery disease and concluded that, E/A ratio and Isovolumic relaxation time are significantly altered in non-insulin dependent diabetic patient without coronary artery disease [9].

Gough SC, et al. in 1999 evaluated 92 type 1 patients without known cardiac disease and 50 controls with Doppler echocardiography and concluded that even young type 1 diabetic patients with normal systolic ventricular function suffer a diastolic dysfunction which serves as a marker of a diabetic cardiomyopathy [10].

Gaasch WH, et al. in 2001 evaluated 40 diabetic patients without clinical evidence of cardiac disease by Doppler echocardiography and came to the conclusion that diastolic function in diabetic patients were impaired even though they had normal systolic function [11].

Ceruttti F., et al. in 1994 evaluated left ventricular diastolic function in 50 insulin dependent diabetic children by M. mode and Doppler echocardiography and concluded that early diastolic dysfunction, expressed by reduced left ventricular compliance, can be found in children with type 1 D.M of relatively short duration. Doppler echocardiography is a reliable non invasive method to assess early impairment of cardiac function [12].

Gough, et al. evaluated 20 normotensive patients with a new diagnosis of type 2 diabetes mellitus with normal cardiac function without any evidence of coronary artery disease and followed up them for 6 months and concluded that in patients with type 2 diabetes mellitus and normal systolic function, diastolic function was impaired at diagnosis and was not affected by an improvement in the glycemic control.

Peak velocity of early mitral flow 'E' was significantly lower. Other study results regarding this were similar to earlier studies (**Table – 1**).

Table – 1: Comparison of peak velocity of early mitral flow ('E').

	Diabetics	P
Present study	69.44	0.001
Gaasch WH, et al. [11]	56±10mls	0.001
Gough SC, et al. [10]	54 ± 0.07m/s	<0.01
Fiorini G, et al. [9]	70±11	0.001

Table – 2: Comparison of peak velocity of late mitral flow (A).

	Diabetics	P
Present study	67.62	0.001
Gaasch WH, et al. [11]	71±13	0.001
Gough SC, et al. [10]	76 ± 0.05	<0.01
Fiorini G, et al. [9]	89±0.17	0.001

Table – 3: Comparison of isovolumic relaxation time (IRT).

	Diabetics	P
Present study	83.51	0.001
Gough SC, et al. [10]	129 ± 23	<0.01
Gaasch WH, et al. [11]	109 ±11	0.001

There was a significant increase in A value. Similar observation was seen in other studies (**Table – 2**).

All the 3 studies shows increase in isovolumic relaxation time in diabetic patients compared to controls which is statistically significant (**Table – 3**).

Early diastolic dysfunction, expressed by reduced left ventricular compliance can be found in diabetics of relatively short duration of disease. Doppler echocardiography is a reliable non-invasive means to assess early diastolic dysfunction of left ventricle [12] and there is good correlation with HbA1c%. It identifies diastolic dysfunction of left ventricle before abnormalities are detected clinically or by ECG.

Echocardiography with measurements of systolic and diastolic functional parameters appears to be a sensible method for evaluating the course of diabetic cardiomyopathy.

The intentional assessment of diastolic function is advisable for early detection of LV dysfunction before clinical symptoms appear, with follow-up to detect further deterioration of cardiac status.

HbA1c% can be a very good indicator of long term prognosis.

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.

Doppler echocardiography is a valuable non-invasive method to defect left ventricular diastolic impairment and the intentional assessment of diastolic function is advisable for early detection of LV dysfunction before clinical symptoms appear with follow up to detect further deterioration of cardiac status irrespective of type of diabetes.

Compared to radionucleotide and catheterization studies Doppler echocardiography is faster, safer, non-invasive and more economical. It can be done at bedside without any risks to patient. It is simple and reproducible. It identifies large percentage of as symptomatic diabetic subjects with left ventricular diastolic dysfunction before abnormalities are detected clinically or by ECG.

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References

1. Glycosylated hemoglobin and left ventricular diastolic dysfunction in patients with type 2 diabetes mellitus] [Article in Polish] Leszek Markuszewskietal. Pol Merkur Lekarski., 2006.
2. Zabalgoitia M, Ismaeil MF, Anderson L, Maklady FA. Prevalence of diastolic dysfunction in normotensive, asymptomatic patients with well-controlled type 2 diabetes mellitus. Am J Cardiol., 2001; 87: 320–3.
3. Iribarren C, Karter AJ, Go AS, Ferrara A, et al. Glycemic control and heart failure among adult patients with diabetes. Circulation, 2001; 103(22): 2668–73.
4. Shapiro L.M., et al. Left ventricular function in diabetes mellitus. Relation between clinical features and left ventricular function. Br. Heart. J, 1981; 45: 129-132.
5. Nathan DM, Singer DE, Hurxthal K, Goodson JD. The clinical information value of the Glycosylated hemoglobin assay. NEJM, 1984; 310: 341-6.
6. Guglielmi, Maria D., et al. Impaired left ventricular diastolic function and vascular post ischemic vasodilation associated with microalbuminuria in IDDM patients. Diabetes Care, 1995; 18: 353-360.
7. Quinones Miguel A. Doppler assessment of left ventricular diastolic function. Ch. 19 in Doppler echocardiography. Nanda Navin C, Philadelphia, Lea and Febiger, 19th edition, 1993, p. 197.
8. Demaria Arathony N, et al. Doppler echocardiographic evaluation of diastolic dysfunction. Circulation, 1991; 84: 288-295.
9. Fiorini G, et al. An echocardiographic

study of left ventricular diastolic function in patients with D.M. type-2. G. Ital. Cardiol., 1995; 25: 17-28.

10. Gouch S.C., et al. Diastolic dysfunction is not related to changes in glycemic control over 6 months in type - 2 diabetes mellitus. A cross sectional study. Acta. Diabetol. J, 1995; 32: 110-115.
11. Gaasch William Hand Martin M. Le Winter. Left ventricular diastolic dysfunction and heart failure, Philadelphia, Lee and Febriger, 1993, p. 498.
12. Raev D.C., et al. Which left ventricular function is impaired earlier in the evaluation of diabetic cardiomyopathy. An echocardiographic study of young type-1 diabetic patients. Diabetes care, 1994; 17: 633.