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ORIGINAL ARTICLE

LEFT ATRIUM VOLUME INDEX AND DIASTOLIC DYSFUNCTION IN NORMOTENSIVE DIABETIC PATIENTS

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ABSTRACT

Background: Diabetes mellitus causes hyperglycemia owing to insulin secretion, action, or both. This study evaluates left ventricular diastolic function in diabetics without cardiac symptoms who have left ventricle impairment early and late. To link LVDD to Type 1 and Type 2 diabetes duration, HbA 1c, fasting sugar, and smoking.

Materials & Methods: This prospective cross-sectional study was conducted at Marjan Teaching Hospital and the Diabetic Endocrine Center in Babylon province from December 2019 to July 2022. It included 104 referred patients. Demographic data such as age, gender, blood pressure, height, weight, Body Surface Area, disease duration. 5 ml of blood was collected from group for the purpose of measuring hematological parameters (fasting blood sugar (FBS), glycated hemoglobin (HbA1C)). Left Atrium volume index (LAVI), Time of Deceleration (DT), and Isovolumic relaxation time (IVRT) were collected by the trans-mitral Doppler. Inclusion criteria: Any patient with normotensive diabetic and Diastolic Dysfunction**.** Exclusion criteria was patients with blood pressure equal or above 140/90 on more than 3 readings.

Results: HbA1C levels varied from 6 to 15%. Among the patients, 72 had moderate to severe HbA1C levels, 27.9% had normal HbA1C, and 2.9% had mild HbA1C levels. The mean (LAVI) was 38. Normal LAVI was observed in 34.6% of patients, while 42.3% had Grade 1 LAVI, 16.3% had Grade 2, and 6.7% had Grade 3. Diastolic dysfunction was present in 42% of patients (Grade 1), with 16.3% having Grade 2 and 6.7% having Grade 3 DD. A negative correlation was found between gender, smoking, and (LVDD). Positive correlations were observed between age, HbA1C, disease duration, and LAVI with diabetes severity and DD grades.

Conclusion: Patients with higher HbA1C and longer diabetes duration had higher LAVI. Additionally, older diabetic patients exhibited more severe diastolic dysfunction.

Key words: Diabetes Mellitus; Diastolic Dysfunction; FBS; HbA1C; LAVI; DT.

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INTRODUCTION

Diabetes is a collection of metabolic illnesses that cause high blood sugar due to inadequate insulin manufacturing, cell responsiveness, or both.[1,2] Environmental and genetic risk factors can cause type 1 diabetes, which impairs insulin production. [3]

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Two sorts of difficulties exist. The first type is quick and manageable.[4] The other kind, called chronic, is caused by high blood glucose. Extremely high levels might cause serious problems.[5] It damages neurons and blood vessels. Atherosclerosis and plaque, Metabolic Syndrome, Diabetes with No Insulin Response, CHD, HBP, and Diabetes Interaction may cause diabetic heart disease. [6] Long-term blood vessel damage can cause strokes, heart attacks, renal failure, blindness, slow wound healing, infection, and amputations owing to inadequate circulation. Cardiovascular disease, a chronic, non-communicable disease, causes many deaths and illnesses.[7] The American College of Cardiology/American Heart Association now lists diabetes as a risk factor for CHF since it affects CHF development. Hyperglycemia contributes to diabetic cardiomyopathy. This heart

muscle sickness may be caused by altered substrate supply and utilization by cardiac cells, according to emerging data.[8] The "fetal gene program" disruption, which impairs myocardial calcium management, and altered gene and myosin heavy chain control are also linked to diastolic dysfunction in diabetics. Systolic function is unaltered, while diastolic function is compromised in several illnesses, including hypertension, hypertrophic cardiomyopathy, and coronary artery disease.[9] Normal diastolic function is the left ventricle fully filled and efficiently at physiological pressures.[10] This suggests that the left ventricle can fill without an extremely high left atrial pressure. Isovolumic relaxation opens the mitral valve, and elastic rebound and active chamber relaxation occupy the first third of diastole.[11] E wave indicates this period. The mitral annulus moves swiftly during early filling as the chamber expands to receive blood. This process may be measured and recorded using tissue Doppler. Mid-diastole filling is little, and heart rate shortens or vanishes the diastasis.[12]

The impact of type 2 diabetes on left atrial remodeling: We can determine how diabetes affects LA remodeling using echocardiographic, computed tomography, and cardiac magnetic resonance studies of diabetic left atrial volume, function, and mechanics.[13, 14] Diabetic cardiomyopathy causes the heart muscle to expand, thicken, and/or stiffen, impairing its ability to pump blood and causing arrhythmias and heart failure.[15] Diabetics' metabolic changes cause it.[16] Subclinical myocardial damage may result from loss of coronary flow reserve, metabolic problems, autonomic dysfunction, and myocardial fibrosis, although the exact causes of LV changes in diabetics remain unclear.[17] On echocardiography, diabetic cardiomyopathy causes heart failure, which is characterized by left atrial chamber hypertrophy and dilatation and systolic and diastolic dysfunction.[18] It's intriguing that Wang et al. observed left atrial energy loss and deformation mechanics hampered even in type 2 diabetic individuals with normal LA size.[19] Similar to the association between insulin resistance and CV problems in overt diabetes, recent studies have linked higher insulin resistance to cardiac and vascular dysfunction in non-diabetics.[20] Diabetes increases cardiovascular risk by 2-4 times. Additionally, women with diabetes had the same age-adjusted cardiovascular risk as males.[21] LVH may affect 7% of diabetics, according to a Russian research, and it may rise owing to high blood pressure from distant nephropathy.[22] Both men and women who consume cigarettes have greater inflammatory markers. Smoking may diminish platelet-derived NO and platelet sensitivity to exogenous NO, which may increase platelet activation, adhesion, fibrinogen, and fibrinolysis.[23] It reduces plasma paraoxonase, an LDL-oxidation-fighting enzyme. Recent research links smokers' triglycerides and HDL abnormalities to insulin resistance.[24] This study evaluates left ventricular diastolic function in diabetics without cardiac symptoms who have left ventricle impairment early and late. To link LVDD to Type 1 and Type 2 diabetes duration, HbA 1c, fasting sugar, and smoking.

MATERIAL AND METHODS

2.1 Study design: is a prospective cross-sectional study including (104) patients with normotensive diabetic and Diastolic Dysfunction.

2.2 Sampling Technique: The technique of collecting study samples was done very accurately based on a set of specific criteria to complete this study. Patients suffering from diabetes were selected. Patients referred to the hospital and diabetic center during the study December 2019 to July 2022 were included in the study.

2.3 Inclusion Criteria: Cases: Individuals aged 28-69 years diagnosed with diabetic (If a patient has a FBS concentrations 126 mg/dL or higher and is a known diabetic receiving treatment, and the patients with Diastolic Dysfunction, [25] attending the (Marjan Teaching Hospital, and Diabetic, Endocrine Center) in Babylon province.

All patients:

- Before collecting samples, we got the patients' oral permission.
- Patients consent for blood sample collection and clinical examinations.
- Patients with all data available (name, age, gender, duration of illness, other illnesses, height, weight, blood pressure, BSA and treatment used).

Exclusion Criteria includes individuals with angina pectoris, patients with hypertension, significant alcoholics, thyroid diseases, renal failure, and other underlying heart diseases such as (Valvular heart disease, and by history, chest X-ray (CXR) poster anterior (PA) view, and echocardiography (Echo) are considered to have myocardial infarction.

2.4 Sample collections:

This study was conducted at Marjan Teaching Hospital and the Diabetic and Endocrine Center in Babylon Province, from December 2019 to July 2022. The study involved 104 patients (79 males and 21 females) suffering from diabetic and Diastolic Dysfunction and aged between 28 and 69 years.

A 5 ml medical disposable syringe was used to take 5 ml of blood, which was then put in a tube containing anti-coagulants to avoid clotting and analyzed to determine fasting blood sugar and HbA1C. Trans mitral Doppler measured left atrium volume index (LAVI), Time of Deceleration (DT), and Isovolumic relaxation time (IVRT). The A-wave, which is linked to atrial contraction, and the E-wave, which features rapid early filling, cause normal diastolic flow.[26,27]

E-wave DT (140-240MS) and EIA ratio 0.9-1.5 indicate transmittal flow. Normal, delayed relaxation (G1), pseudonormal (G2), and restricted filling (G3) samples.[28] Three-wave tissue Doppler image: 1-Sa systolic cardiac tissue Doppler velocity above baseline, 2-Ea early diastolic relaxation below baseline, and Aa atrial contraction velocity. Sample volume (2-3mm) in the myocardial septum, then lateral to ideal location by cursor sample volume below mitral annulus, low gain, aliasing velocity 15-20 ms.[29] Time of Deceleration (extrapolated from peak E wave velocity to baseline along velocity deceleration slope).[30, 31]

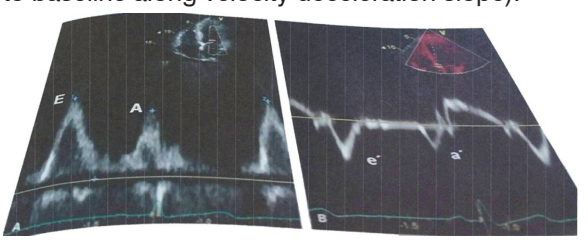

Fig (1) Tissue Doppler image [30]

2.3 Statistical Analysis

The data was analyzed by SPSS 15 using ANOVA, t-test, correlation coefficient, and discriminant analysis. *P* value 0.05 was significant .[32]

RESULTS

All T2DM patients at Marjan teaching hospital in Babylon Governorate were included in this cross-sectional research. Most patients were 50 years old (15 individuals). The mean age was 47. Only 15 (14.4%) of the research group were under 30, while 19 (18.3%) were over 60. While 23.1% and 44.2% of patients were 31-45 and 46-60 years old.

Male patients made up 79.8% of the trial, while female patients 21%. Male patients averaged 48 years old and females 43. Male participants had 191 mg/dl mean FBS, whereas female participants had 235 mg/dl. Systolic blood pressure means for the overall sample (males, and females) is 119 mm/hg. The recruited patients are non-smokers, while the rest are light, moderate, or heavy smokers (fig. 2). None of the women smoke.

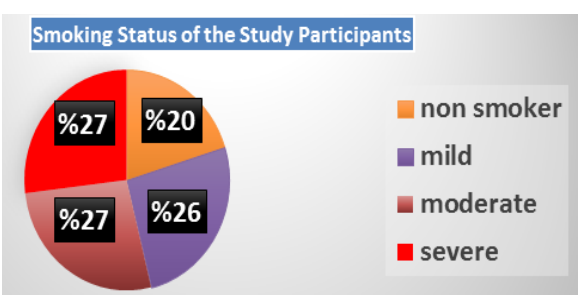

Fig. (2): The smoking status, N=104

The research participants had diabetes for 8.8 years on average. Only 2 individuals had diabetes for more than 30 years, while 7 (6.7%) had it for one year. One quarter of the study sample (26 individuals) had short-term diabetes, whereas 38.5% and 36.5% had medium-term diabetes. It was unfortunate that the mean FBS was 200 mg/dl. Minimum and highest FBS levels were 100 and 480 mg/dl (fig. 3).

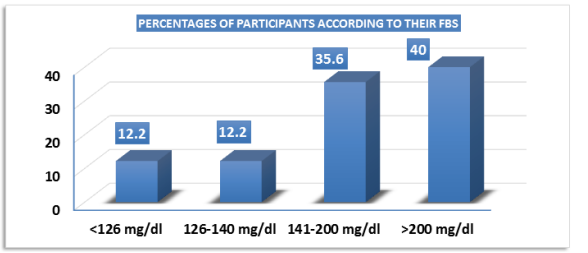

Fig. (3): Percentages of the study participants according to their FBS, N=104.

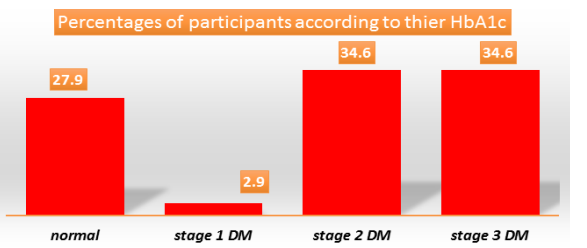

Fig. 4: Percentages of participants according to their HbA1C, N=104.

The mean for the measured left atrial volume index for the study sample (fig. 5).

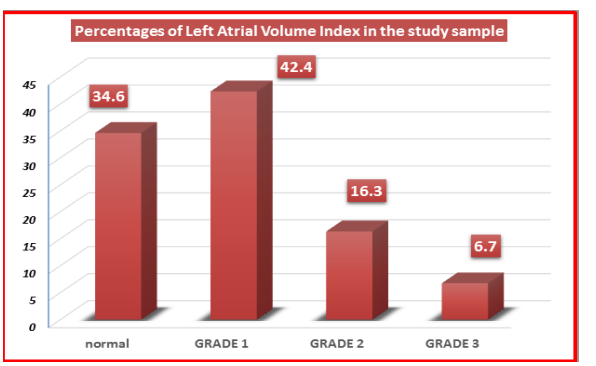

Fig. 5: Percentages of the study sample According to their LAVI, N=104.

More over half of patients (55 individuals) had Grade 1 diastolic dysfunction, whereas 14.4% and 1% had Grade 2 and 3. The remaining 33 have normal diastolic function.

Diastolic function is strongly correlated with patient age (Table 1).

The duration of the disease, also shown to be significantly correlated with Diastolic function (Table 2).

Furthermore, FBS, also exhibit a significant correlation with Diastolic Function, (Table 3).

Jointly, the results of the HbA1C tests have exhibit a significant correlation with their Diastolic

Function (Table 4).

The correlation of the age and LAVI has also been tested and found to be a significant correlation (Table 5).

Table 1: The Correlation between Diastolic Function and the Age, N=104.

Age group	DD grade				Total	P value
	normal DF	Grade 1	Grade 2	Grade 3		
<30 y	9	4	1	1	15	0.000
31-45 y	11	6	7	0	24	
46-60 y	9	34	3	0	46	
>60 y	4	11	4	0	19	
Total	33	55	15	1	104	

Table 2: The Correlation between disease Duration and Diastolic Function, N=104.

Duration of disease	DD grade				Total	*P value*
	normal DF	Grade 1	Grade 2	Grade 3		
Short D.	22	3	1	0	26	**0.000**
Medium D.	10	29	1	0	40	
Long D.	1	23	13	1	38	
Total	33	55	15	1	104	

Table 3: The Correlation between FBS and Diastolic Function, N=104.

FBS	DD grade				Total	*P value*
	Normal DF	Grade 1	Grade 2	Grade 3		
<126 mg/dl	12	1	0	0	13	**0.000**
126-140 mg/dl	7	3	3	0	13	
141-200 mg/dl	10	24	3	0	37	
>200 mg/dl	4	27	9	1	41	
Total	33	55	15	1	104	

Table 4: The Correlation between hbA1c levels and Diastolic Function, N=104.

HbA1C	DD grade				Total	P value
	Normal DF	Grade 1	Grade 2	Grade 3		
Normal	28	1	0	0	29	0.000
stage 1 DM	2	0	1	0	3	
stage 2 DM	3	33	0	0	36	
stage 3 DM	0	21	14	1	36	
Total	33	55	15	1	104	

The duration of the disease for the patient also shown significantly correlated with their LAVI (Table 6).

Similar to its correlation with the Diastolic Function, Fasting Blood Sugar has also exhibit a significant correlation with LAVI (Table 7).

In the same context, the HbA1c level has demonstrated a significant correlation with the LAVI (Table 8).

Lastly, the correlation between the LAVI and Diastolic Function was a significant correlation (Table 9).

Table 5: The Correlation of the Age with LAVI, N=104.

AGE	Lt Atrial Vol. Index				Total	*P value*
	Normal DF	Grade 1	Grade 2	Grade 3		
<30 y	10	3	1	1	15	
31-45 y	12	4	7	1	24	
46-60 y	10	26	8	2	46	**0.001**
>60 y	4	11	1	3	19	
Total	36	44	17	7	104	

Table 6: Correlation of the Duration of the disease with the LAVI, N=104

Duration of disease	Lt Atrial Vol Index				Total	P value
	Normal	Grade 1	Grade 2	Grade 3		
Short Duration	23	2	1	0	26	
Medium Duration	12	24	3	1	40	**0.000**
Long Duration	1	18	13	6	38	
total	36	44	17	7	104	

Table 7: Correlation of Fasting Blood Sugar with LAVI, N=104.

FBS	Lt Atrial Vol Index				Total	*P value*
	Normal	Grade 1	Grade 2	Grade 3		
<126 mg/dl	**12**	**1**	**0**	**0**	13	
126-140 mg/dl	**7**	**3**	**2**	**1**	13	
141-200 mg/dl	**11**	**20**	**5**	**1**	37	**0.000**
>200 mg/dl	**6**	**20**	**10**	**5**	41	
Total	36	44	17	7	104	

Table 8: Correlation of HbA1C with LAVI, N=104.

HbA1C	LT Atrial Vol. Index				Total	*P value*
	Normal	Grade 1	Grade 2	Grade 3		
Normal	29	0	0	0	29	
stage 1 DM	2	0	1	0	3	
stage 2 DM	5	28	2	1	36	**0.000**
stage 3 DM	0	16	14	6	36	
Total	36	44	17	7	104	

Table 9: Correlation of the LAV with Diastolic Function, N=104.

DD grade	LT Atrial Vol. Index				Total	*P value*
	Normal	Grade 1	Grade 2	Grade 3		
Normal DF	33	0	0	0	33	0.000
Grade 1 DD	3	44	7	1	55	
Grade 2 DD	0	0	10	5	15	
Grade 3 DD	0	0	0	1	1	
	36	44	17	7	104	

DISCUSSIONS

Besides vascular cardiac disease, diabetes can cause diabetic cardiomyopathy, LVDD systolic. In metabolic syndrome patients, diastolic dysfunction predicts mortality and morbidity.[33] Even without cardiovascular illness, European guidelines prescribe echocardiography for diabetes type 2 patients' diagnostic work-up.[34] According to several articles, symptom-free diabetes type 2 individuals have variable diastolic dysfunction rates. After removing all patients with micro- or macro-vascular issues, Cosson et al. found 0% prevalence, while Boyer et al. found 75% frequency using wide criteria for diastolic dysfunction.[35] Diastolic abnormalities are common in Diabetes Mellitus, with 68.3% of patients having them. Similar findings were found by Boyer et al.[36] (75%), Nikhil [37] (66%), and Fawad[38] (48%). Studies demonstrate Diabetes Mellitus patients' lower LVD function.

Kapappu found that 78% of Diabetes Mellitus patients had diastolic dysfunction, and 33% had Grade 2 or more DD.[39] Diabetic cardiomyopathy's complex changes in the heart's mechanical, metabolic, anatomical, and electrical characteristics may cause early diastolic dysfunction and an increased risk of cardiac arrhythmias. Diabetic heart energy may be reduced by improper use of free fatty acid as a metabolic substrate. Intra-myocardial lipolysis and re-esterification of fatty acids can accumulate dangerous intermediates, limit glucose metabolism, and lower the phosphocreatine/adenosine triphosphate ratio. Myocardial, cardiac contractile, and diastolic function may be altered by heart energy metabolism problems.[40] The mean age of our volunteers was 47 years, lower than Diamant study patients' 56 years.[41] This research had 80% smokers, while Kadappu had 48%.[42] Due to gender differences, Kadappu study has virtually equal male and female percentages whereas our study has just 20% females. Indeed, it exceeds Poirier study participants' fasting blood sugar.[41], studies with mean FBS of 184, 180, and 144 mg/dl. The study group's mean HbA1c was the highest among comparable trials (6.1%, 6.5, 7.3%, and 8.3%).[42] However, the mean HbA1c of the enrolled patients was 8.8%, indicating inadequate diabetes management[43], and Platil's 11-year investigation.[44] but the Diamant group had 6.1% HbA1c despite a 14-year illness duration.[42] Previous scientific research showed a favorable association between illness duration and diastolic dysfunction. In our study, almost 97% of individuals with long-term diabetes exhibited diastolic dysfunction, while 86% of those with short-term diabetes had normal diastolic function. Platil found a link between diabetes duration and diastolic dysfunction.[44]This study's patients' diastolic dysfunction is highly linked with fasting blood sugar and HbA1C. Diastolic dysfunction is more common in patients with FBS over 140 mg/dl. In reciprocal, diastolic dysfunction was more common in individuals with HbA1C beyond 7.5%. These findings correlate with Abhay et al. [45], who reported that LVDD patients have a higher mean HbA1C than the general population. In multivariate analysis, males had far higher rates of diastolic abnormalities than females.[44] Smoking was another sociodemographic factor that did not correlate with diastolic performance in our study. Similar studies poorly studied smoking as a predictor for diastolic function, but Fischer's[45] and kapappu investigations found no significant link.[41] Left atrium size predicts stroke, atrial fibrillation, and mortality.[46] LAVI independently and incrementally predicts cardiovascular mortality and morbidity in diabetics without cardiovascular disease.[47] Other studies found that diabetic cardiomyopathy induces atrial fibrosis and lowers LA compliance.[48] Thus, Diabetes Mellitus may have more atrial fibrosis. Surrogate markers for DD include LA enlargement and dysfunction. LA function in Diabetes Mellitus patients may indicate underlying DD, hence examination is crucial.[41] Interestingly, about 65% of research participants had left atrial volume index. Over 40% of patients had grade 1 LAVI, whereas 6.7% had grade 3. In the first study to rigorously measure Left Atrial Volume in a large sample with T2 Diabetes Mellitus, a third of 305 participants had moderate-to-severe LA enlargement. Age and LAVI of the research patient were also shown to be significantly correlated. About

80% of individuals over 60 have abnormal LAVI. LAV dilatation increased with age. In agreement. Our data showed that LAVI rises with diabetes duration. Medium and long-term diabetics have greater LAVI than short-term diabetics, Tomasz Zapolski et al. found that LAVI is strongly and directly linked with HbA1C, supporting our findings ,We identified a strong association between the recruited group's LAVI and Diastolic Function. Patients with normal Left Atrial Volume Index had normal Diastolic Function, while all Grade3 LAVI patients had Grade3 DD. In the same context, 80% of Grade1 and 66.4% of Grade2 Left Atrial Volume Index patients had DD. Kadappu found that 40% of patients with greater LAVI had diastolic impairment.[41] In a cross-sectional study of individuals aged 45+, Diamant showed that Left Atrial Volume Index was linked to DD severity.[46]

CONCLUSIONS

Higher prevalence of diastolic dysfunction in DM patients and it increases with increasing age of patient, period of diabetes and with high HbA1C, there is significant association between increments of LAVI with severity of DD grades. Patient with higher HbA1C and those with longer duration of diabetes had higher LAVI.

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CONFLICT OF INTEREST
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	HN, ZCH
Acquisition, Analysis or Interpretation of Data:	HN, ZCH
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All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.