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Gender Differences of Pulsed and Tissue Doppler Indices of Left Ventricular Diastolic Function in Type II Diabetic Patients

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Abstract

Background: LV diastolic dysfunction is one of the first signs of diabetic cardiomyopathy, often developing before systolic dysfunction. Diastolic dysfunction in women differs in many aspects from that of men. Some of these differences may have a pathophysiological basis. These sex differences may have widespread implications in the field of heart failure with normal ejection fraction. **Objective:** To assess gender differences of left ventricular diastolic function by pulsed and tissue Doppler echocardiographic indices in patients with type II diabetes mellitus. **Patients and Methods:** The study included 300 patients with type II diabetes mellitus and was conducted in the Cardiology Department (Faculty of Medicine, Azhar University). It is an observational case control study started from January 2017 to March 2019. 150 age and gender matched healthy volunteers as control. **Results:** Our study showed that there is no statistically significant difference between diabetic males and diabetic females as regard LA dimensions, E/é lateral, e' lateral, E/A ratio, A velocity. It was significant for E/e' septal, E velocity, EF, LVEDD and LVESD with p values 0.033, 0.006, 0.001, 0.007 and 0.001 respectively. **Conclusion:** Diabetic patients should be evaluated for subclinical diastolic dysfunction by Doppler studies as well as good control of diabetes for deceleration of the development of clinical cardiomyopathy, and decreased morbidity and mortality.

Keywords: DM, HF, LV, CVD.

INTRODUCTION

Diabetes mellitus (DM) may be considered as one of the challenges even in the highly developed medical field of the 21st century. It is becoming an epidemic health threat [(1)]. It affects 350 million people around the world, and the World health organization (WHO) has projected that diabetes deaths will be doubled between 2005 and 2030 [(2)].

Number of epidemiological, clinical and autopsy studies have proposed the presence of diabetic heart disease as a distinct clinical entity. Diastolic heart failure (HF) is also referred to as HF, with preserved left ventricular systolic function. Many studies have reported that the incidence of heart failure in diabetic subjects is high even in the absence of hypertension and coronary artery disease. Studies have reported a high prevalence of pre-clinical diastolic dysfunction among subjects with DM. The evidence indicates that myocardial damage in diabetic subjects affects diastolic function before the systolic function. The pathogenesis of this left ventricular (LV) dysfunction in diabetic subjects is not clearly understood [(3)].

Diabetic cardiomyopathy has been proposed as an independent cardiovascular disease, and many mechanisms, such as microvascular disease, autonomic dysfunction, metabolic disorders, and interstitial fibrosis, have been suggested as causative factors. However, the exact etio-pathogenesis of diabetic cardiomyopathy still remains unclear. So far, very few population-based studies have been carried out in India, to demonstrate the prevalence of diastolic dysfunction in diabetic subjects in the Indian patients. The objective of our study was to determine whether there is any association between diastolic dysfunction and type 2DM, even in the asymptomatic subjects. Thus, this prospective case control study was conducted with the aim of determining the prevalence of asymptomatic LV diastolic dysfunction in type 2 diabetes subjects, and its relation to age, duration of DM, HbA1c, obesity indices and other diabetic complications such as microangiopathies [(3)]. Cardiovascular diseases has been singled out as a major cause of death in patients with DM as diabetes increases the risk of developing heart disease by several folds. Heart involvement in diabetes goes beyond the damage to coronary arteries due to the progress of atherosclerotic process. Diabetes and its pathophysiological consequences are able to induce direct alterations and abnormalities in the cardiac muscle functions [(4)].

Diabetes may affect the heart in three ways: (a) coronary artery disease due to accelerated atherosclerosis; (b) cardiac autonomic neuropathy; and (c) diabetic cardiomyopathy. Several studies have suggested that diabetes may be associated with left ventricular (LV) structural and functional abnormalities in addition to, and independent of atherosclerosis [(5)].

Echocardiography plays a central role in the evaluation of diastolic function and conventional pulsed-wave (PW) Doppler is usually performed to obtain mitral inflow velocities to assess left ventricular filling. Doppler pattern of impaired left ventricular relaxation, characterized by decreased early and increased late diastolic flow, which is an early sign of diastolic dysfunction [(6)].

Compared with epidemiological studies on cardiovascular disease (CVD), less attention is given

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for examining whether disparities in CVD risk management create gender differences among an already high-risk population like those with diabetes. Although differences exist between men and women with T2DM regarding CVD occurrence, gender differences in composite control of cardiovascular risk factors are less understood [7].

AIM OF THE WORK

To assess gender differences of left ventricular diastolic function by pulsed and tissue Doppler echocardiographic indices in patients with type II diabetes mellitus.

PATIENTS AND METHODS

This study was conducted in the Cardiology Department Faculty of Medicine, Azhar University El Hussein. It was an observational case control study started from January 2017 to March 2019. Patients with type 2 DM were age and sex matched with healthy volunteers as control. **The study was approved by the Ethics Board of Al-Azhar University and an informed written consent was taken from each participant in the study.**

The study included 300 patients (159 (53%)) % males and (141 (47%)) % females) with type II Diabetes Mellitus, in addition to 150 (75 (50%)) % males and (75 (50%)) % females) age and gender matched healthy volunteers as control. So the study enrolled 450 subjects, (300 (66.7%) %) patients and (150 (33.3%) %) control.

All subjects in study and control groups were subjected to the following:

A) History:

- Demographic data.
- Diabetes mellitus.
- Hypertension
- Family history of premature coronary artery disease (CAD)
- Symptoms suggestive of cardiac disease and current medications.

B) Full clinical examination including: Detailed general and local examinations were done for assessment of blood pressure, Heart rate and signs of valvular or myocardial disease.

C) Laboratory assessment:

Including fasting blood sugar and HbA1c with diagnosis of DM according to ADA 2015.

D) 12-lead surface Electrocardiogram:

Standard 12 leads ECG were done to exclude evidence of (1) LVH, (2) Ischemic heart disease and (3) tachyarrythmias e.g. AF.

E) Transthoracic echocardiography:

All patients underwent TTE using commercially available echocardiography systems equipped with frequency range 2-4MHz multifrequency phased array transducer (PHILIPS Affiniti 50C Japan) and has tissue Doppler facility. All patients were ECG connected. Detection of any cardiac abnormality listed in exclusion criteria and the following indices of cardiac function were evaluated.

Transthoracic echocardiogram: (Lang *et al.* [8]).

1. Routine 2-dimensional echocardiography was performed.
2. Images were obtained at rest with the patient in the left lateral decubitus position parasternal long axis view (PSLAV).
3. Systolic LV function assessment and estimation of ejection fraction were done by M-mode.
4. Left atrial dimensions only not volume were measured.
5. Assessment of LV wall motion contractility to exclude any significant wall motion abnormality.
6. Assessment of mitral flow by pulsed-wave Doppler with measurements of E and A wave amplitude, E/ A ratio and E wave deceleration time (DT).
7. Tissue Doppler of septal and lateral mitral annulus with measurements of E´ and E/ E´ ratio.

Left ventricular systolic function: As shown in figure (12), left ventricular end diastolic dimension (EDD), end systolic diameter (ESD) and Ejection fraction (EF), were obtained in the short axis-papillary level view using M mode and the leading edge methodology [8].

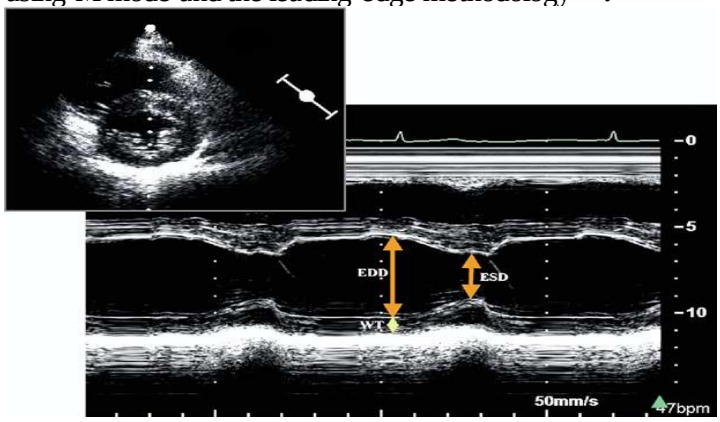

Figure (1): Measurement of left ventricular end-diastolic diameter (EDD) and end-systolic diameter (ESD) from M-mode, guided by parasternal short-axis image (upper left) to optimize medial-lateral beam orientation [8].

Left ventricular diastolic function:

Pulsed-wave Doppler measurements were obtained in the apical four chamber view. The Doppler beam has been aligned perpendicular to the plane of the mitral annulus and a 5 mm pulsed wave Doppler sample volume was placed between the tips of the mitral leaflets during diastole. The following variables have been calculated: maximum velocity of early mitral filling (E), maximum velocity of late mitral filling (A), ratio of early to late velocity (E/A), and deceleration time (DT).

Diastolic dysfunction was graded into: [6]

- Impaired relaxation (grade I): **E/A**<0.8, **DT**>200ms.
- Pseudonormal filling (grade II): **E/A** 0.8-1.5, **DT** 160-200ms.

- Restrictive filling (grade III): **E/A**>2.0, **DT**<160ms.

F) Tissue Doppler imaging (TDI)

Tissue Doppler imaging was used to measure myocardial tissue velocities and times. These velocities have been obtained with the (M4S) transducer in the apical four and the sampling volume at the lateral and septal mitral annular regions; and the peak velocity of early diastolic mitral inflow in lateral and septal regions.

- Diastolic function was calculated by measuring:

- Average of E` (E prime) of lateral and septal of mitral annulus.
- Average of E (e) of lateral and septal of mitral annulus.
- Ea/Aa ratio.

- E/E` ratio(E/e` prime); where E is the early diastolic velocity of the mitral valve inflow obtained by Echo-Doppler & E` is the average velocity of lateral and septal parts of the mitral annulus obtained by Tissue-Doppler**.**

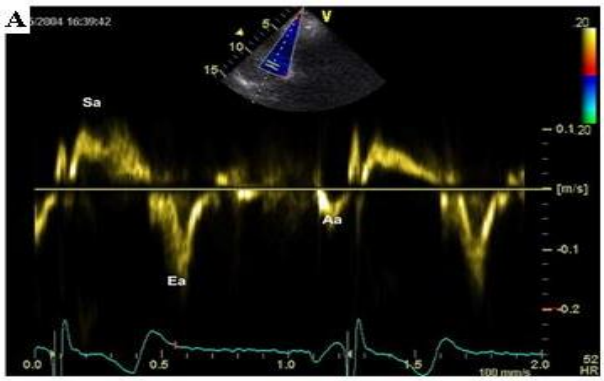

Figure (2): Illustration of Pulsed Wave-TDI and Color-TDI with quantitative analysis of the septal motion recorded in a healthy patient. Ea: peak early diastolic velocity at the septal mitral annulus. Aa: peak late diastolic velocity at the septal mitral annulus. Sa: peak systolic velocity at the septal mitral annulus [8]**.**

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 25.0 for windows (SPSS Inc., Chicago, IL, USA).

Quantitative data were expressed as mean ± standard deviation (SD). Median and range (minimum – maximum) were also calculated for quantitative data. Qualitative data were expressed as frequency and percentage.

The following tests were done:

- Mann Whitney U test was used to compare differences between two independent groups when the dependent variable is continuous, but not normally distributed.
- Chi-square (X^2) test also called Pearson's chi-square test or the chi-square test of association, was used to discover if there is a relationship between two categorical variables.

• Probability (p-value): p-value ≤0.05 was considered significant, p-value ≤0.001 was considered as highly significant and p-value >0.05 was considered insignificant.

RESULTS

Study population:

This study was conducted in the Cardiology Department (Faculty of Medicine, Al-Azhar University hospitals), it was an observational case control study started from January 2017 to March 2019. Patients with type 2 DM were age and sex matched with healthy volunteers as control.

The study included 300 patients (159 (53%)) % male and (141 (47%)) % females) with type II Diabetes Mellitus, in addition to 150 (75 (50%)) % males and (75 (50%)) % females) age and gender matched healthy volunteers as control. So the study enrolled 450 subjects, (300 (66.7%) %) patients and (150 (33.3%) %) control.

Table (1) showed that the study group enrolled 300 (66.7%) diabetics, and 150 (33.3%) controls. The mean age of all patients was 34.8 ± 4.9 years. While the duration of DM (years) = 4.1 ± 1.8 years For diabetics only (N = 300).

Table (1): Baseline demographic data of age of the whole study population.

Demographic data	**All patients**
Count (%)	450 (100%)
Age (years)	
Mean ± SD	34.8 ± 4.9
Median (Range)	35 (20 – 47)
Gender	
Male	234 (52%)
Female	216 (48%)
Study group	
Diabetics	300 (66.7%)
Controls	150 (33.3%)
Duration of DM (years)	**For diabetics only (n=300)**
Mean ± SD	4.1 ± 1.8
Median (Range)	4 (1 – 14)

The median (range) of age (years) of diabetic males was 37 (23 – 43), while the median (range) of age (years) of diabetic females was 34 (20 – 40). The median (range) of DM duration (years) of diabetic males 4 (1 – 14), while the median (range) of DM duration (years) of diabetic females 4 (1 – 10).

Table (2) showed that there is a statistically non-significant difference between diabetic males and diabetic females as regard age (years), DM duration (years) (P=0.051), (P=0.122) respectively.

Table (2): Comparison between diabetic males and diabetic females regarding the Age (years) and DM duration (years) demographic data.

Demographic data	Diabetic males	Diabetic females	Test	P-value (Sig.)
Count	159	141		
Age (years)				
Median (Range)	37 (23 – 43)	34 (20 – 40)	1.950 •	0.051 (NS)
DM duration (years)				
Median (Range)	4 (1 – 14)	4 (1 – 10)	1.546 •	0.122 (NS)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (3) showed that there was a statistically non-significant difference between diabetic males concerning HbA_1C (%), 7.8 (5.1 – 13.2) and creatinine (mg/dL) 1.16 (0.6 – 1.53) compared to diabetic females HbA_1C (%) 7.8 (5.1 – 12.2) and creatinine (mg/dL) 1.2 (0.6 – 1.6) (P=0.280), (P=0.945) respectively. However, there was a statistically high significant difference between diabetic males regarding Hb (gm/dL), 13.9 (10.3 – 16.6) and hematocrit (%), 45 (29 – 52) compared to diabetic females Hb (gm/dL), 13 (9.9 – 15.6) and hematocrit (%), 41 (27 – 49) p (<0.001).

Table (3): Comparison between diabetic males and diabetic females regarding the laboratory data.

Laboratory data	Diabetic males	Diabetic females	Test	P-value (Sig.)
Count	159	141		
HbA_1C (%)				
Median (Range)	7.8 (5.1 – 13.2)	7.8 (5.1 – 12.2)	1.081•	0.280(NS)
Creatinine (mg/dL)				
Median (Range)	1.16 (0.6 – 1.53)	1.2 (0.6 – 1.6)	0.070•	0.945(NS)
Hb (gm/dL)				
Median (Range)	13.9 (10.3 – 16.6)	13 (9.9 – 15.6)	4.844•	<0.001 (HS)
Hematocrit (%)				
Median (Range)	45 (29 – 52)	41 (27 – 49)	4.893•	<0.001 (HS)

• Mann Whitney U test . p< 0.05 is significant. Sig.: significance.

Table (4) showed a statistically significant difference between diabetic males 8.2 (3.8 – 34.5) compared to diabetic females 9.8 (3.8 – 36.5) regarding E/e' septal (P=0.033).

Table (4): Comparison between diabetic males and diabetic females regarding the E/e' septal echocardiographic data.

Echocardiographic data	Diabetic males	Diabetic females	Test	P-value (Sig.)
Count	159	141		
E velocity (cm/s)				
Median (Range)	72.8 (36.4 – 127)	78.6 (44.6 – 169)	-2.767 •	0.006 (S)
A velocity (cm/s)				
Median (Range)	59.2 (28.1 – 104)	65 (29.1 – 133)	-1.847 •	0.065 (NS)
E/A				
Median (Range)	1.3 (0.6 – 3.1)	1.3 (0.5 – 3.0)	0.082 •	0.935 (NS)
e' septal velocity (cm/s)				
Median (Range)	8.7 (2.6 – 18.0)	7.7 (3.2 – 18.8)	1.069 •	0.285 (NS)
E/e' septal				
Median (Range)	8.2 (3.8 – 34.5)	9.8 (3.8 – 36.5)	-2.128 •	0.033 (S)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (5) showed that median of LVEDD (cm) of diabetic males 4.7 (3.1 – 7.5), while median LVEDD (cm) of control males was 4.7 (4.2 – 5.0). Median of LVESD (cm) of diabetic males was 3.3 (2.0 – 6.2), while median LVESD (cm) of control males 3.3 (2.5 – 3.9). The table showed a statistically non-significant difference between diabetic males compared to control males regarding LVEDD (cm) and LVESD (cm) [P=0.286 and P=0.0060] respectively.

Table (5): Comparison between diabetic males and control males regarding the LVEDD (cm) and LVESD (cm), echocardiographic data.

Echocardiographic data	Diabetic males	Control males	Test	P-value (Sig.)
Count	159	75		
LVEDD (cm)				
Median (Range)	4.7 (3.1 – 7.5)	4.7 (4.2 – 5.0)	1.067 •	0.286 (NS)
LVESD (cm)				
Median (Range)	3.3 (2.0 – 6.2)	3.3 (2.5 – 3.9)	1.883 •	0.060 (NS)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (6) showed a statistically high significant difference between diabetic males 72.8 (36.4 – 127) and 59.2 (28.1 – 104) compared to control males110.4 (78 – 130.7) and 86.5 (65.4 – 112) regarding E velocity (cm/s) and A velocity (cm/s) (P <0.001).

Table (6): Comparison between diabetic males and control males regarding the E velocity (cm/s) and A velocity (cm/s) echocardiographic data

Echocardiographic data	Diabetic males	Control males	Test	P-value (Sig.)
Count	159	75		
E velocity (cm/s)				
Median (Range)	72.8 (36.4 – 127)	110.4 (78 – 130.7)	-10.482 •	<0.001 (HS)
A velocity (cm/s)				
Median (Range)	59.2 (28.1 – 104)	86.5 (65.4 – 112)	-9.253 •	<0.001 (HS)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (7) showed a statistically high significant difference between diabetic males 8.7 (2.6 – 18.0) and 9.8 (4.0 – 23.9) compared to control males18 (110.9 – 24.5) and 18.9 (13.5 – 23.2) concerning e' septal velocity (cm/s) and e' lateral velocity (cm/s) (P<0.001).

Table (7): Comparison between diabetic males and control males regarding the e' septal velocity (cm/s) and e' lateral velocity (cm/s) echocardiographic data

Echocardiographic data	Diabetic males	Control males	Test	P-value (Sig.)
Count	159	75		
e' septal velocity (cm/s)				
Median (Range)	8.7 (2.6 – 18.0)	18 (110.9 – 24.5)	-11.946 •	<0.001 (HS)
e' lateral velocity (cm/s)				
Median (Range)	9.8 (4.0 – 23.9)	18.9 (13.5 – 23.2)	-10.821 •	<0.001 (HS)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (8) showed a statistically high significant difference between diabetic males 8.2 (3.8 – 34.5) and 7.1 (3 – 26.5) in comparison with control males 5.9 (4.1 – 7.9), 5.8 (3.1 – 7.1) as regard E/e' septal and E/e' lateral (P<0.001).

Table (8): Comparison between diabetic males and control males regarding the E/e' septal and E/e' lateral echocardiographic data

Echocardiographic data	Diabetic males	Control males	Test	P-value (Sig.)
Count	159	75		
E/e' septal				
Median (Range)	8.2 (3.8 – 34.5)	5.9 (4.1 – 7.9)	8.417 •	<0.001 (HS)
E/e' lateral				
Median (Range)	7.1 (3 – 26.5)	5.8 (3.1 – 7.1)	5.290 •	<0.001 (HS)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (9) showed that median of age (years) of diabetic females was 34 (20 – 40), While median of age (years) of control females was 35 (23 – 47). Median (Range) of DM duration (years) of diabetic females 4 (1 – 10).

Table (9): Comparison between diabetic females and control females regarding age (years) and DM duration (years) demographic data

Demographic data	Diabetic females	Control females	Test	P-value (Sig.)
Count	141	75		
Age (years)				
Median (Range)	34 (20 – 40)	35 (23 – 47)	-0.078 •	0.938 (NS)
DM duration (years)				
Median (Range)	4 (1 – 10)	-	-	-

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Regarding E velocity (cm/s), A velocity (cm/s), table (10) showed a statistically highly significant difference between diabetic females [78.6 (44.6 – 169) and 65 (29.1 – 133)] compared to control females105 [(85.5 – 130.7) and 88 (65.5 – 113)] as (P<0.001). While the difference between diabetic females 1.3 (0.5 – 3.0 and control females 1.2 (1.1 – 1.4) as regard E/A was highly significant (P=0.001).

Table (10): Comparison between diabetic females and control females regarding the E velocity (cm/s), A velocity (cm/s) and E/A echocardiographic data

Echocardiographic data	Diabetic females	Control females	Test	P-value (Sig.)
Count	141	75		
E velocity (cm/s)				
Median (Range)	78.6 (44.6 – 169)	105 (85.5 – 130.7)	-8.506 •	<0.001 (HS)
A velocity (cm/s)				
Median (Range)	65 (29.1 – 133)	88 (65.5 – 113)	-8.690 •	<0.001 (HS)
E/A				
Median (Range)	1.3 (0.5 – 3.0)	1.2 (1.1 – 1.4)	3.392 •	0.001 (S)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (11) showed a statistically highly significant difference between diabetic females and control females as regard e' septal velocity (cm/s), E/e' septal, e' lateral velocity (cm/s) and E/e' lateral (P<0.001).

Table (11): Comparison between diabetic females and control females regarding the e' septal velocity (cm/s), E/e' septal, e' lateral velocity (cm/s), E/e' lateral echocardiographic data

Echocardiographic data	Diabetic females	Control females	Test	P-value (Sig.)
Count	141	75		
e' septal velocity (cm/s)				
Median (Range)	7.7 (3.2 – 18.8)	19.6 (13 – 23)	11.885 •	<0.001 (HS)
E/e' septal				
Median (Range)	9.8 (3.8 – 36.5)	5.5 (4.3 – 7.9)	8.994 •	<0.001 (HS)
e' lateral velocity (cm/s)				
Median (Range)	9.9 (4.1 – 19.9)	18 (13.5 – 23.4)	11.198 •	<0.001 (HS)
E/e' lateral				
Median (Range)	7.9 (3.6 – 28.1)	5.8 (4.0 – 7.9)	5.996 •	<0.001 (HS)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

Table (12) showed a statistically highly significant difference between diabetic females and control females as regard e' septal velocity (cm/s), E/e' septal, e' lateral velocity (cm/s) and E/e' lateral (P<0.001).

Table (12): Comparison between diabetic females and control females regarding the e' septal velocity (cm/s), E/e' septal, e' lateral velocity (cm/s), E/e' lateral echocardiographic data

Echocardiographic data	Diabetic females	Control females	Test	P-value (Sig.)
Count	141	75		
e' septal velocity (cm/s)				
Median (Range)	7.7 (3.2 – 18.8)	19.6 (13 – 23)	11.885 •	<0.001 (HS)
E/e' septal				
Median (Range)	9.8 (3.8 – 36.5)	5.5 (4.3 – 7.9)	8.994 •	<0.001 (HS)
e' lateral velocity (cm/s)				
Median (Range)	9.9 (4.1 – 19.9)	18 (13.5 – 23.4)	11.198 •	<0.001 (HS)
E/e' lateral				
Median (Range)	7.9 (3.6 – 28.1)	5.8 (4.0 – 7.9)	5.996 •	<0.001 (HS)

• Mann Whitney U test. p< 0.05 is significant. Sig.: significance.

DISCUSSION

This study aimed at assessing gender differences of left ventricular diastolic function by pulsed and tissue Doppler echocardiographic indices in patients with type II diabetes mellitus. Comparison between the 2 groups was done regarding patient demographics, history, clinical presentation and echocardiography parameters.

In our study, there was no statistically significant difference between the two groups as regarding **age** and **sex** (p value 0.225, 0.548 respectively). As regarding age, this is similar to **Mitrovska *et al.* [9],** who studied the role of TDI in the early detection of diastolic dysfunction in asymptomatic diabetic patients. They found that there was no statistically significant difference between patients and control group (40 ± 6.56 years vs. 43 ± 7.5 years, p >0.05: respectively). In contrast, **Leung *et al.* [10]** studied left ventricular diastolic reserve in patients with type 2 diabetes mellitus and found that patients with diabetes mellitus were older than control group (54 ± 10 years vs. 50 ± 12 years, respectively; p =0.005: respectively).

As regarding sex, **Akçay *et al.* [11],** studied assessment of the left ventricular function in normotensive pre-diabetics. They found that the sex ratio was similar between diabetic patients and normal persons (p =0.270).

When comparing diabetic group with control one in our study, there was statistically significant difference between them as regarding, **HbA1C, serum creatinine** and **hematocrit value** with p value < 0.001. These results are consistent with **Parving *et al.* [12],** as regarding serum creatinine but not for HbA1C and hematocrit, they analyzed serum urea and serum creatinine level in type 2 diabetic patients. They observed an increase in levels of serum urea and serum creatinine in type 2 diabetic patients when compared with healthy controls**.**

In our study, when we compared between the two groups as regarding echocardiographic parameters, we founded that there was highly statistically significant difference as regarding EF, LA dimensions, E velocity, A velocity, E/A and E/e' septal and lateral with p value less than 0.001for the all parameters. There was no statistically significant difference as regarding LVEDD and LVESD between the two groups with p value 0.792 and 0.836 respectively. According to **Parving *et al.* [12],** who studied diastolic dysfunction in asymptomatic diabetic versus non-diabetic population. They found that left ventricular ejection fraction was significantly reduced in diabetic group, compared to non-diabetic group. In contrast, **Akçay *et al.* [11]** found that there was no significant difference between case and control groups regarding LVEF.

Similar to our study, **Jani *et al.* [13],** showed significant difference of the Doppler parameter of diastolic function between the patients with type 2 diabetes and the control group. The acquired results pointed out that in patients with type 2 diabetes there was a pathological transmitral flow-velocity profile, or, a characteristic model of delayed (late) relaxation, reduced speed of transmitral flow in the phase of early ventricular filling (E-wave), decreased E/A relation <1.0 and prolongation of the isovolumetric relaxation time (>100mil/s).

As regarding gender, there was no statistically significant difference as regarding age and duration of diabetes when comparing diabetic males and females with each other with p valves 0.051 and 0.122 respectively. As regards duration of diabetes, there are several studies similar to ours, **Jani *et al.* [13]** did not prove an influence of the duration of type 2 diabetes in the distribution of the subclinical left ventricular diastolic dysfunction, nor in the structural and functional changes of the myocardium at the patient with type 2 diabetes.

Our study showed that there was no statistically significant difference between diabetic males and diabetic females as regard LA dimensions, E/é lateral, e' lateral, E/A ratio and A velocity. However, it was significant for E/e' septal, E velocity, EF, LVEDD and LVESD with p values 0.033, 0.006, 0.001,0.007, 0.001 respectively. In the **Fang study**, the influence of sex in the distribution of subclinical left ventricular diastolic dysfunction at the ones with type 2 diabetes was not proven **[14].** In addition, a study by **Suys *et al.* [15]** stated that the changes in the diastolic function and dimension of the left ventricle at women with type 2 diabetes were more significant. They stated that increased early and late filling velocities compensate for the smaller mitral annular size (reflecting smaller body size) in women. A multicenter EACVI Euro-Filling study, reported that female gender is independently associated with higher peak E velocity, which was similar to our results in control group (females 15.88 cm/s and males 15.35 cm/s) but not as E/A ratio where transmitral flow velocity ratios were similar between men and women **[16].**

In a study by **Otsuka *et al.* [17],** it was conducted on 467 male and 455 female healthy subjects, the aim was to determine the normative Doppler values and gender differences in left ventricular (LV) diastolic function in healthy subjects at each decade of life. The tissue Doppler method showed significantly lower early diastole velocity of the mitral annulus (E) in females especially females older than 50 years than in males (10.7 ± 3.7 versus 11.2 ± 3.7 cm/s, p < 0.025). They concluded that there were gender differences in Doppler indices of LV diastolic function in healthy subjects and in clinical settings, assessment of LV diastolic function should take into account patient

gender. **Ha *et al.*** [18] found that women have higher peak E and A velocities than men, but both men and women have similar E/A ratios.

In our study, when we compared between diabetic males and control males, we founded that there was significant correlation in-between regarding all laboratory data, HbA1c, creatinine, Hb and hematocrit value with p value less than 0.001. In addition, for female diabetics and control, it was significant for all laboratory parameters except for hematocrit value. Our results are consistent with **Ishimura et al.** [19] where they stated that poor glycemic control is an independent predictor of poor prognosis in diabetic hemodialysis patients. HbA1C is a clinically useful parameter for identifying the risk for mortality, both for cardiovascular and non-cardiovascular mortality and for careful management of glycemic control**.**

Berria *et al.* [20] stated that after 4 months of diabetes, both the Hb and Hct fell significantly in the diabetic group. In treated diabetic patients, platelet count fell from 21279 to 19778 10^3 /mm^3 (P0.02) and white blood cell (WBC) count decreased from 6.870.2 to 6.070.2 10^3 /mm^3 (P0.0001). In the control group, there were no significant changes in Hct, Hb, WBC, or platelet count.

In our study we founded that there was significant correlation between all echocardiographic parameters (FS (%), EF (%), LA dimension (cm), E velocity (cm/s), A velocity (cm/s), E/A, e' septal velocity (cm/s), E/e' septal, e' lateral velocity (cm/s) and E/e' lateral) when comparing diabetic males to control males Significant increase. The same results also when comparing diabetic females to control females Significant decrease except for LA dimensions, which was insignificant.

Gurdal *et al.* [21] agreed with us as their study aimed to assess Doppler-derived annular and myocardial tissue velocities in healthy subjects as well as in patients with T2 DM, and to determine the role of LV length as a possible mechanistic explanation for discrepancies between genders. **Form *et al.*** [22]**,** have reported before that e′ was significantly lower in diabetic patients without hypertension than in normal subjects**.**

CONCLUSION

Study showed that there are statistically significant differences of left ventricular diastolic function by pulsed-wave and tissue Doppler echocardiographic indices according to E/E` septal and lateral in patients with type II diabetes mellitus in comparison to non-diabetics.

There are insignificant statistical differences in diastolic functions between diabetic males and females. This study might provide important view about differences in left ventricular diastolic dysfunction in diabetic patients free from hypertension and ischemic heart disease.

RECOMMENDATIONS

1- Diabetic patients should be evaluated for subclinical diastolic dysfunction by Doppler studies as well as good control of diabetes for deceleration of the development of clinical cardiomyopathy, and decreased morbidity and mortality.

2- It is suggested that all patients of NIDDM should be routinely and repeatedly subjected to 2-D colour Doppler echocardiographic assessment of cardiac functions in the long-term management of this metabolic disease. This has important therapeutic implications and helps physicians planning early intervention strategies.

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