Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

Study of echocardiographic assessment of Left ventricular diastolic dysfunction in normotensive Type 2 Diabetes mellitus patients

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Received Date: 25/04/2023 Acceptance Date: 23/06/2023

Abstract

Background: Diabetes mellitus is one of the most common diseases in the world and is acquiring epidemic proportions. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome. Diabetes mellitus also can affect cardiac structure and function in the absence of changes in blood pressure and coronary artery disease, a condition called diabetic cardiomyopathy. **Methodology-** The study was conducted at Department of Medicine of Pravara Rural Hospital, Loni from September 2014 to August 2016. 50 patients who were newly detected as well as known case of diabetes mellitus type 2 were included in the study. All the subjects underwent resting transthoracic 2-dimensional echocardiography and Doppler imaging, to assess left ventricular diastolic function. Data was analyzed using SPSS-16 for windows. **Result-**Out of total study population, diastolic dysfunction was present in 27 (54%) cases. Out of 50 cases 24 (48%) had grade I, 3 cases (6%) had grade II diastolic dysfunction and 23 cases (46%) had no diastolic dysfunction. Presence of diastolic dysfunction in population with age more than 45 years was found to statistically significant in male population as compared to female population. E/A ratio was found to be very significantly low in diabetic patients with diastolic dysfunction as compared to diabetic patients without diastolic dysfunction. **Conclusion-** Diastolic dysfunction in type 2 DM is significantly dependent on the duration of diabetes mellitus. As the duration of diabetes increases presence of diastolic dysfunction increases in asymptomatic type 2 DM population.

Keywords- Diabetes mellitus, echocardiography, left ventricle, diastolic, dysfunction

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Introduction

Diabetes mellitus is one of the most common diseases in the world and is acquiring epidemic proportions. Its prevalence is growing in both developed and developing countries. More than 5 % of adults have this disease, with prevalence of about 1 % in the youth to 13 % in those older than 60 years.[1] Based on current trends, the International Diabetes Federation projects that 592 individuals will have diabetes by the year 2035.[2] Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also

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accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the non-ketotic hyperosmolar syndrome. Long-term complications of diabetes include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction.[3] Diabetes mellitus also can affect cardiac structure and function in the absence of changes in blood pressure and coronary artery disease, a condition called diabetic cardiomyopathy. Diastolic heart failure (HF) is also referred to as HF, with preserved left ventricular systolic function.[4] 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.[5] Assessment of diastolic dysfunction requires an understanding of diastole and various means to evaluate diastolic function. Assessment of diastolic dysfunction should be an integral part of an evaluation of cardiac function because about 30 % of patients with heart failure have a preserved LVEF.
Therefore, this study was carried out for the echocardiographic assessment of Left ventricular diastolic dysfunction in normotensive Type 2 Diabetes mellitus patients.

Materials And Methodology

Study place- The study was conducted at Department of Medicine of Pravara Rural Hospital, Loni from September 2014 to August 2016.

Study design- Prospective observational study.

Inclusion criteria- All cases of normotensive type 2 diabetes mellitus, patients aged less than 30 years, having good left ventricular systolic function with EF of more than or equal to 55% and those who were willing to give written and informed consent were included for the study.

Exclusion criteria- Systemic Hypertension (BP ≥140/90) and Normotensive individual taking anti-hypertensive agents, having Ischemic heart disease (abnormal E.C.G. and RWMA on Echo), patients with signs and symptoms s/o congestive cardiac failure, Congenital or Acquired Valvular Heart Disease, cardiac signs and symptoms like exertional dyspnoea, chest pain, palpitation, raised JVP, subjects with poor transthoracic window, Diabetic Nephropathy and anaemia, and those who were not willing to give consent were excluded from the study.

Sample size- 50 patients from OPD as well as IPD from the Department of Medicine were taken into consideration for the study.

Data analysis- Data was analyzed by using SPSS-16 (Statistical Package for the Social Sciences) for Windows. Descriptive variables were tabulated for Mean, percentage, standard deviation. Relation and association of the variable was analyzed using chi square test for the qualitative data and t test for quantitative data. Correlation between the variable was established using Pearson's correlation test. Observations were interpreted with '*P*' value < 0.05 was considered statistically significant.

Ethical considerations- Ethical committee permission was taken before beginning the study. Written informed consent was taken from the patients.

Detailed medical history was collected from each eligible subject and they underwent physical examination and biochemical investigations. Physical examination including routine general examination, systemic examination and anthropometric evaluation was done. All the subjects underwent resting transthoracic 2-dimensional echocardiography and Doppler imaging, to assess left ventricular diastolic function. A transthoracic 2-dimentionsional echocardiogram (TTE) with pulsed Doppler evaluation of transmitral inflow and Tissue Doppler Imaging (TDI) and 2D echocardiography was performed to minimize the errors in

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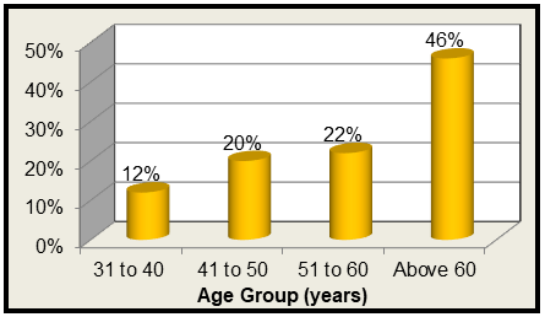
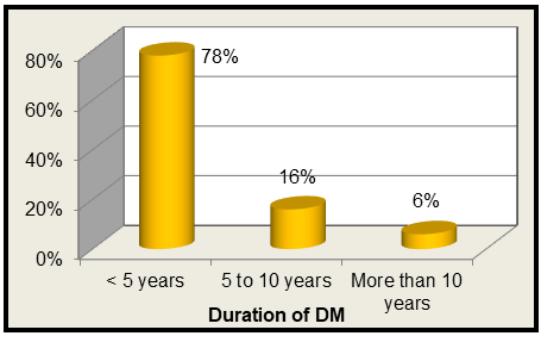
assessing the diastolic dysfunction. Echocardiography was performed by a "Micromaxx Ultrasound System Sonosite". Pulsed-wave Doppler (PWD)- derived transmitral inflow velocities was obtained in the apical 4-chamber view, with the sample volume placed at the mitral valve leaflet tips. Diastolic dysfunction was labelled according to the standard guidelines. Left ventricular overall ejection fraction (systolic function) was calculated by modified Simpson's method; and, LVEF ≥ 50% was considered as normal.[6]

Results



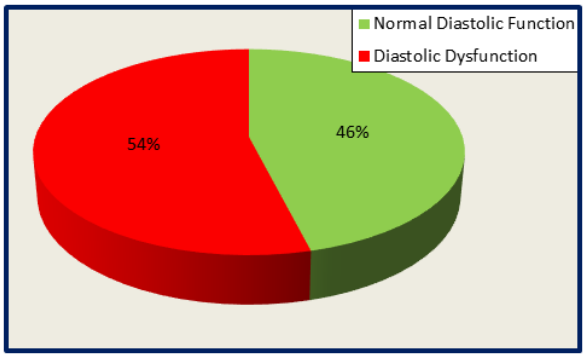
Graph 1: Age Group of Type 2 DM patients

Maximum, 23 (46%), patients were above the age group of 60 yrs. 12% patients with Type 2 DM were within 31 to 40 years of age, 20% patients were 41 to 50 years old, 22% had age within 51 to 60 years and 46% patients age was more than 60 years.



Graph 2: Duration of Type 2 DM in patients.

In the present study, 39 (78%) patients the duration of diabetes was less than 5 years. In 8 (16%) patients the duration was from 5 to 10 years and in 3 (6%) patients the duration was more than 10 years.



Graph 3: Diastolic dysfunction in Type 2 DM patients

Out of the 50 studied patients 27 (54%) had diastolic dysfunction.

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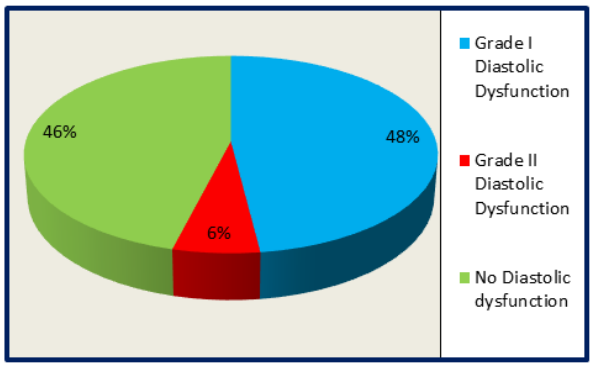

Graph 4: Various grades of diastolic dysfunction in the study population

Out of 27 patients having diastolic dysfunction, in 24 (48%) diastolic dysfunction was of grade I. in 3 (6%) cases the diastolic dysfunction was of grade II. However, grade III and IV was not found in any patient in the present study.

Table 1: Showing E/A Ratio of Type 2 DM patients.

E/A ration	No of patients	Percent
≤0.75	24	48.0
>0.75	26	52.0
Total	50	100.0

Table 1. shows, of 50 patients studied E/A ratio was less than or equal to 0.75 in 48% patient while in 52%patients E/A ratio was more than 0.75.

Table 2: Diastolic dysfunction in the study population according to age group, sex and Duration of DM.

Parameters		Diastolic Dysfunction		P value
		No of patients	Percent	
Age Group	≤ 45 years	2	25%	<0.05
	>45 years	25	59.5%	
Sex	Female	12	52.2%	0.811
	Male	15	55.6%	
Duration of Diabetes mellitus (years)	< 5	18	45%	0.035
	5 to 10	6	85.7%	
	> 10	3	100%	

Out of 50 patients with type 2 DM, age of 42 patients was above 45 years while 8 patients age was less than or equal to 45 years. Table 5.9 shows out of 8 patients of age less than or equal to 45years, 2 (25%) had diastolic dysfunction and out of 42 patients of age above 45 years 25 (59.5%) had diastolic dysfunction. There was statistically significant ($p<0.05$) difference of higher proportion of type 2 DM patients above 45 year's age group having diastolic dysfunction than those up to 45 year's age. In female type 2 DM patients 12 (52.2%) had Diastolic dysfunction while in male type 2 DM patients 15 (55.6%) had developed diastolic dysfunction as shown in table 5.9. There was statistically no significant ($p>0.05$) difference of proportion of type 2 DM patients having diastolic dysfunction according to sex. out of 40 patients having type 2 DM for less than or up to 5 year's duration, 18 (45%) had diastolic dysfunction. Of 7 patients having type 2 DM for 5 to 10 years of duration 6 (85.7%) had diastolic dysfunction while all i.e. 100% patients having type 2 DM from more than10 years had developed diastolic dysfunction. There was statistically significant ($p<0.05$)

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association of increasing proportion of DM patients with diastolic dysfunction with increasing duration of DM.

Table 3: Diastolic dysfunction in the study population according to 5 year's duration of Type 2 DM.

Duration of DM		Diastolic Dysfunction		P value
		Grade I	Grade II	
Groups (years)	<5	17(43.6%)	0	0.003
	5 to 10	5(62.5%)	2(25%)	
	>10	2(66.7%)	1(33.3%)	

Out of 39 patients of less than 5 year's duration of DM 17 (43.8%) had Grade 1 diastolic dysfunction, out of 8 patients with 5 to 10 year's duration of DM 5 (62.5%)patients had Grade 1 diastolic dysfunction and 2 (25%) had Grade II diastolic dysfunction. While out of 3 patients of more than 10 year's duration of type 2 DM 2 (66.7%) had Grade 1 and 1 (33.3%) patient had Grade II diastolic dysfunction i.e. none of them had normal diastolic dysfunction. There was statistically highly significant ($p<0.01$) difference of proportions of Grade of diastolic dysfunction with the increasing duration of DM.

Table 4: Diastolic dysfunction in the study population according to obesity indices.

Obesity Parameter		Diastolic Dysfunction		Total
		Absent	Present	
BMI	Normal	18	13	31
		78.3%	48.1%	62.0%
	Obese (M>27 BMI; F>25 BMI)	5	14	19
		21.7%	51.9%	38.0%
	Total	23	27	50
		100.0%	100.0%	100.0%
WHR	Raised (M>0.9; F>0.8)	23	27	50
		100.0%	100.0%	100.0%
	Total	23	27	50
		100.0%	100.0%	100.0%

Chi-Square Test

		Value	df	p value
BMI	Pearson Chi-Square	4.780	1	0.029
WHR	Pearson Chi-Square	0.00	1	1.00

Risk factor	Unadjusted odds ratio and 95% CI
Raised BMI (obesity)	3.877 (1.116-13.73)

In 27 (51.9%) DM patients with diastolic dysfunction had raised body mass index i.e. more than cut-off value thus obese while 13 (48.1%) had normal BMI. Also obesity was found in 5 (21.7%) patients with normal diastolic function. There was statistically significantly ($p<0.05$) higher proportion of obese patients in diastolic dysfunction group than in the normal patients with odds ratio of 3.877. All patients with diastolic dysfunction and with normal diastolic

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function had raised waist to hip ratio. There was statistically no significant (p>0.05) difference.

Table 5: Sex wise Diastolic dysfunction in the study population according to 45-years age group.

Sex	Diastolic Dysfunction	Age group (years)		Total	Pearson Chi-Square test		Odds ratio
		≤ 45	>45		X^2 value	P value	Unadjusted odds ratio and 95% CI
Female	Absent	0	12	12	0.831	0.362	1.857 (1.301-2.651)
			46.2%	44.4%			
	Present	1	14	15			
		100.0%	53.8%	55.6%			
	Total	1	26	27			
		100.0%	100.0%	100.0%			
Male	Absent	6	5	11	5.789	0.016	13.2(1.24-140.68)
		85.7%	31.3%	47.8%			
	Present	1	11	12			
		14.3%	68.8%	52.2%			
	Total	7	16	23			
		100.0%	100.0%	100.0%			

Diastolic dysfunction was noted in all females up to 45 year's age group while in 14 (53.8%) out of 26, females with age more than 45 years old had diastolic dysfunction. Statistically there was no significant (p>0.05) difference of presence of diastolic dysfunction in DM female patients with 45 year's age group with odds ratio of 1.857. In male DM patients of up to 45 year's age only 1 (14.3%) had diastolic dysfunction while 11 (68.8%) male more than 45 years old had diastolic dysfunction. There was statistically significant (p<0.05) difference of higher proportion of male patients more than 45 year's age having diastolic dysfunction with odds ratio of 13.2

Table 6: Grades of Diastolic dysfunction according to sex patients with DM.

Diastolic dysfunction	Sex		Total
	Female	Male	
Grade I	13	11	24
	48.1%	47.8%	48.0%
Grade II	2	1	3
	7.4%	4.3%	6.0%
Grade III	0	0	0
Grade IV	0	0	0

Chi-Square Test

	Value	df	p value
Pearson Chi-Square	0.225	2	0.894

Out of 50 patients, of 27 female DM patients 13 (48.1%) had Grade I diastolic dysfunction and 2 (7.4%) had grade II diastolic dysfunction. In Male DM patients 11 (47.8%) had Grade I diastolic dysfunction while 1 (4.3%) had Grade II diastolic dysfunction. There was

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statistically no significant difference of proportion of Grades of diastolic dysfunction according to sex of DM patients.

Table 7: Comparison of parameters in between Type 2 DM patients according to presence of diastolic dysfunction

Parameter	No Diastolic Dysfunction	Diastolic Dysfunction	Mean difference	T value	P value
Duration of DM (years)	1.5±2.1	4.2±4.2	-2.63	-2.742	0.009
Age (years)	56.2±11.0	59.2±11.3	-3.01	-.951	0.346
BSL-F (mg/dl)	193.2±70.1	219.3±90.6	-26.08	-1.123	0.267
BSL-PP (mg/dl)	246.2±95.1	271.0±67.5	-24.78	-1.074	0.288
BMI (kg/m^2)	23.3±3.9	26.4±4.8	-3.0599	-2.428	0.019
WC-HC ratio	1.0±0.2	1.0±0.1	0.0175	.388	0.700
E/A	1.1±0.2	0.8±0.2	.3153	5.498	<0.001
E/e’	8.7±1.1	9.5±0.7	-.7473	-2.891	0.006

The above table shows s mean duration of DM was 1.5 years (SD 2.1 years) in patients with normal diastolic function and in those with diastolic dysfunction had 4.2 years (SD 4.2 years) mean duration of DM. There were higher mean years of DM duration in diastolic dysfunction patients than those with normal diastolic function which was statistically highly significant ($p<0.01$). Mean age in patients with normal diastolic function was 56.2 years (SD 11 years) and those with diastolic dysfunction had 59.2 years (SD 11.3 years) mean age. There was statistically no significant ($p>0.05$) mean difference of mean age in diastolic dysfunction patients than those with normal diastolic function. Mean fasting BSL in patients with normal diastolic function was 193.2 mg/dl (SD 70.1 mg/dl) and those with diastolic dysfunction had 219.3 mg/dl (SD 90.6 mg/dl) mean fasting BSL. Mean post prandial BSL in patients with normal diastolic function was 246.2 mg/dl (SD 95.1 mg/dl) and those with diastolic dysfunction had 271 mg/dl (SD 67.5 mg/dl) mean post prandial BSL. Though there was higher mean fasting and post prandial BSL in diastolic dysfunction patients than those with normal diastolic function it was statistically not significant ($p>0.05$). In normal diastolic function patients mean BMI was 23.3 kg/m^2 (SD 3.9 kg/m^2) while those with diastolic dysfunction had 26.4 kg/m^2(SD 4.8 kg/m^2) mean BMI. There was higher mean BMI in diastolic dysfunction patients than those with normal diastolic function which was statistically significant ($p<0.05$).

Both patients with and without diastolic dysfunction had mean waist to hip ratio of 1. There was statistically no significant ($p>0.05$) mean difference of mean waist to hip ratio in DM patients with and without diastolic dysfunction. E/A ratio in normal diastolic function DM patients was 1.1 (SD 0.2) while those with diastolic dysfunction had 0.8 E/A ratio. There was higher E/A ratio in normal diastolic function DM patients than those with diastolic dysfunction which was statistically very highly significant ($p<0.001$). In normal diastolic function DM patients mean E/e’ ratio was 8.7 (SD 1.1) while in those with diastolic dysfunction E/e’ ratio was 9.5(S.D 0.7). DM patients with diastolic dysfunction patients had higher mean difference of E/e’ ratio than those with normal diastolic function which was statistically highly significant ($p<0.01$).

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Table 8: Correlation of E/e' and E/A with the parameters in type 2 DM patients.

		E/A	E/e'
Duration of DM	Pearson Correlation	-0.117	0.353
	Sig. (2-tailed)	0.419	0.012*
AGE	Pearson Correlation	-0.168	0.195
	Sig. (2-tailed)	0.243	0.174
BSL-F	Pearson Correlation	-0.030	-0.161
	Sig. (2-tailed)	0.835	0.264
BSL-PP	Pearson Correlation	0.000	-.387
	Sig. (2-tailed)	0.998	0.006**
BMI	Pearson Correlation	-0.023	0.318
	Sig. (2-tailed)	0.872	0.024*
WC-HC ratio	Pearson Correlation	-0.110	-0.162
	Sig. (2-tailed)	0.449	0.261
E/A	Pearson Correlation	1.000	0.039
	Sig. (2-tailed)	.	0.787
	Sig. (2-tailed)	.034*	0.073
E/e'	Pearson Correlation	.039	1.000
	Sig. (2-tailed)	.787	.

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).

There was negative correlation of E/A ratio with duration of DM, age, fasting BSL, body mass index, waist to hip ratio. E/A ratio was positively correlated with E/e' ratio while no relation at all with BSL PP. Statistically the relation of E/A with DT is very highly significant ($p<0.001$) and IVRT is significant ($p<0.05$). E/e' ratio had positive correlation with duration of DM, Age, BMI, E/A. There was negative correlation of E/e' ratio with Fasting and postprandial BSL, waist to hip ratio. Statistically the relation of E/e' ratio with duration of DM, BMI was significant ($p<0.05$) and with BSL –PP it was highly significant ($p<0.01$).

Discussion

In the present study, maximum subjects i.e. 23 (46%) were above the age group of 60 yrs. 12% patients with Type 2 DM were within 31 to 40 years of age, 20% subjects were 41 to 50 years old, 22% had age within 51 to 60 years. There was statistically no significant ($p>0.05$) difference of age group of patients according to the status of diastolic function in type 2 DM patients. Mean age of study population with diastolic dysfunction was 59.2±11.3. Similarly, in Soldatos et al [7] mean age was found to be 62±9 and in Masugata et al [8] 63±11. Whereas, in Boyer et al [9] it was 45.6±8 and in Zabalgoitia et al [10] it was 46.

In our study, out of 50 subjects, 27 (54%) were female and 23 (46%) were male population. Similarly, in Boyer et al study out of 61 study population 31 were male and 30 were females and in Masugata et al [8] study out of 77 subjects 40 were males and 37 were females and in the study by Dikshit et al.[11] Male to female ratio was 1.94:1 in 50 cases of diabetes.

In the present study, mean duration of diabetes mellitus in subjects with diastolic dysfunction was 4.2±4.2. Risk of developing diastolic dysfunction in males is 55 times more if duration of diabetes more than 5 years whereas in females it was found to be 5.5 times. Similarly, in

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Boyer et al [9] study mean duration of diabetes mellitus in patients with diastolic dysfunction was 5.8±5.5. However, In Soldatos et al [7] study out of 55 cases of diabetes mean duration of diabetes mellitus was 10±7 years.

In the present study, out of 50 subjects studied E/A ratio was less than or equal to 0.75 in 24 (48%) subjects while in 26 (52%) subjects E/A ratio was more than 0.75. Mean E/A ratio in normal diastolic function DM patients was 1.1 (SD 0.2) while those with diastolic dysfunction had 0.8±2 E/A ratio. There was higher E/A ratio in normal diastolic function DM patients than those with diastolic dysfunction which was statistically very highly significant ($p<0.001$). Similarly, in Soldatos et al [7] E/A ration in diabetic population was 0.8±0.2 and in Dikshit et al[11] E/A ratio of 0.9±0.27 was present in study population which was statistically significant in both studies. However, Masugata et al [8] observed that the E/A ratio in the patients with type 2 diabetes was not different from that in the control subjects in their 40s (1.17± 0.35 versus 1.20±0.36). However, E/A was significantly lower in the diabetic patients than in the control subjects in their 50s (0.87 ± 0.28 versus 1.14± 0.24), 60s (0.78±0.22 versus 0.97±0.27), and 70s (0.66 ± 0.19 versus 0.84±0.21) ($p < 0.05$). It was observed in the present study that there was negative correlation of E/A ratio with duration of DM as it was observed in Masugata et al [8] study and Mishra et al [12] study.

Mean fasting blood glucose level (FBG) in cases with diastolic dysfunction was 219.3±90.6. Whereas Dikshit et al [12] found mean fasting blood glucose level of 180.8±78.41 while in Soldatos et al [7] mean FBG was 160±43. As all the study population involved in the present study was rural because of infrequent follow up and badly controlled diabetes in turn result into high mean fasting blood sugar.

In the present study, diastolic dysfunction was present in 27 (54%) out of 50 cases. Similarly, VC Patil et al [13] also found diastolic dysfunction in 54.33% in case group of the study and Soldatos et al [7] study also found that diastolic dysfunction was present in a significant proportion of population with type 2 DM. There was statistically no significant difference of proportion of Grades of diastolic dysfunction according to sex of DM patients.

Conclusion

We conclude, that diastolic dysfunction in type 2 DM is significantly dependent on the duration of diabetes mellitus. As the duration of diabetes increases presence of diastolic dysfunction increases in asymptomatic type 2 DM population. Presence of diastolic dysfunction in type 2 DM is more significant in male than female population. Presence of diastolic dysfunction is significant in male type 2 DM population with age more than 45 years. Diastolic dysfunction is present more significantly in female type 2 DM population.

Limitations

The sample size was 50 which was small. But these subjects had isolated diabetes mellitus so that all other causes of diastolic dysfunction were excluded. We recommend same study with large sample size.

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