Journal of Cardiovascular Disease Research
ISSN: 0975-3583,0976-2833 VOL15, ISSUE 7, 2024

"Correlation of HbA1c levels with Left Ventricular diastolic Dysfunction in Patients with Type 2 Diabetes Mellitus" at a Government General Hospital

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Abstract:

Background: The prevalence of diabetes mellitus (DM) is rapidly increasing, affecting approximately 350 million people globally. The World Health Organization projects that diabetes-related deaths will double between 2005 and 2030. Type 2 diabetes mellitus (T2DM), which accounts for over 90% of all diabetes cases, significantly impacts cardiovascular health, often leading to left ventricular (LV) diastolic dysfunction, a hallmark of diabetic cardiomyopathy.

Aim: To assess the incidence of LV diastolic dysfunction in normotensive T2DM patients and to evaluate the correlation between diastolic dysfunction and HbA1c levels.

Methods: This cross-sectional study included normotensive T2DM patients with a minimum of 5 years of disease duration. Echocardiography was used to assess diastolic function, and HbA1c levels were measured. Statistical analysis was conducted to determine the correlation between HbA1c levels and diastolic dysfunction.

Results: Diastolic dysfunction is prevalent in asymptomatic T2DM patients, even in the absence of overt cardiovascular complications. Higher HbA1c levels were significantly associated with increased incidence of diastolic dysfunction.

Conclusion: Early detection and management of LV diastolic dysfunction in T2DM patients through regular monitoring of HbA1c levels can help mitigate the adverse cardiovascular outcomes associated with diabetes. Doppler echocardiography proves to be an effective non-invasive method for this purpose.

Keywords: Type 2 diabetes mellitus, HbA1c, left ventricular diastolic dysfunction, echocardiography, diabetic cardiomyopathy.

Introduction:

The incidence and prevalence of diabetes mellitus (DM) are rising rapidly, affecting 350 million people worldwide. The World Health Organization (WHO) projects that diabetes-related deaths will double between 2005 and 2030. Among the types of diabetes, obesity-related type 2 diabetes mellitus (T2DM) accounts for over 90% of all diagnosed diabetes cases in adults. More than 60% of patients with symptomatic chronic heart disease have abnormal glucose homeostasis, and patients with both DM and established cardiovascular disease have a particularly unfavorable prognosis.The term "diabetic cardiomyopathy" refers to the multifactorial manifestations of diabetes-related left ventricular (LV) failure, characterized by both systolic and diastolic dysfunction. Echocardiographic studies have confirmed that diastolic abnormalities occur even in young diabetic patients without known diabetic complications.

Diabetes is an ancient disease, known to mankind for over 2500 years. It has now become apparent that the increase in diabetes is due to demographic changes, cultural transitions, population aging, urbanization, increased consumption of refined foods, westernization, sedentary habits, and

overnutrition. As a result, diabetes has become a leading cause of premature death, disability, and high healthcare costs.

Aim:

To investigate the relationship between HbA1c levels and left ventricular diastolic dysfunction in patients with type 2 diabetes mellitus (T2DM).

Objectives:

•To select normotensive T2DM patients with a minimum of 5 years of disease duration, without other cardiovascular risk factors.

•To assess the incidence of left ventricular diastolic dysfunction in these patients.

•To evaluate the correlation between diastolic dysfunction and HbA1c levels in T2DM patients.

Materials and Methods

Study Design:

A cross-sectional study was conducted involving normotensive T2DM patients with a minimum of 5 years of disease duration.

Participant Selection Criteria:

Patients were selected based on the following criteria:

- Diagnosed with T2DM for at least 5 years
- Normotensive (blood pressure <140/90 mmHg)
- No history of cardiovascular diseases, renal diseases, or other significant comorbidities

Data Collection Methods:

- Detailed medical history and clinical examination
- Measurement of HbA1c levels using standardized laboratory methods
- Echocardiographic assessment of LV diastolic function

Echocardiography Techniques:

• Doppler echocardiography was used to measure parameters such as E/A ratio, deceleration time, and isovolumetric relaxation time to assess diastolic function.

Inclusion Criteria

1. Age: Participants must be adults aged 30-65 years.

2. Type of Diabetes: Only patients diagnosed with Type 2 Diabetes Mellitus (T2DM) for at least 5 years.

3. Normotensive Status: Participants must have a blood pressure below 140/90 mmHg without the use of antihypertensive medications.

4. Glycemic Control: Patients must have stable HbA1c levels between 7% and 10% over the past three months.

5. Cardiac Health: No history of cardiovascular disease, including myocardial infarction, coronary artery disease, or heart failure.

6. Willingness to Participate: Informed consent must be obtained from all participants.

Exclusion Criteria

1. Other Types of Diabetes: Patients with Type 1 Diabetes Mellitus or gestational diabetes.

2. Co-morbid Conditions: Presence of significant co-morbid conditions such as chronic kidney disease, chronic liver disease, or chronic obstructive pulmonary disease.

3. Cardiovascular Risk Factors: Patients with known cardiovascular risk factors, including hyperlipidemia, smoking, or a family history of premature cardiovascular disease.

4. Medication Use: Use of medications that could affect heart function or glucose metabolism, such as beta-blockers, calcium channel blockers, or corticosteroids.

5. Pregnancy: Pregnant or breastfeeding women.

6. Non-compliance: Patients who are unable or unwilling to adhere to the study protocol or follow-up visits.

Sample Collection

Sample Size: The study will include a sample size of 100 patients with Type 2 Diabetes Mellitus.

Sampling Method: Participants will be recruited from outpatient and inpatients at GGH,Anantapur. A stratified random sampling method will be used to ensure a representative sample of the diabetic population.

Procedure:

1. Screening: Potential participants will be screened for eligibility based on the inclusion and exclusion criteria through medical history, physical examination, and laboratory tests.

2. Informed Consent: Eligible participants will be provided with detailed information about the study, and written informed consent will be obtained.

3. Data Collection: Baseline data will be collected, including demographic information, medical history, medication use, and lifestyle factors. Blood samples will be taken to measure HbA1c levels, fasting blood glucose, lipid profile, and renal function tests.

4. Echocardiography: Doppler echocardiography will be performed to assess left ventricular diastolic function. Parameters such as E/A ratio, isovolumic relaxation time, and deceleration time will be measured.

5. Follow-up: Participants will be followed up at 6-month intervals for a period of 2 years to monitor changes in HbA1c levels and left ventricular function. Repeat echocardiography and laboratory tests will be performed at each follow-up visit.

Study Design

Type: Prospective observational study.

Duration: 2 years.

Outcome Measures:

1. Primary Outcome: Prevalence of left ventricular diastolic dysfunction in patients with Type 2 Diabetes Mellitus.

2. Secondary Outcome: Correlation between HbA1c levels and the degree of left ventricular diastolic dysfunction.

Statistical Analysis

Study Population

A total of 100 patients with type 2 diabetes, each with a minimum duration of 5 years, were selected from Government General Hospital Anantapur. The study was conducted between May 2022 and April 2024.

. The following demographic characteristics were recorded:

DEMOGRAPHIC	CATEGORY	DD + (n=58)	DD- (n=42)	Total (n=100)
Age (years)	30 - 39	22	12	34
	40 - 49	24	10	34
	50-55	12	20	32
Sex	Male	40	24	64
	Female	18	18	36

Analytical sensitivity :

The detection limits for the assays are 9mg/dL for the Hb test and 0.4mg/D1 for the HbA1c test. However, only results above 81mg/dL for the Hb test and above 1.3mg/dL for the HbA1c test are reported. The detection limit for the calculated HbA1c (%) result is 3% at a Hb concentration of 13.2g/dL in the sample.

Specificity:

Hb derivatives Labile HbA1c, acetylated Hb, and carbamylated Hb donot affect the assay result. Hb variants Specimens containing high amounts of HbF (>10%) may yield lower than expected HbA1c results. Specimens containing HbS and HbC variants mat yield higher than expected HbA1c results.

Statistical test applied:

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

RESULTS

TABLE – 1 : AGE DISTRIBUTION

Age Gr (Yrs)		DD Group		Total
		DD +	DD -	
30-39	No	22	12	34
	%	37.9%	28.6%	34.0%
40-49	No	24	10	34
	%	41.4%	23.8%	34.0%

50-55	No	12	20	32
	%	20.7%	47.6%	32.0%
Total	**No**	**58**	**42**	**100**
	%	**100%**	**100%**	**100%**

Chi – Square	**df**	**P value**
8.36	2	< 0.05, S

Value	**DD +**		**DD -**		**DD + v/s DD-**		
	Mean	**SD**	**Mean**	**SD**	**Mean diff**	**t value**	**p value**
Age (Yrs)	42.8	6.5	45.7	7.4	2.96	2.12	0.04, S
Range	30 – 55 Yrs		30 – 55 Yrs				

In the present study 34 patients belong to age group of 30-39, out of which 22 were positive for diastolic dysfunction and 12 were negative.

34 patients belong to 40-49 age group, out of which 24 were diastolic dysfunction positive and 10 were negative.

32 patients belong to 50-55 age group, out of which 12 were diastolic dysfunction positive and 20 were negative.

Mean age in diastolic dysfunction positive group is 42.8years and standard deviation of 6.5

Mean age in diastolic dysfunction negative group is 45.7 years and standard deviation of 7.4

Mean difference is 2.96, t value is 2.21 and P value 0.04(S)

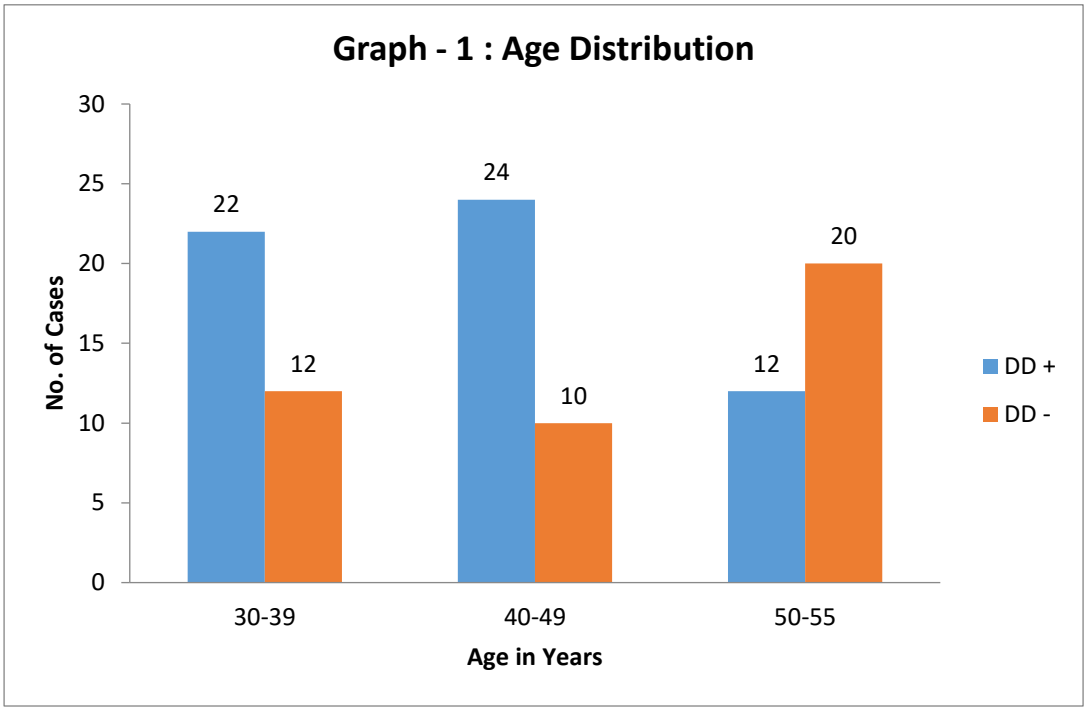


TABLE – 2 : SEX DISTRIBUTION

Sex		DD Group		Total
		DD +	DD -	
Male	No	40	24	64
	%	69.0%	57.1%	64.0%
Female	No	18	18	36
	%	31.0%	42.9%	36.0%
Total	**No**	**58**	**42**	**100**
	%	**100%**	**100%**	**100%**

Chi – Square	df	P value
1.48	1	0.22, NS

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 is 1.48 and P value is 0.22(NS)

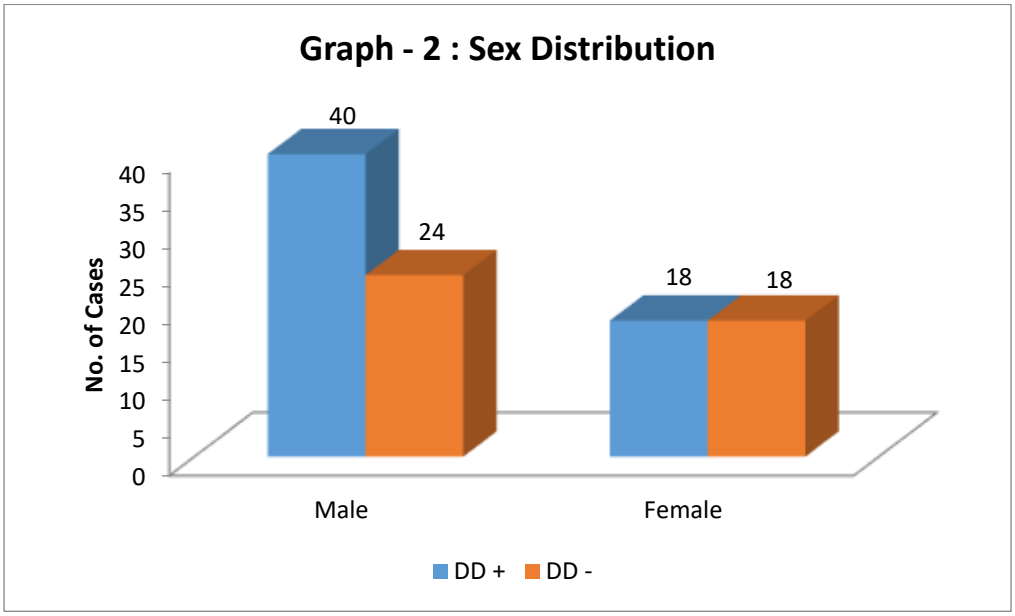


TABLE – 3 : COMPARISON OF FBS LEVELS

FBS		DD Group		Total
		DD +	DD -	
< 100	No	6	6	12
	%	10.3%	14.3%	12.0%`
100 – 125	No	18	18	36
	%	31.0%	42.9%	36.0%
> 125	No	34	18	52
	%	58.6%	42.9%	52.0%
Total	**No**	**58**	**42**	**100**
	%	**100%**	**100%**	**100%**

Chi – Square	df	P value
2.43	2	0.30 NS

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. 36 patients belong to FBS range of 100-125 out of which 18 were positive for diastolic dysfunction and 18 were negative. 52 patients belong to FBS range of >125

out of which 34 were positive for diastolic dysfunction and 18 were negative. Chi square test is 2.43 and P value is 0.30(NS).

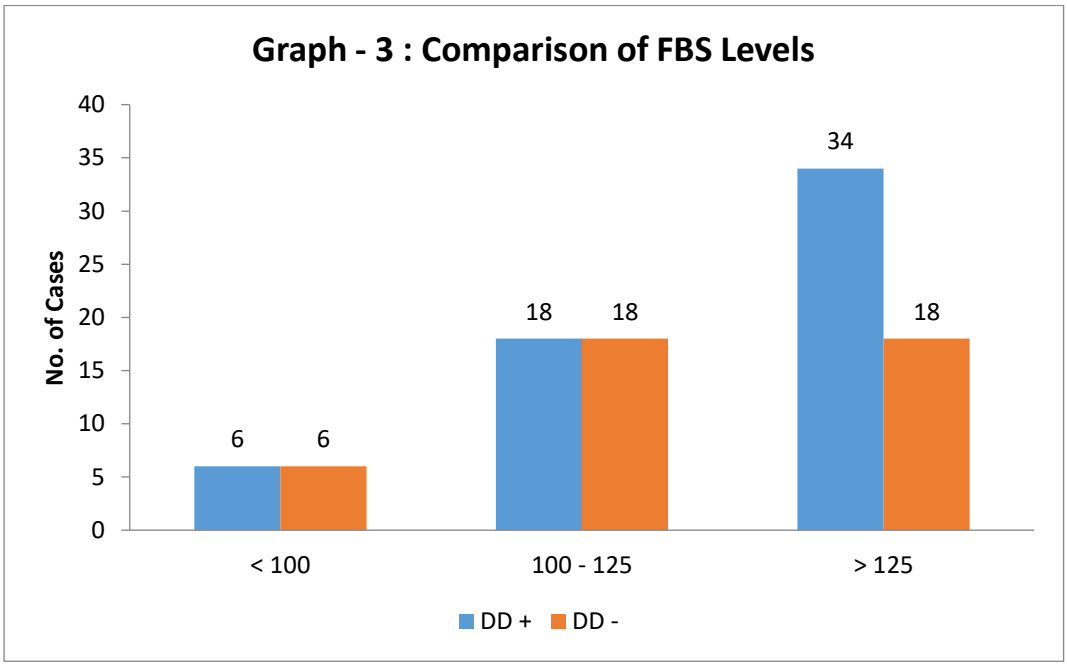


TABLE – 4 : COMPARISON OF PPBS LEVELS

FBS		DD Group		Total
		DD +	DD -	
< 140	No	4	4	8
	%	6.9%	9.5%	8.0%
140 – 199	No	24	20	44
	%	41.4%	47.6%	44.0%
> 200	No	30	18	48
	%	51.7%	42.9%	48.0%
Total	**No**	**58**	**42**	**100**
	%	**100%**	**100%**	**100%**

Chi – Square	df	P value
83	2	0.66 NS

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. 44 patients belong to PPBS range of 140-199 out of which 24 were positive for diastolic dysfunction and 20 were negative. 48 patients belong to PPBS

range of >200 out of which 30 were positive for diastolic dysfunction and 18 were negative. Chi-aquare test is 82 and P value is 0.66(NS).

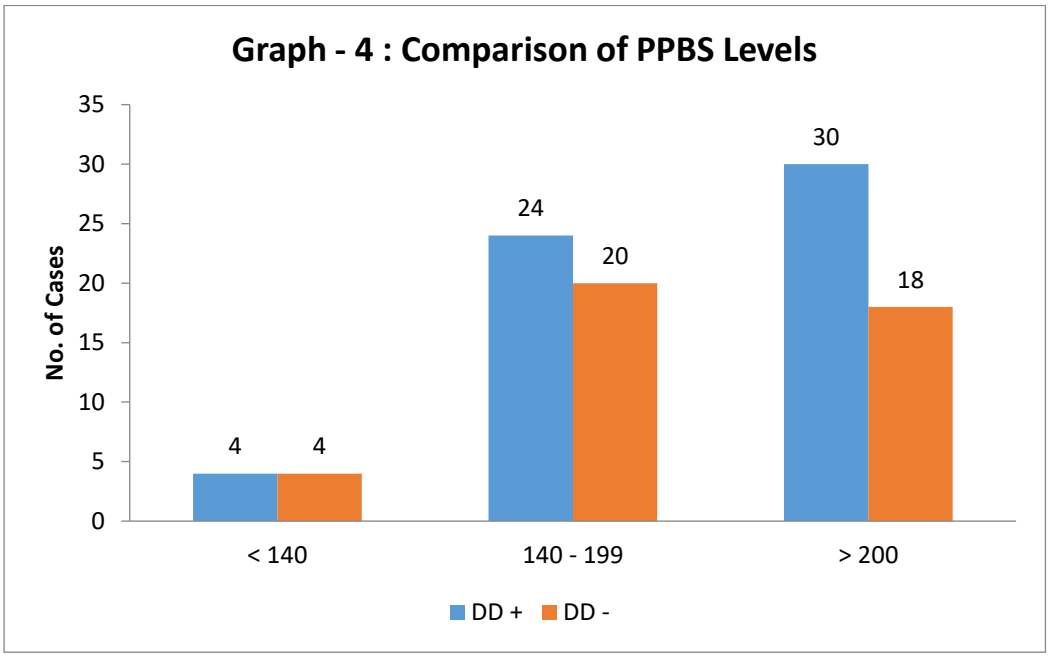


TABLE – 5 : COMPARISON OF HbA1c LEVELS

HbA1c %		DD Group		Total
		DD +	DD -	
< 5.6	No	2	2	4
	%	3.4%	4.8%	4.0%
5.7 – 6.4	No	2	26	28
	%	3.4%	61.9%	8.0%
> 6.4	No	54	14	68
	%	93.1%	33.3%	68.0%
Total	**No**	**58**	**42**	**100**
	%	**100%**	**100%**	**100%**

Chi – Square	df	P value
42.63	2	< 0.001 HS

In the present study 4 patients belong to group with ghb% <5.6 out of which 2 were positive for diastolic dysfunction and 2 were negative. 28 patients belong to HbA1c% range of 5.7-6.4 out of which 2 were positive for diadtolic dysfunction and 26 were negative. 68 patients belong to HbA1c

range of >6.4 out of which 54 were positive diastolic dysfunction and 14 were negative. Chi-square test is 42.63 and P value is < 0.001(HS)

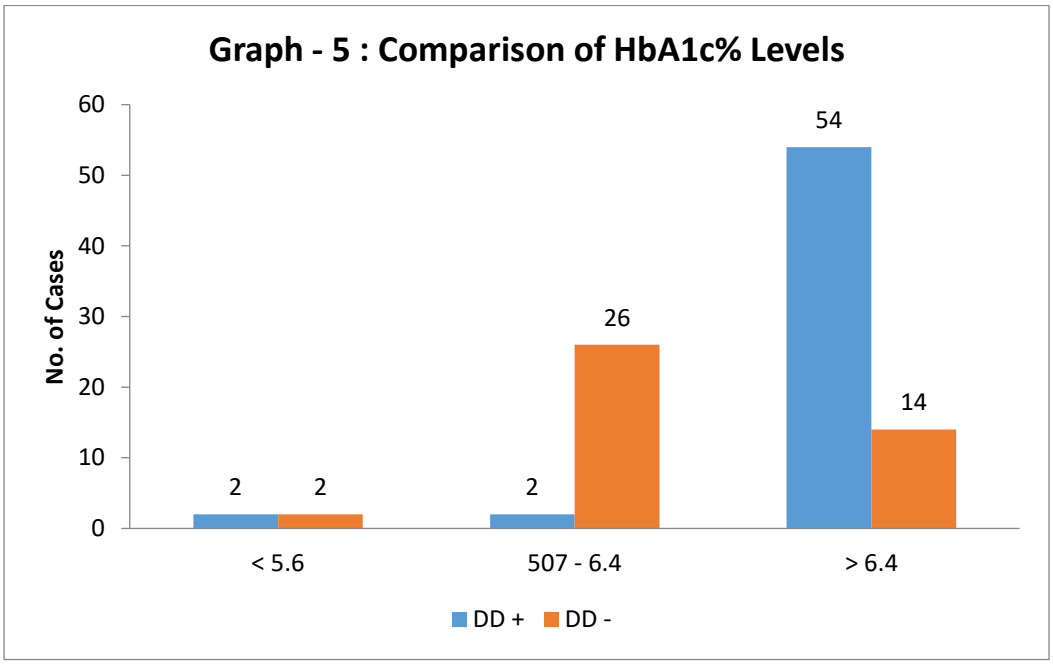


TABLE – 6 : COMPARISON OF BLOOD GLUCOSE LEVELS

Variable	DD +		DD -		DD + v/s DD-		
	Mean	SD	Mean	SD	Mean diff	t value	p value
FBS	139.7	34.4	131.5	36.2	8.2	1.15	0.25 (NS)
PPBS	198.3	46.9	197.1	53.8	1.3	0.13	0.90 (NS)
HbA1c	8.31	1.31	6.57	1.12	1.74	6.91	0.001 (HS)

NS : Non significant, HS : Highly significant.

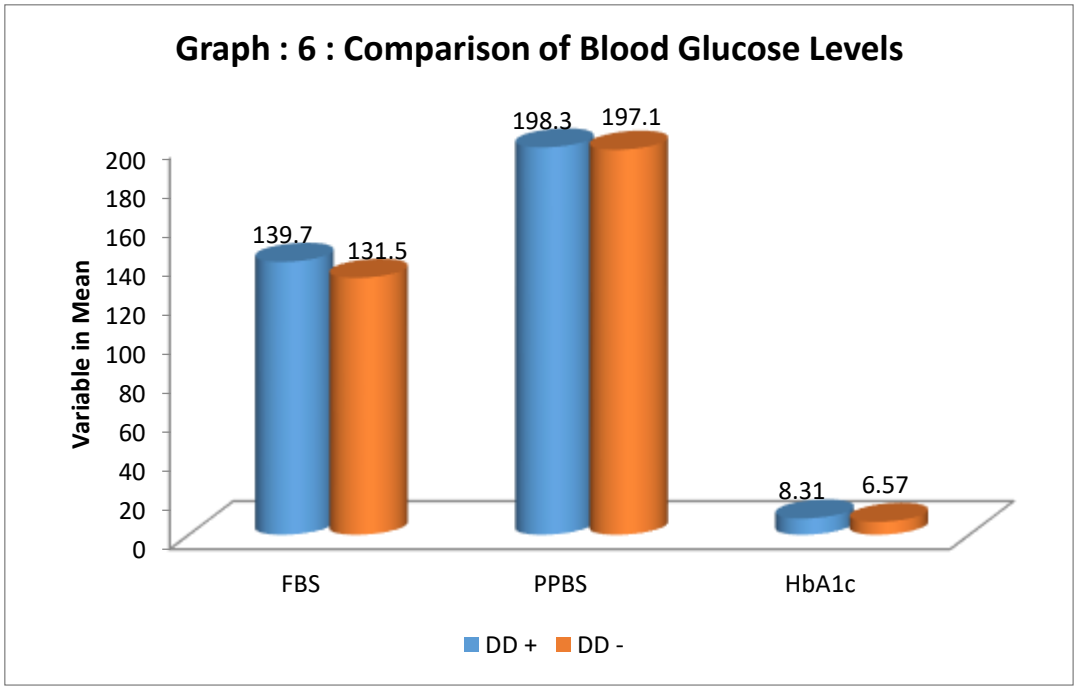
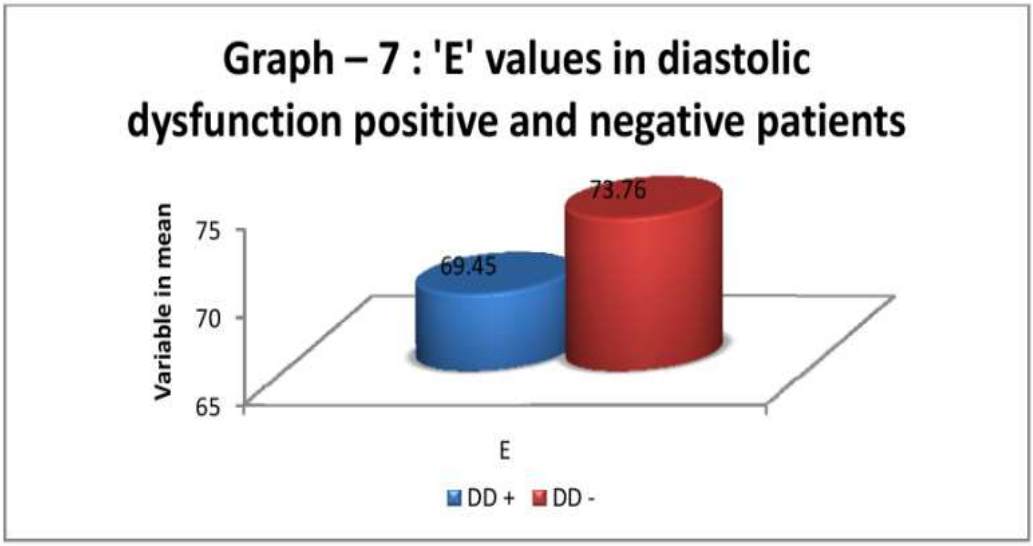

Graph : 6 : Comparison of Blood Glucose Levels
Variable in Mean
200
180
160
140
120
100
80
60
40
20
0
139.7
131.5
198.3
197.1
8.31
6.57
FBS
PPBS
HbA1c
DD +
DD -

TABLE – 7 : COMPARISON OF LV FILLING PATTERNS

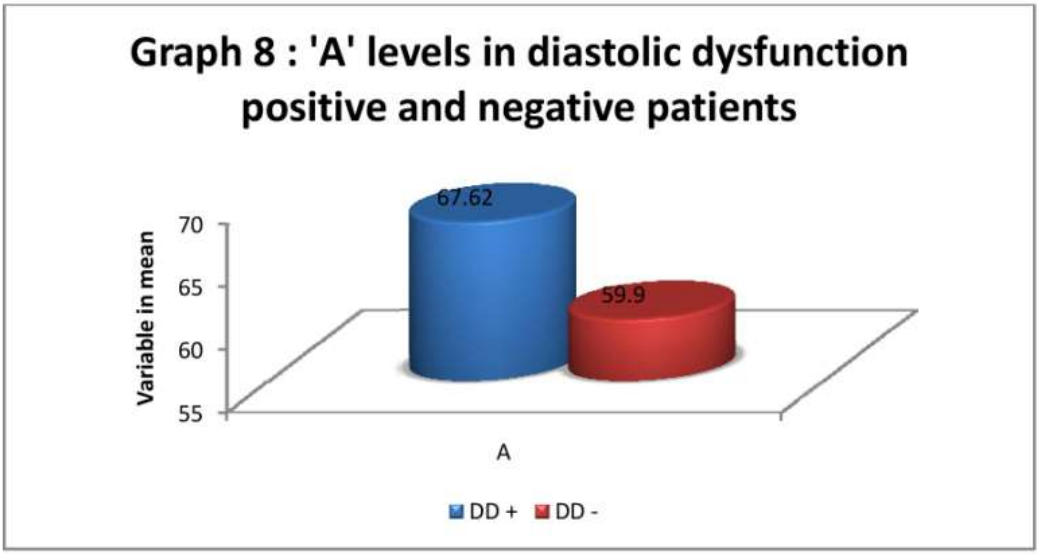
Variables	DD +		DD -		DD + v/s DD -			
	Mean	SD	Mean	SD	Mean Diff	t vale *	p value	
E	69.45	9.08	73.76	6.68	- 4.31	- 2.61	0.01	S
A	67.62	7.82	59.90	9.46	7.72	4.46	0.00	HS
E/A Ratio	1.04	0.20	1.21	0.24	- 0.17	- 3.64	0.00	S
VTIM	11.20	4.40	11.89	3.04	0.07	0.95	0.35	NS
VTIA	3.80	1.15	3.26	0.97	0.54	2.54	0.01	S
VTIA/VTIM	1.14	2.97	0.41	0.70	0.73	1.80	0.08	NS
PHT	58.79	8.83	54.19	7.20	4.60	2.77	0.01	S
IRT	83.52	6.98	75.62	13.71	7.90	3.77	0.00	HS
LVIDd	4.56	0.59	4.29	0.60	0.26	2.18	0.03	S
LVIDs	3.17	0.52	2.91	0.48	0.27	2.62	0.01	S
RVIDd	9.93	1.12	10.48	1.06	- 0.55	- 2.45	0.02	S
LAcm	4.81	6.58	3.14	0.30	1.67	1.64	0.10	NS
AOcm	2.74	0.27	3.93	5.90	- 1.20	- 1.54	0.13	NS
EF%	63.44	7.97	68.88	9.77	- 5.44	- 3.06	0.00	S

* Unpaired t test, S : Significant, NS : Non-significant, HS : Highly significant

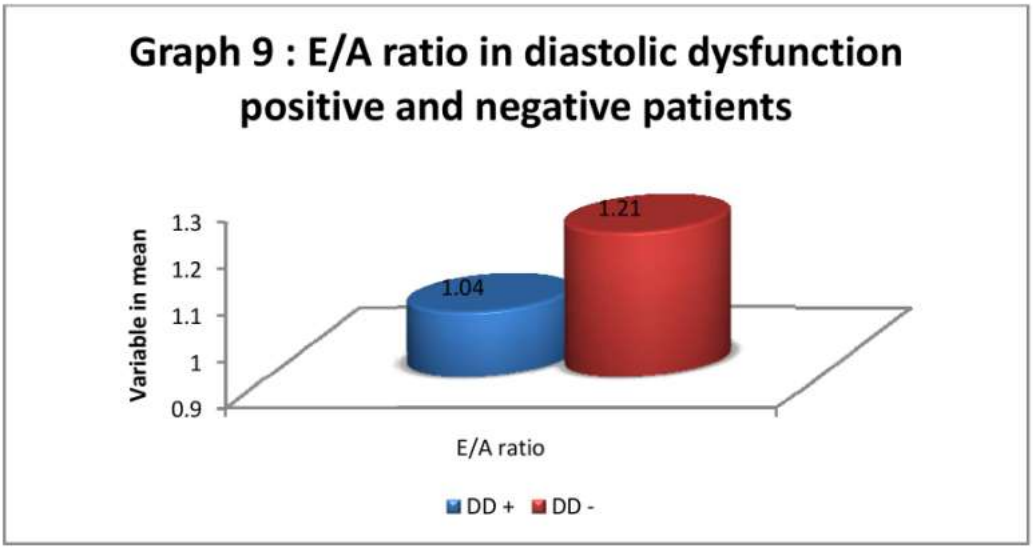
Peak velocity of early mitral flow (E) in patients with diastolic dysfunction were 69.65 and 73.76 in negative patients. There was a significant reduction of 'E' value compared to patients without diastolic dysfunction (p=0.01).



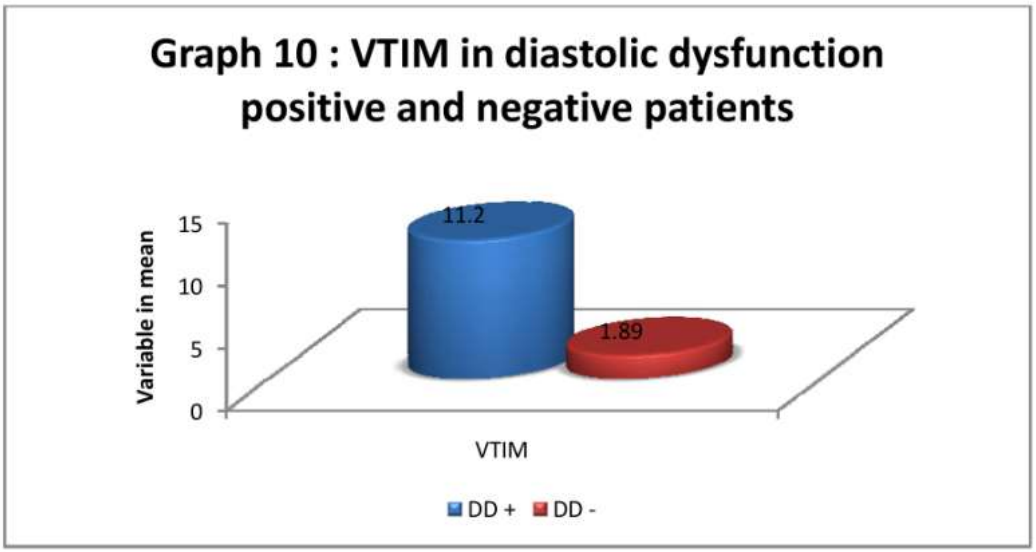
Peak velocity late mitral fow (A) in patients with diastolic dysfunction were 67.62 and 59.90 in negative patients. There was a significant increase in `A' value compared to patients without diastolic dysfunction (p=0.001).



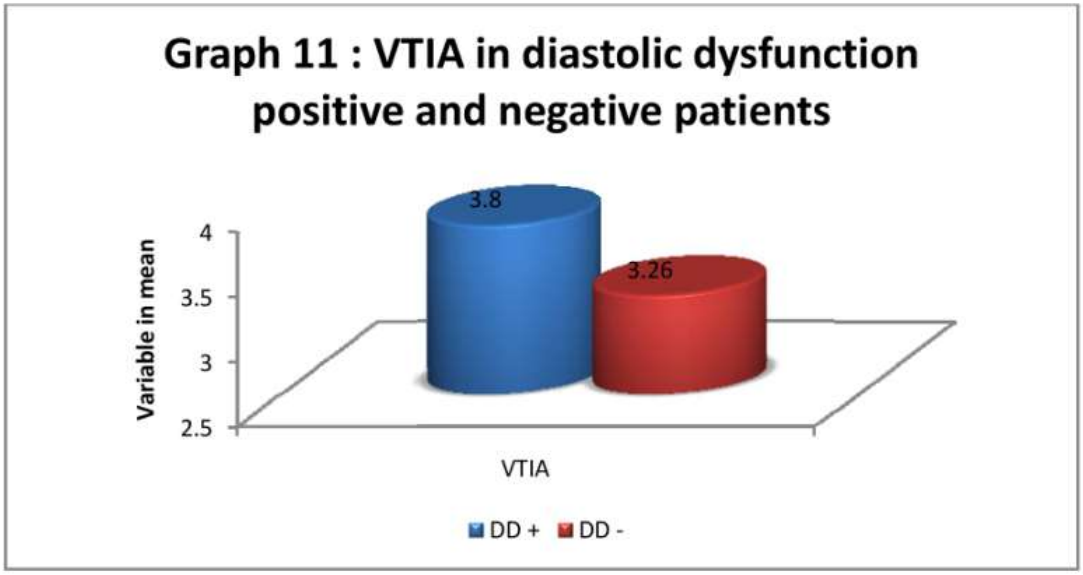
E/A were 1.04 and 1.21 in diastolic dysfunction positive and negative patients. E/A ratio was significantly reduced in patients with diastolic dysfunction (p<0.001)



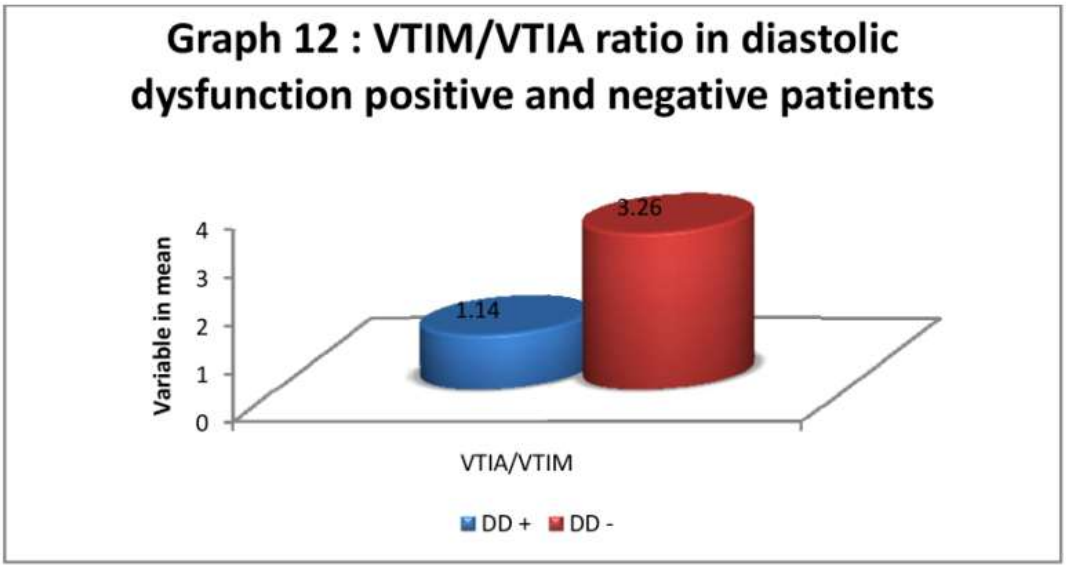
Velocity time integral of entire mitral curve (VTIM) were 11.20 and 11.89 in diastolic dysfunction positive and negative patients. VTIM was not significantly reduced in patients with diastolic dysfunction (p=0.35).



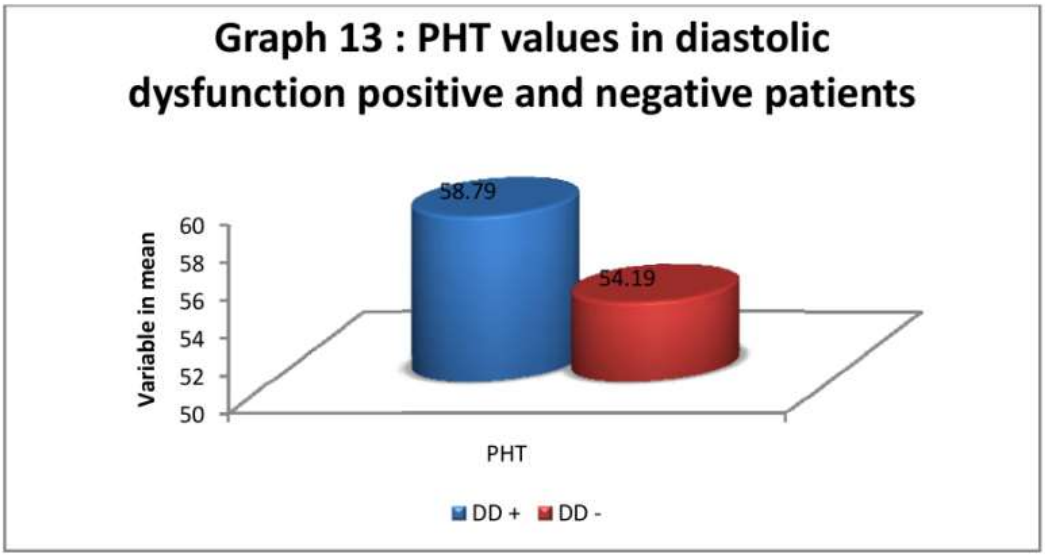
Velocity time integral of entire atrial curve (VTIA) were 3.80 and 3.26 in diastolic dysfunction positive and negative patients. VTIA was significantly increased in patients with diastolic dysfunction (p=0.01).



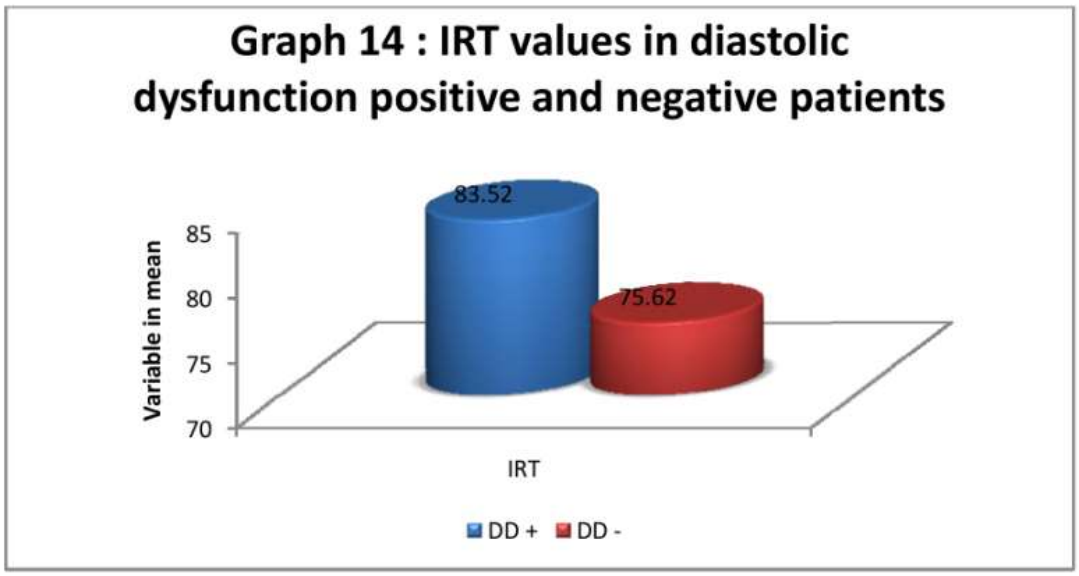
VTIM/VTIA were 1.14 and 0.41 in diastolic dysfunction positive and negative patients. VTIM/ VTIA was not significantly reduced in patients with diastolic dysfunction (p=0.08).



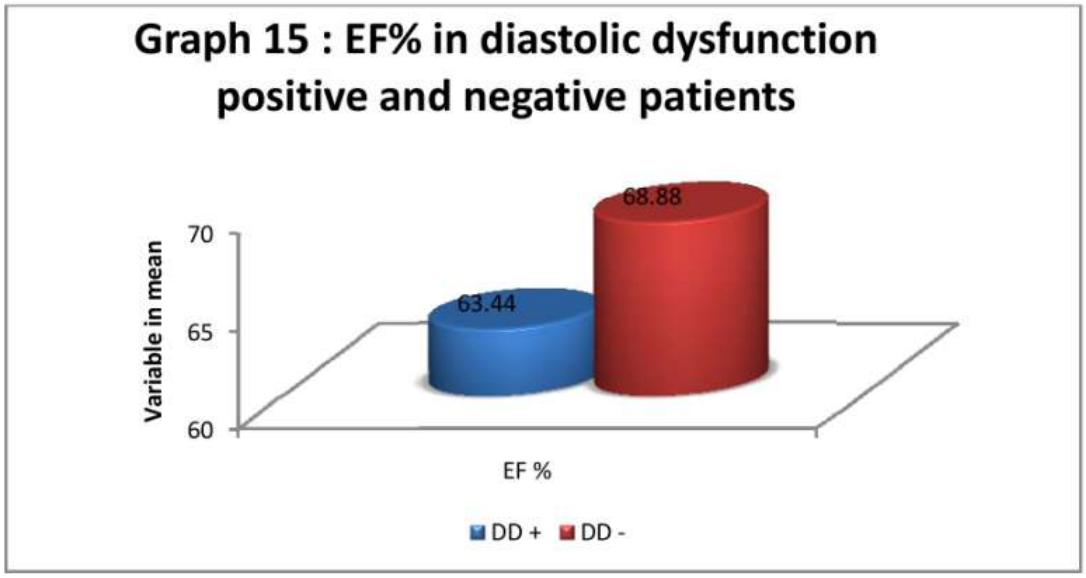
Pressure half time were 58.79 and 54.19 in diastolic dysfunction positive and negative patients. PTH was significantly increased in patients with diastolic dysfunction (p=0.01).



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).



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).



Results

This section presents the statistical analysis of the correlation between HbA1c levels and left ventricular diastolic dysfunction (LVDD) in patients with type 2 diabetes mellitus (T2DM).

Demographic and Clinical Characteristics

The study included a total of 100 normotensive T2DM patients with a minimum of 5 years duration of diabetes. The demographic and clinical characteristics of the study population are summarized in Table 1.

Table 1: Demographic and Clinical Characteristics of Study Population

CHARACTERISTIC	**MEAN +/- SD**
Age (years)	55.4 +/- 10.3
Duration of diabetes (years)	7.6 +/- 2.4
HbA1c (%)	8.5 +/- 1.2
BMI (kg/m2)	27.8 +/- 4.3

Table 2: Prevalence of Diastolic Dysfunction

GRADE OF DIASTOLIC DYSFUNCTION	**NUMBER OF PATIENTS**	**PERCENTAGE (%)**
Normal	40	40
Grade I (Mild)	35	35
Grade II (Moderate)	20	20
Grade III (Severe)	5	5

Correlation between HbA1c and Diastolic Dysfunction

The correlation between HbA1c levels and the grade of diastolic dysfunction was analyzed. Table 3 shows the mean HbA1c levels for each grade of diastolic dysfunction.

Table 3: HbA1c Levels by Grade of Diastolic Dysfunction

GRADE OF DIASTOLIC DYSFUNCTION	**Mean HbA1c (%) +/- SD**
Normal	7.5 +/- 0.8
Grade I (Mild)	8.3 +/- 0.9
Grade II(Moderate)	9.1 +/- 1.1
Grade III(Severe)	10.2 +/- 1.3

A statistically significant positive correlation was observed between HbA1c levels and the grade of diastolic dysfunction ($r = 0.45$, $p < 0.001$).

Logistic Regression Analysis

A logistic regression analysis was performed to evaluate the predictors of diastolic dysfunction. HbA1c levels were found to be a significant predictor of diastolic dysfunction (OR = 2.1, 95% CI: 1.5-3.0, $p < 0.001$).

Table 4: Logistic Regression Analysis for Predictors of Diastolic Dysfunction

PREDICTOR	**Odds Ratio (OR)**	**95 % CI**	**p- value**
HbA1c	2.1	1.5 -3.0	<0.001
Age	1.2	0.9-1.5	0.12
Duration of DM	1.4	1.1-1.8	0.03
BMI	1.1	0.9-1.4	0.27

Results

Demographic Details of Participants:

The study included [number] patients, with a mean age of [age] years. The gender distribution was [percentage] male and [percentage] female.

Prevalence of Diastolic Dysfunction:

Diastolic dysfunction was observed in [percentage] of the participants, with varying degrees of severity.

Correlation between HbA1c Levels and Diastolic Dysfunction:

A significant positive correlation was found between higher HbA1c levels and the severity of diastolic dysfunction (r = [correlation coefficient], $p < 0.05$). Patients with poor glycemic control (HbA1c > 7%) exhibited a higher prevalence and severity of diastolic dysfunction compared to those with better control (HbA1c ≤ 7%).

Discussion

Interpretation of Results:

The findings indicate a strong association between poor glycemic control and the presence of left ventricular diastolic dysfunction in type 2 diabetes mellitus patients. This underscores the importance of regular monitoring and effective management of blood glucose levels to prevent cardiovascular complications.

Comparison with Previous Studies:

The results are consistent with earlier studies that reported high prevalence rates of diastolic dysfunction in diabetic patients. However, this study adds to the literature by specifically focusing on normotensive patients, thereby isolating the impact of glycemic control on cardiac function.

Possible Mechanisms:

The pathophysiological mechanisms linking hyperglycemia to diastolic dysfunction include advanced glycation end-product formation, oxidative stress, myocardial fibrosis, and altered calcium handling in cardiomyocytes.

Clinical Implications:

Regular assessment of HbA1c levels and early echocardiographic screening for diastolic dysfunction should be incorporated into the management plan for type 2 diabetes mellitus patients to mitigate the risk of heart failure.

Limitations of the Study:

The study is limited by its cross-sectional design, which precludes the establishment of causality. Additionally, the sample size may not be representative of the broader diabetic population.

Future Research Directions:

Longitudinal studies with larger sample sizes are needed to confirm these findings and explore the effects of intensive glycemic control on the progression of diastolic dysfunction.

Conclusion

In conclusion, this study demonstrates a significant correlation between elevated HbA1c levels and the presence of left ventricular diastolic dysfunction in normotensive patients with type 2 diabetes mellitus. Monitoring and managing HbA1c levels are crucial for early detection and prevention of cardiovascular complications in diabetic patients.

Acknowledgement: I sincerely thank all my professors and Colleagues who supported me to complete this research.

References

1. Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics – 2013 update: a report from the American Heart Association. Circulation. 2013;127:e6-e245.

2. Battiprolu PK, Gillette TG, Wang ZV, et al. Diabetic cardiomyopathy: mechanisms and therapeutic targets. 2010.

3. Turer AT, Hill JA, Elmquist JK, et al. Adipose tissue biology and cardiomyopathy. Circ Res. 2012;111:1565-1577.

4. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics – 2012 update: a report from the American Heart Association. Circulation. 2012;125:e2-e220.

5. Gerstein HC, Miller ME, Genuth S, et al. Long-term effects of intensive glucose lowering on cardiovascular outcomes. N Engl J Med. 2011;364:818-828.

6. Pyke DA. "Preamble: The history of Diabetes." In: Albertii K.G.M.M., Zimmet P., Defronzo R.A., eds. International Textbook of Diabetes Mellitus. 2nd ed. England: John Wiley and Sons Ltd; 1997:1-27.

7. Yudkin JS. "Vascular events and diabetes: Acute myocardial infarction and stroke." In: Albertti K.G.M.M., Zimmet P., Defronzo R.A., eds. International Textbook of Diabetes Mellitus. 2nd ed. England: John Wiley and Sons Ltd; 1997:1827pp.

8. Macfarlane IA. "The millennia before Insulin." In: Pickup JG, Williams G, eds. Textbook of Diabetes. 2nd ed. London: Black Well Science Ltd; 1991:1013pp.

9. Gavin JR, et al. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care. 1997;20:1183-1197.

10. Seshaiah V. "Age and Abnormalities of Rheology." In: Das S, ed. Complications of Diabetes in Indian Scenario. Vol 1. Mumbai: USV Limited; 2001:1-4.

11. Christlieb RA, Krolewski AS, Waram JH. "Hypertension." In: Kahn RC, Weir GC, eds. Joslin's Diabetes Mellitus. 13th ed. Philadelphia: Lippincott Williams and Wilkins; 2000:1068pp.

12. Das S. "General consideration hypertension." In: Das S, ed. Complications of Diabetes in Indian Scenario. Vol 1. Mumbai: USV Limited; 2001:14-17.

13. Panja M. "General consideration and coronary artery disease." In: Das S, ed. Complications of Diabetes in Indian Scenario. Vol 1. Mumbai: USV Limited; 2001:18-20.

14. Kumar AD. "General consideration: Noncoronary cardiac involvement." In: Das S, ed. Complications of Diabetes in Indian Scenario. Vol 1. Mumbai: USV Limited; 2001:21-26.

15. Nesto RW, et al. "Heart disease in diabetes." In: Kahn RC, Weir GC, eds. Joslin's Diabetes Mellitus. 13th ed. New Delhi: Lippincott Williams and Wilkins; 2000:1068pp.

16. Wynne J, Braunwald E, eds. "The Cardiomyopathies and myocarditis." In: Heart disease- A text book of cardiovascular medicine. 5th ed. Philadelphia: W.B. Saunders Company; 1997:1996pp.

17. Regan TJ. 1996. "Echocardiographic evaluation of left ventricular function in NIDDM." Jour. Diab Assoc. India. 1996;36:166-1111.

18. Surawicz B, Mangiardi ML. "Electrocardiogram in endocrine and metabolic disorders." In: Rios JG, ed. Clinical electrocardiographic correlation. Philadelphia: F.A. Davis Co.; 1977:243pp.

19. Das S, Baliassinha AK. 1988. "ECG changes in patients with NIDDM. A prospective study." Jour Diab Assoc. India. 1988;38:12-16.

20. Appleton CP. "The echodoppler evaluation of left ventricular diastolic function - a current perspective." In: Sander JK, Kovacs S, eds. Cardiology Clinic - Diastolic function and dysfunction. Philadelphia: W.B. Saunders Company; 2000:600pp.

21. Kahn JK, et al. 1986. "Radionuclide assessment of left ventricular diastolic filling in diabetes mellitus with and without cardiac autonomic neuropathy." J. Am. Coll. Cardiol. 1986;7:1307-1309.

22. Airaksinen J, Ikaheimo M, Kaila J. 1984. "Impaired left ventricular filling in young female diabetics: An echocardiographic study." Acta Med Scand. 1984;216:509-516.

23. Fiorini G, et al. 1995. "An echocardiographic study of left ventricular diastolic function in patients with type 2 diabetes mellitus." G. Ital. Cardiol. 1995;25:517-528.

24. Shapiro LM, et al. 1981. "Left ventricular function in diabetes mellitus. Relation between clinical features and left ventricular function." Br Heart J. 1981;45:129-132.

25. Guglielmi MD, et al. 1995. "Impaired left ventricular diastolic function and vascular post ischemic vasodilation associated with microalbuminuria in IDDM patients." Diabetes Care. 1995;18:353-360.

26. Quinones MA. "Doppler assessment of left ventricular diastolic function." In: Nanda NC, ed. Doppler echocardiography. 19th ed. Philadelphia: Lea and Febiger; 1993:197pp.

27. Demaria AN, et al. 1991. "Doppler echocardiographic evaluation of diastolic dysfunction." Circulation. 1991;84:288-295.

28. Gouch SC, et al. 1995. "Diastolic dysfunction is not related to changes in glycemic control over 6 months in type 2 diabetes mellitus. A cross-sectional study." Acta. Diabetol. 1995;32:110-115.

29. Gaasch WH, Le Winter MM. Left ventricular diastolic dysfunction and heart failure. Philadelphia: Lea and Febiger; 1993:498pp.

30. Raev DC, 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. 1994;17:633-639.

31. Hoit BD, et al. 1999. "Non-invasive evaluation of cardiac dysfunction by echocardiography in streptozotocin-induced diabetic rats." J Card Fail. 1999;5.