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ECHOCARDIOGRAPHIC EVALUATION OF LV DIASTOLIC DYSFUNCTION IN ASYMPTOMATIC TYPE 2 DIABETES MELLITUS PATIENTS WITH NORMAL LVEF.

General Medicine

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ABSTRACT

Introduction: Diabetes mellitus is one of the most common disease in the world and is acquiring epidemic proportions. India is the Diabetic capital of the world. Indians are genetically more susceptible to diabetes compared to other races. Cardiovascular complications are known to be the main cause of morbidity and death in diabetic patients. Left ventricular diastolic dysfunction in diabetic patients is very common and represents an early stage of heart failure without any clinical manifestations before systolic dysfunction. The incidence of heart failure in diabetic subjects is high even in the absence of hypertension and coronary artery disease. In the view of these above facts the present study was done to assess the diastolic dysfunction in asymptomatic diabetic patients.

Aims: The aim of this study was to detect the incidence of LV diastolic dysfunction in asymptomatic Diabetic subjects and its relation to various parameters

Settings and Design: This was an observational & descriptive study conducted at the teaching hospital during a one year period.

Materials and Methods: This study included 165 asymptomatic patients with type 2 diabetes mellitus, without evidence of cardiovascular involvement and blood pressure less than 130/80 mmHg. LVDD was evaluated by Doppler Echocardiography, which included PWD MV - E/A ratio, DT, IVRT, Average E/e' ratio, TDI MV septal diastolic e' Velocity & Indexed left atrial volume . LVDD was assessed in relation with age, sex, duration of diabetes, Fasting, PP BSL level, HbA1c level, obesity, Lipid profile, urine microalbuminurea & LV mass.

Results: Results showed that out of 165 studied patients LV diastolic dysfunction was present in 122 (73.9 %) patients. Among Males & females patients diastolic dysfunction was present in 84 cases (86.6%) & 65cases (95.6%) respectively with more prevalence in females. Increased prevalence of LV Diastolic dysfunction was associated with increase in age, duration of diabetes, uncontrolled diabetes as assessed by HbA1c levels, Obesity, dyslipidemia, Microalbuminurea, increased LA Volume & LV mass.

Conclusions: Present study reveals high incidence of diastolic dysfunction in asymptomatic Diabetic subjects and this finding was correlated with the age, sex, duration of diabetes, HbA1c Levels, obesity, Lipid profile, urinary microalbuminurea, and LA Size & LV mass. The findings in our Study indicate that early myocardial damage in patients with diabetes mellitus affects left ventricular diastolic function before systolic function. Combination of Conventional Doppler & Tissue Doppler echocardiography parameters is a simple, noninvasive, cheap, easily available and a valuable tool in diagnosing diastolic dysfunction. In diabetics before they develop cardiac symptoms, echocardiography should be done routinely on every diabetic patients to assess the cardiac function.

KEYWORDS

Left Ventricular Diastolic Dysfunction, Diabetes Mellitus, Echocardiography.

INTRODUCTION

Diabetes mellitus is one of the most common diseases in the world and is acquiring epidemic proportions. Its prevalence is increasing in both developed and developing countries. India is known as "Diabetes capital of the world"[1]. The so called "Asian Indian Phenotype" refers to certain unique clinical and biochemical abnormalities in Indians which include increased insulin resistance, greater abdominal adiposity i.e., higher waist circumference despite lower body mass index, lower adiponectin and higher high sensitive C-reactive protein levels. This phenotype makes Asian Indians more prone to diabetes and premature coronary artery disease. At least a part of this is due to genetic factors. 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. Diastolic heart failure (HF) is also referred to as HF with preserved left ventricular systolic function (HFNEF). Studies have reported a high prevalence of pre-clinical diastolic dysfunction among subjects with DM [2]. The evidence indicates that myocardial damage in diabetic subjects affects diastolic function before the systolic function. [3].

Diabetic cardiomyopathy has been proposed as an independent cardiovascular disease and many mechanisms for diabetic cardiomyopathy have been proposed including small and microvascular disease, autonomic dysfunction, metabolic derangements, interstitial fibrosis and the development of fibrosis, possibly caused by the accumulation of a periodic acid- Schiff-positive glycoprotein, leading to myocardial hypertrophy and diastolic dysfunction.[4,13] However the exact etio-pathogenesis of diabetic cardiomyopathy still remains unclear. The objective of our study was to Grade & to determine the prevalence of LV diastolic dysfunction in asymptomatic type 2DM subjects and its correlation to age, Sex, duration of DM, F & PP BSL, HbA1c, obesity, Lipid profile, Urine Microalbuminurea, LA volume & LV mass.

The objectives of our study:

The objective of our study was to Grade & to determine the prevalence of LV diastolic dysfunction in asymptomatic type 2DM subjects and its correlation to age, Sex, duration of DM, F & PP BSL, HbA1c, obesity, Lipid profile, Urine Microalbuminurea, LA volume & LV mass.

MATERIALS AND METHODS

For the study, we hypothesized that the diastolic dysfunction, [as assessed by the mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (e') i.e. (E/e') ratio], worsens with age, duration of DM, HbA1c, Lipid profile, Urine microalbuminurea and obesity indices. A total of 165 subjects with type 2 DM with no clinical evidence of hypertension & cardiac disease were studied. This observational study was designed to determine the prevalence of asymptomatic left ventricular diastolic dysfunction in type 2 DM subjects and its relation to subjects age, sex, duration of DM, control of diabetes as determined by HbA1c levels, Lipid profile, Urine microalbuminurea and obesity indices. This study was conducted at the Prakash Institute of Medical Sciences, Urun - Islampur, over a period of one year period from January 2018 to December 2018. This study was approved by the ethical committee of Prakash Institute of Medical Sciences Urun -Islampur.

Inclusion criteria for study:

All type 2 DM patients with normal left ventricular systolic function (LVEF: ≥ 50%).

Exclusion criteria for study:

- Patients with evidence of coronary artery disease, valvular heart disease, heart failure, hypertension, renal failure, thyroid disease, left ventricular hypertrophy on echocardiography.
- Patients with poor transthoracic echo window.

Methodology for study:
Detailed medical history was taken from each eligible subject and they underwent general physical examination and biochemical investigations. After a 12-hour fast, a venous blood sample was collected. Informed consent was obtained from the subjects.
The following investigations were done:

- Blood glucose on admission: FBS, PPBS, Glycosylated hemoglobin (HbA1c).
- Fasting Lipid profile, Renal function tests.
- Urine routine, microscopy, Albumin & Micral Test,
- ECG, Echocardiography was done under standard protocol
- Detail anthropometric evaluation including height (meter), hip circumference in centimeter (HC), waist circumference in centimeter (WC) and weight in kilogram was measured, Body Mass Index (BMI) was calculated as: weight (kg) ÷ [height (m)]².

Echocardiography:
All transthoracic echocardiographic examinations were obtained using GE Vivid T8 ultrasound machine with 4 MHz probe and performed according to the recommendations of American Society of Echocardiography (ASE) [10]. Subjects were examined using standard parasternal long axis, short axis and apical two and four chambers views. Conventional techniques (two-dimensional-2D, M-mode echocardiography, Mitral pulsed wave Doppler (MV-PWD) and Tissue Doppler Imaging (MD TDI) were performed to minimize the errors in assessing the diastolic dysfunction. Echocardiography was performed by harmonic imaging mode. Pulsed-wave Doppler (PWD) - derived transmitral inflow velocities were obtained in the apical 4-chamber view, with the sample volume placed at the mitral valve leaflet tips. [5,6,10]. Measurements included the transmitral early diastolic rapid filling (E-wave) and atrial contraction late filling (A-wave) velocities to calculate E/A ratio, isovolumteric relaxation time (IVRT) and deceleration time (DT). For tissue Doppler imaging, the mitral annulus diastolic e' Velocity was obtained with a 2 mm sample volume placed at the septal and lateral side of the mitral annulus. Diastolic dysfunction was labeled according to the standard ASE guidelines .Diastolic function was classified into 4 groups: 1-Normal (E/A=0.7-1.3, DT=140-240 ms, IVRT=76±13 ms), 2-Mild LVDD / Gr-I (E/A <1, DT>240 ms, IVRT>90 ms), 3- Moderate LVDD / Gr-II (E/A=1.0-1.5, DT=160-240 ms, IVRT=76 ±13 ms), 4-Severe LVDD / Gr - III (E/A>2, DT< 160 ms, IVRT<60 ms). Left ventricular overall ejection fraction (systolic function) was calculated by modified Simpson's method; and LVEF ≥ 50% was considered as normal. All echocardiographic measurements were averaged over three consecutive cardiac cycles, measured by a single investigator blinded to all other variables.

Diagnostic criteria:

- Dyslipidemia: was defined if TC ≥ 200 mg/dl; LDL cholesterol ≥ 130 mg/dl; HDL cholesterol <40 mg/ dl; and, TG ≥ 150 mg/dl.[7]
- Obesity indices: Cut-off for high Body Mass Index (BMI) was ≥ 25 for females and ≥ 27 for males. Cut-off for high waist to hip ratio (WHR) was ≥ 0.9 for males, and ≥ 0.8 for females. Cut-off for high WC was
- > 85 cm for females and > 90 cm for males. [8].
- Diabetes Mellitus (DM) [9] According to ADA 2017 Guidelines: Fasting blood sugar (FBS) ≥ 126 mg/dL (7.0 mmol/L) or PP BSL / 2-h blood sugar ≥ 200 mg/dL (11.1 mmol/L). or HbA1c ≥ 6.5% or Classic diabetes symptoms + random plasma glucose ≥ 200 mg/dL (11.1 mmol/L)
- Definition Of diastolic dysfunction: LV diastolic dysfunction is considered to be present if any 3 or more criteria of the following findings are seen:[5,6,10,11]
- E/A ratio < 0.8 or > 1.5
- DT < 140 or > 240 ms,
- IVRT <70 or > 100 ms,
- E/e' ratio > 10
- TDI Septal e Vel. <7 cm/sec ,
- LA volume index >34 ml/m

Statistical analysis
Data was summarized to mean, percentage, standard deviation. Further chi square test & t test was carried out by using SPSS-200 (Statistical Package for the Social Sciences) for Windows (SPSS, Chicago, IL). '*P*' value < 0.05 was considered statistically significant.

RESULTS:
In present study total 165 subjects with asymptomatic type-2 diabetes mellitus were studied. Out of 165 subjects Age wise distribution of Minimum, Maximum & Mean age was 25, 84 & 57.115 Years with Std. deviation of 11.40037 respectively. Results showed that out of 165 studied patients diastolic dysfunction was present in 122 (73.9 %) patients. [Table 1]

Table 1: Comparison of diastolic dysfunction with other studies

Studies	Percentage
Shrestha NR [3]	71
Poirier et al [14]	60
Suresh Chandravanshi [15]	70
Bajraktari [18]	68.8
Patil VC [19]	54
Present study	73.9

Baseline demographic, anthropometric & biochemical indices of study participants without & with LV diastolic dysfunction with mean & standard deviation with't' Test &' p' values were obtained. (N=165) [Table 2].

Parameter	LV Diast. Dysfunction. Absent		LV Diast. Dysfunction. Present		't 'Value	'p' Value	Significance
	n = 16		n = 149				
	Mean	Std Devi.	Mean	Std Devi.			
Age	48.93	± 10.0	57.99	±11.21	-3.097	0.002	S
BMI	23.96	±3.90	24.47	±4.80	-0.412	0.681	NS
WHR	0.953	±0.0702	0.959	±0.086	-0.243	0.808	NS
DM Dur.	1.88	±2.66	6.37	±5.91	-3.003	0.003	S
HBA1C	8.23	±1.95	8.46	±1.68	-0.517	0.606	NS
FBSL	126.81	±33.64	123.7	±38.60	-0.309	0.757	NS
PPBSL	222.125	±61.44	199.44	±65.21	-1.329	0.186	NS
Tot. Chol.	190.5	±15.38	192.28	±13.56	-0.495	0.621	NS
Trigl	183.43	±86.83	144.87	±26.15	4.043	0.000	S
HDL	43.06	±4.58	43.52	±3.47	-0.488	0.626	NS
LDL	108.93	±15.07	119.12	±12.50	-3.033	0.003	S
VLDL	33.66	±9.87	29.12	±5.54	2.841	0.005	S
TC -HDL ratio	4.44	±0.631	4.41	±0.452	0.214	0.831	NS
HDL-LDL ratio	21.35	±75.10	2.77	±0.40	3.099	0.002	S

Relation of diastolic dysfunction with various dependent variables in type 2 diabetes mellitus subjects in the study (N=165) [Table 3].

Parameter		LVDD Absent n = 16	LVDD Present n = 149	Total	'T' Value	' p ' Value	Significance
1)Age	25-40	3 (27.3%)	8(72.7%)	11(100%)	7.132	0.028	S
	40-60	10(12.3%)	71(87.7%)	81(100%)			
	>60	3(4.1%)	70(95/9%)	73(100%)			
2)Sex	Male	13(13.4%)	84(86.6%)	97(100%)		0.938	
	Female	03(4.4%)	65(95.6%)	68(100%)		0.032	S
	Total	16(9.7%)	149(90.%)	165(100%)	3.690	0.055	S
3)HbA1c	<7.5	09(16.7%)	45(83.3%)	54(100%)	4.523	0.104	
	7.51 - 10	06(6.7%)	84(93.3%)	90(100%)			
	>10	1(4.8%)	20(95.2%)	21(100%)			
4)F BSL	Up to 110	05(11.9%)	37(88.1%)	42(100%)	0.905	0.636	NS
	110 - 150	10(9.9%)	91(90.1%)	101(10%)			
	>150	01(4.5%)	21(95.5%)	22(100%)			
5) P P BSL	Up to 140	0 (0%)	06(100%)	06(100%)	2.689	0.611	NS
	141 - 200	10(11.6%)	76(88.4%)	86(100%)			
	210-250	03(6.1%)	46(93.9%)	49(100%)			
	251-300	01(7.1%)	12(92.3%)	13(100%)			
	>300	2(18.2)	9(81.8)	11(100%)			
6)Duration of DM(Yrs)	<5	13 14.8%)	75(85.2%)	88(100%)	7.328	0.026	S
	5-10	03(9.1%)	30(90.9%)	33(100%)			
	>10	0(0%)	44(100%)	44(100%)			

Relation of diastolic dysfunction with various dependent variables in type 2 diabetes mellitus subjects in the study (N=165) [Table 4].

Parameter		LVDD Absent n = 16	LVDD Present n = 149	Total	't' Value	'p' Value	Significance
1)Obesity	Underweight (<18)	01(11.1%)	08(88.9%)	09(100%)	0.498	0.919	NS
	Normal (18-24)	07 (10.4%)	60(89.6%)	67(100%)			
	Overweight (24.1-29.99)	7(10.0%)	63(90%)	70(100%)			
	Obese (>30)	1(5.3%)	18(94.7%)	19(100%)			
2)WHR	Male (n-97)	13(13.4%)	84(86.6%)	97(100%)		0.938	NS
	Female (n-68)	03 (4.4%)	65(95.6%)	68(100%)		0.032	S
	Total	16(9.7%)	149(90.3%)	165(100%)	03.690	0.055	S
3)Microalbuminurea	Positive	07 (7.1%)	92(92.9%)	99(100%)	1.949	0.163	NS
	Negative	09(13.6%)	57(86.4%)	66(100%)			
4)Micral Test Value (50,100)	0-20	14 (13%)	94(87%)	108(100%)			
	50 & 100	02(3.5%)	55(96.5%)	57(100%)	8.308	0.051	S
5)Dyslipidemia	Absent	05(6.3%)	74(93.7%)	79(100%)			
	Present	11(12.8%)	75(87.2%)	86(100%)	1.963	0.161	NS
6) Total Cholesterol	Normal(<200)	13(11%)	105(89.0%)	118(100%)			
	Abnormal(>200)	03(6.4%)	44(93.6%)	47(100%)	1.963	0.364	NS
7)Triglyceride	Normal(<150)	06(6.3%)	89(93.7.0%)	95(100%)			
	Gr - I(151-200)	06(9.7%)	56(90.3%)	62(100%)			
	Abnormal(>200)	04(50.0%)	04(50.0%)	08(100%)	16.080	0.001	S
8)HDL	Best (>50)	05(23.8%)	16(76.2%)	21(100%)			
	Good(45-50)	08(10.8%)	66(89.2%)	74(100%)			
	Bad(<35-40)	00(00%)	08(100%)	08(100%)	7.411	0.060	S
	Very bad(<35)	03(4.8%)	59(95.2%)	62(100%)			
9)LDL	Best (<100)	06(42.9%)	08(57.1%)	14(100%)			
	Good(101-130)	09(07.1%)	118(92.9%)	127(100%)			
	Bad(> 130)	01(4.2%)	23(95.8%)	24(100%)	19.407	0.001	S

Relation of diastolic dysfunction with various dependent variables in type 2 diabetes subjects: N=165 [Table 2,3&4].

1) **Age -** Mean age without & with diastolic dysfunction was 48.93± 10.0 &57.99 ±11.21 respectively with **'p' Value 0.002.** Out of 11 subjects with age group 25-40 years 08 (72.7%) had diastolic dysfunction; and out of 81 subjects with age group 40-60 years 71 (87.7) had diastolic dysfunction and Out of 73 subjects with age group > 60 years 70 (95.9.7%) had diastolic dysfunction**.** Diastolic dysfunction was significantly high in patients with age > 40 years as compared to age < 40 years which is statistically significant**. (*'P'*= 0.028).**
2) **Sex -** Out of 97 Male subjects 84 (86.6%) had diastolic dysfunction and out of 68 Female subjects 65 (95.6%) subjects had diastolic dysfunction**.** Female subjects had more prevalence of diastolic dysfunction than male subjects**. (*'P'* = 0.055).**
3) **HbA1c -** Mean HbA1c without & with diastolic dysfunction was 8.23±1.95 &8.46 ±1.68 respectively with **'p' Value 0.606**. Out of 54 subjects with HbA1c < 7.5%, 42 (85.7%) had diastolic dysfunction and out of 86 subjects with HbA1c between 7.5 - 10%, 79 (91.9%) had diastolic dysfunction & out of 30 Subjects with HBA1c > 10% 28(90.3%) had diastolic dysfunction. Subjects with HBA1c > 7.5% had more prevalence of diastolic dysfunction than subjects with HBA1c < 7.5% **(*'P'* = 0.104).**
4) **F BSL -** Mean F BSL without & with diastolic dysfunction was 126.81±33.64 &123.70 ±38.60 respectively with **'p' Value 0.757**. Out of 42 subjects with FBSL level <110 mg/dl 37 (88.1%), Out of 101 subjects with FBSL level <111-150 mg/dl 91 (90.1%) & Out of 22 subjects with FBSL level >150 mg/dl 21(95.5%), had diastolic dysfunction. Comparing to FBSL level as level increases, prevalence of diastolic dysfunction increases.**(*'P'*= 0.636).**
5) **PP BSL -** Mean PP BSL without & with diastolic dysfunction was 222.125±61.44 &199.44 ±65.21 respectively with **'p' Value 0.186.** Out of 6 subjects with PPBSL level <140 mg/dl 06 (100%), Out of 86 subjects with PPBSL level <141-200 mg/dl 76 (88.4%), Out of 49 subjects with PPBSL level 201-250 mg/dl 46 (93.9%), Out of 13 subjects with PPBSL level <251-300 mg/dl 12 (92.3.4%) & Out of 11 subjects with PPBSL level >300 mg/dl 09(81.8%) subjects had diastolic dysfunction. Comparing to level of PPBSL as BSL level increases , prevalence of diastolic dysfunction increases. **(*'P'*= 0.611).**
6) **Duration of DM -** Mean duration of DM without & with diastolic dysfunction was 1.88±2.66 &6.37 ±5.91 Yrs respectively with **'p' Value 0.003(S)** . Out of 88 subjects with the duration of diabetes < 5 years 75 (85.2) , and Out of 33 subjects with the duration of diabetes 5-10 years 30 (90.9%) & Out of 44 subjects with the duration of diabetes > 10 years 44 (100%) had diastolic dysfunction. Comparing duration of diabetes in years as duration increases, prevalence of diastolic dysfunction increases. **(*'P'*= 0.026).**
7) **Obesity indices – a) BMI** : Mean BMI without & with diastolic dysfunction was 23.96±3.90 &24.47 ±4.80 respectively with **'p' Value 0.681**. Out of 89 total overweight (70) & obese (19) subjects 63 (90%) & 18 (94.7%) had diastolic dysfunction respectively. Comparing to normal & underweight subjects prevalence of diastolic dysfunction increases with severity of obesity. **(*'P'*= 0.919).**

b) **WHR :** Mean WHR without & with diastolic dysfunction was 0.953±0.070 &0.959 ±0.086 respectively with **'p' Value 0.809** & 149(90.3%) had diastolic dysfunction with **'p' Value 0.055.** Out of 97 Male subjects 84 (86.6%) had diastolic dysfunction **(*'P* ' = 0.938)** and out of 68 Female subjects 65 (95.6%) subjects had diastolic dysfunction **(*'P* ' = 0.032).** Female subjects had more prevalence of diastolic dysfunction than male subjects.

8) **Microalbuminurea** - Out of 99 Micral test positive subjects 92 (92.9%) subjects had diastolic dysfunction with **(*'P'*= 0.163).** But out of 57 positive Micral test subjects with value 50 & 100, 55(96.5%) subjects had diastolic dysfunction. **(*'P'*= 0.051).**
9) **LIPID PROFILE** –

a) **Dyslipidemia** - Out of 79 Non dyslipidemic subjects' 74(93.7%) subjects had diastolic dysfunction. Out of 86 dyslipidemic subjects 75(87.2%) subjects had diastolic dysfunction with **(*'P'*= 0.161).**

b) **Total Cholesterol** - Mean Total Cholesterol without & with diastolic dysfunction was 190.5±15.38 &192.28 ±13.56 respectively with **'p' Value 0.621.** Out of 118 subjects with normal cholesterol level (<200mg/dl), 105(89%) & out of 47 High cholesterol level(>200mg/dl),44 (93.6%) subjects had diastolic dysfunction with**(*'P'*= 0.364).**

c) **Triglyceride** - Mean Triglyceride without & with diastolic dysfunction was 183.43±86.83.64 &144.87 ±26.15 respectively with **'p' Value 0.000 .** Out of 95 subjects with normal Triglyceride level (<150mg/dl), 89(93.7%) & out of 70 High Triglyceride level (>150 mg/dl), 60 (85.71%) subjects had diastolic dysfunction with **(*'P'*= < 001).**

d) **HDL** - Out of total 165 subjects, Mean HDL without & with diastolic dysfunction was 43.06±4.58 &43.52 ±3.47 respectively with **'p' Value 0.626.** Out of 95 subjects with normal HDL level (> 40mg/dl), 82(86.31%) & out of 70 Low HDL level(< 40mg/dl), 67 (95.71%) subjects had diastolic dysfunction with **(*'P'*= 0.060).**

e) **LDL** - Out of total 165 subjects, Mean LDL without & with diastolic dysfunction was 108.93±15.07 &119.12 ±12.50

respectively with **'p' Value 0.003.** Out of 14 subjects with normal LDL level (< 100mg/dl) 8 subjects (57.1%), out of 127 subjects with LDL level (100-130mg/dl) 118(92.9%) subjects & out of 24 subjects with LDL level (>130mg/dl) 23(95.8%) subjects had diastolic dysfunction with **('*P*'= < 0.001).**

Relation of diastolic dysfunction with various Echocardiographic parameters in type 2 diabetes subjects.Mean, standard deviation with't' &' p' values. N=165
[Table 5].

Parameter	LV Diast. Dysfunction. Absent		LV Diast. Dysfunction. Present		't' Value	'p' Value	Significance
	n = 16		n = 149				
	Mean	Std Devi.	Mean	Std Devi.			
E	0.68	±0.095	0.76	±0.26	-1.255	0.211	NS
A	0.56	±0.125	0.77	±0.26	-3.015	0.003	S
E/A Ratio	1.21	±0.19	1.03	±0.44	1.589	0.114	NS
DT	169.18	±23.77	178.66	±8.58	-0.641	0.522	NS
IVRT	111.67	±22.10	115.55	±29.78	-0.512	0.609	NS
A Dur	126.5	±28.32	139.79	±37.17	-1.387	0.167	NS
Sep.e' mtr/sec.	0.096	±0.011	0.067	±0.21	5.324	0	S
E/e' Sep. ratio	6.93	±0.900	11.74	±4.40	-4.349	0	S
E/e' Av Ratio	6.23	±0.73	10.57	±4.94	-3.491	0.001	S
Sep.e'cms /sec.	8.12	±2.33	7.02	±2.13	1.939	0.054	S
Sep.a'cms /sec.	10.5	±1.86	10.16	±2.15	0.592	0.554	NS
Sep.e-a Ratio	0.78	±0.22	0.71	±0.24	1.171	0.243	NS
LAV	47.00	±2.83	62.45	±10.41	-2.357	0.02	S
IND LAV	28.07	±1.41	37.37	±6.19	-2.391	0.018	S
LVM INDX	73.48	±17.61	91.8	±26.87	-2.662	0.009	S

1) Grading of LVDD – Out of 165 studied patients, 122(73.9%) subjects with LV Diastolic dysfunction, 87 (71.39%) had grade I (Delayed relaxation) diastolic dysfunction, 27 (14.75%) had grade II (Pseudo normal) diastolic dysfunction 08 (6.55%) had grade III (Restrictive) diastolic dysfunction.
2) PWD MV Parameters - Mean E, A, E/A ratio, DT & IVRT in patients who had diastolic dysfunction was 0.76±0. 26 (p= 0.211), 0.77±0.26 **(p=0.003),** 1.03±0.44 **(p= 0.114),** 178.66±8.58 (p= 0.522) & 115.55±29.78 **(p= 0.609)** respectively.
3) TDI MV Parameters - Mean Septal e', E/e' Sep. ratio, E/e' Av Ratio, Sep.e'Velocity, Septal a' Velocity & Septal e-a Ratio in patients who had diastolic dysfunction was 6.7±0. 21 **(p= 0.000),** 11.74±4.40 **(p=0.000),** 10.57±4.94 **(p= 0.001),** 7.02±2.13 **(p= 0.054)** & 0.71±24 **(p= 0.554)** respectively.
4) Indexed LA Volume & LV Mass parameters - Mean LAVolume, Indexed LA Volume & LV Mass in patients who had diastolic dysfunction was 62.45±10.41 **(p= 0.020),** 37.37±6.19 **(p=0.018),** 91.80±26.87 **(p= 0.009)** respectively.

Discussion

Epidemiological data indicate a greater risk of cardiovascular morbidity and mortality, particularly congestive cardiac failure, in diabetic subjects as compared with those without diabetes[12].The Left ventricular diastolic dysfunction may represent first stage of diabetic cardiomyopathy, reinforcing the importance of early examination of diastolic function in individuals with diabetes.[13,14]. Van Heerebeek *et al.* [13] in their study of 64 type -2 DM patients stated that, the cardiomyocyte resting tension is more important when LVEF is normal. Excessive diastolic left ventricular stiffness is an important contributor to heart failure in subjects with DM. Diabetes is presumed to increase stiffness through myocardial deposition of collagen and advanced glycation end products. Paul Poirier et al [14] in 2001 evaluated 40 diabetic patients without clinical evidence of cardiac disease by Doppler Echocardiography and came to conclusion that diastolic function in diabetic patients were impaired even though found normal systolic function.

In our study Subjects with HBA1c > 7.5% had more prevalence of diastolic dysfunction than subjects with HBA1c < 7.5% **('*P*' = 0.104).** Comparing to FBSL & PP BSL level as level increases, prevalence of diastolic dysfunction increases with no statistical significance. Prevalence of diastolic dysfunction increased gradually with the rise in HbA1c levels. The relationship between diastolic dysfunction and glycemic control is still a matter of debate. Poirier and colleagues [14] also did not find any difference in the glycemic indices and concluded that fasting blood glucose levels did not correlate with the presence of diastolic dysfunction in type 2 diabetes. Suresh Chandravanshi et al [15] in their study found that prevalence of diastolic dysfunction was more with HbA1c level of more than 9.5 but statistically it was not significant (p<0.71).

In the study 73.9% of subjects had diastolic dysfunction with normal LVEF. This study supports the evidence that LV diastolic function may be impaired early in patients with diabetes mellitus before the development of symptomatic LV systolic or diastolic dysfunction. In our study we have used more TDI parameters (Average E/e' ratio > 10 , Septal e Ve l o c i t y < 7 cm/sec) to increase the accuracy & early detection of Diastolic dysfunction. Mitrovska S. *et al.* [16] in their study of LVDD for comparison of TDI with PWD showed TDI is more sensitive method & unmasks the presence of subclinical LV Diastolic dysfunction & has valuable prognostic importance than PWD. They found prevalence of LV diastolic dysfunction was 60% by PWD & 72% by TDI method.

In our study Diastolic dysfunction was significantly high in patients with age > 40 years compared to age < 40 years which is statistically significant**.('*P*'= 0.028).** Masugata *et al.* [17] in their case control study of 77 normotensive patients found that, the cardiac diastolic dysfunction without LV systolic dysfunction in patients with well-controlled type 2 DM is related neither to hypertension nor LV hypertrophy, but rather to aging and the duration of type 2 DM. Masugata H et al [18] in their study found the presence of LV diastolic dysfunction in NDDM patients is dependent on the age of the patients and duration of diabetes.

Patil VC et al & Shrestha NR et al [19,3] found that LV diastolic abnormalities are correlated with the increasing age & duration of diabetes. In our study comparing duration of diabetes in years as duration increases, prevalence of diastolic dysfunction increases. **('*P*'= 0.026).**

In our study overall prevalence of Diastolic dysfunction is more with high WHR in both sex but in Female subjects had significantly more prevalence of diastolic dysfunction than male subjects. **('*P* ' = 0.032).** Patil VC et al [19] in their study found overall mean of obesity indices like BMI, WC and WHR were significantly higher in subjects with type 2 DM. The Strong Heart study by Devereuex and colleagues in 2000 also demonstrated that diastolic dysfunction is more prevalent in women than in men.[20]. This could be due to hormonal changes that accompany after menopause. Shrestha NR et al [3] in their study found females had almost two times a higher risk for the development of diastolic dysfunction as compared with men. In our study Female subjects had more prevalence of diastolic dysfunction than male subjects. **('*P* ' = 0.055).**

Vinereanu D et al [21] study studies suggest correlation between hyperlipidemia and diastolic dysfunction. Mitrovsca S et al [16] showed most common dyslipidemia in diabetic population is high level of TG and LDL-c (low density lipoproteins) and low level of HDL-high density lipoproteins. In our study 87.2% subjects with dyslipidemia had diastolic dysfunction with **('*P*'= 0.161).** Also showed presence of diastolic dysfunction with high Triglyceride & LDL with low HDL level which is statistically significant. In the majority of study subjects with dyslipidemia were already receiving statins.

TT Shogade et al. [22] in their study states Microalbuminurea showed a strong direct association with LVDD (OR 3.58, 95% CI: 1.99–6.82, p < 0.001). In our study Micral test positive subjects 92.9% had diastolic dysfunction with **('*P*'= 0.163).** But Micral test positive with value 50 & 100, 96.5% had statistically significant diastolic dysfunction. **('*P*'= 0.051).**

Nagueh SF et al & Carolyn Y Ho at al [10,11] stated that in the assessment of LV diastolic dysfunction which depends mainly on the parameters of TDI in addition to LA volume index & TR velocity.

Using these parameters seems to increase the rate of detection of diastolic dysfunction. These new techniques help us to overcome some technical limitations in the conventional Doppler (PWD) echocardiographic techniques of diastolic function. This may be the cause for the discrepancies in the prevalence of diastolic dysfunction that was noted between earlier and recent studies. Ommen et al. [5] in their study found that the ratio of mitral velocity to early diastolic velocity of the mitral annulus (E/e) is better correlated with LV filling pressures than other Doppler parameters.

Boyer et al. detected "LV filling impairment in 46% in asymptomatic normotensive type 2 diabetic patients when screened by conventional Doppler, whilst newer techniques showed diastolic dysfunction in 75% of patients" [23]. Tissue Doppler Imaging is more sensitive method that measures "the velocity of the longitudinal motion (shortening and lengthening) of the mitral annulus" and it is a sensitive method for early detection of diastolic dysfunction. Mitrovska S. *et al.*[16] in their study for comparison of TDI with PWD showed TDI is more sensitive method & unmasks the presence of subclinical LV Diastolic dysfunction & has valuable prognostic importance than PWD.

CONCLUSION

Diabetes has been established as one of the major etiological factor in the development of cardiomyopathy and consequently heart failure. The findings in our study indicate that myocardial damage in patients with diabetes affects LV diastolic function before systolic function, E/A, A, E/e' ratio , Septal e', Left atrial sizes & LV Mass are significantly altered in diabetic patients with diastolic dysfunction. Diabetic dysfunction is significantly associated with Age, duration of disease, glycemic control, Dyslipidemia. Doppler Echo is simple, non – invasive and reproducible. It identifies large percentage of diabetic subjects who have asymptomatic left ventricular dysfunction before abnormalities are detected with ECG or by clinical examination. Therefore by early detection we can start early treatment and can retard the progression of LV diastolic dysfunction. This has important therapeutic implications and helps physicians planning early intervention strategies. Thus, diastolic dysfunction can be used as an early indicator, as it is a precursor to increased LV hypertrophy and clinical.

REFERENCES

1. SR Joshi, Parikh RM. Journal of asso. of physicians of India May 2007; 55; 323-24.
2. Kazik A, Wilczek K, Poloński L. Management of diastolic heart failure. Cardiol J 2010;17:558-65
3. Shrestha NR Sharma SK et al, Echo evaluation of Diastolic function in Asymptomatic type 2 Diabetes, a Cross sectional study. Journal Nepal Medical Association 2009; 48:20-23. From AM, Scott CG, Chen HH. Changes in diastolic dysfunction in diabetes mellitus over time. Am J Cardiol 2009; 103:1463-6.
4. From AM, Scott CG, Chen HH. Changes in diastolic dysfunction in diabetes mellitus over time. Am J Cardiol 2009; 103:1463-6.
5. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: A comparative simultaneous Doppler-catheterization study. Circulation 2000; 102:1788-94.
6. OH JK, Seward JB, Tajik AJ. Assessment of diastolic dysfunction and diastolic heart failure. In: Oh JK, editor. The Echo Manual. 3rd ed. New Delhi: Wolters Kluwer; 2006. p. 120-41.
7. Executive summary of third report of the cholesterol education program (NECP) Expert panel of detection, Evaluation, and treatment of high blood cholesterol In Adults. (Adult Treatment Panel III). JAMA 2001; 285:2486-97.
8. Gupta R, Majumdar S. Correlation of waist-hip ratio with coronary heart disease and risk factor prevalence in a rural male population. Indian Heart J 1994; 46:145-8.
9. American Diabetes Association (2017) Classification and diagnosis of diabetes. Diabetes Care 40: S11-S24
10. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, et al. (2016) Recommendations for the evaluation of left ventricular diastolic function by echocardiography: An update from the American Society of echo-cardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 29: 277-314.
11. Carolyn Y Ho and Scott D Solomon. A Clinician's Guide to Tissue Doppler Imaging. Circulation 2006; 113: 396-e398
12. Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure; The Framingham heart study. Am J Cardiol 1974; 34: 29-34.
13. Van Heerebeek L, Hamdani N, Handoko ML, Falcao-Pires I, Musters RJ, Kupreishvili K, et al. Diastolic stiffness of the failing diabetic heart: Importance of fibrosis, advanced glycation end products, and myocyte resting tension. Circulation 2008; 1; 117:43-51.
14. Poirier P, Bogaty P, Philippon F, Garneau C, Fortin C, Dumesnil JG. Preclinical diabetic cardiomyopathy: Relation of left ventricular diastolic dysfunction to cardiac autonomic neuropathy in men with uncomplicated well-controlled type 2 diabetes. Metabolism 2003; 52:1056-61.
15. Suresh Chandravanshi, Arpan Jain, Shashank Gupta. Echocardiographic evaluation of diastolic dysfunction in asymptomatic type 2 diabetes mellitus
16. Mitrovsca S, Jovanova S, Lazeska B (2014) Tissue Doppler imaging in the early detection of diastolic dysfunction in asymptomatic diabetic patients. Enliven Clinical Cardiology and Research 1: 1.
17. Masugata H, Senda S, Goda F, Yoshihara Y, Yoshikawa K, Fujita N, et al. Left ventricular diastolic dysfunction
18. Bajraktari G, Quinko S, Bakalli A, Rexhepaj N, Elizi S. Reduced left ventricular diastolic function in asymptomatic patients with non insulin dependent diabetes mellitus. Med Arch. 2004; 58(6): 220-41.
19. Patil VC, Patil HV, Shah KB, Vasani JD, Shetty P (2011) Diastolic dysfunction in asymptomatic type 2 diabetes mellitus with normal systolic function. J Cardiovasc Dis Res 2: 213–222.
20. Devereux RB, Roman MJ, Liu JE. Congestive heart failure despite normal left ventricular systolic function in a population based sample. The strong heart study. Am J Cardiol 2000; 86:1090.
21. Vinereanu D, Nicolaides E, Tweddel AC, et al. Subclinical left ventricular dysfunction in asymptomatic patients with Type II diabetes mellitus, related to serum lipids and glycated haemoglobin. Clin Sci (Lond) 2003; 105(5): 591-59.
22. TT Shogade et al. Association of microalbuminuria with left ventricular dysfunction in Nigerian normotensive type 2 diabetes patients
23. Boyer JK, Thanigaraj S, Schechtman KB, Perez JE (2004) Prevalence of ventricular diastolic dysfunction in asymptomatic, normotensive patients with diabetes mellitus. Am J Cardiol 93: 870-875.