

## A Study on Prevalence of Diastolic Dysfunction in Type 2 Diabetes Mellitus in Normotensive Patients

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### ABSTRACT

**Background:** CHD is closely associated with T2DM. This strong relationship has been proved in different studies, beginning with the Framingham study. This study, after 20 years of surveillance, had shown a 2-fold to 3-fold increased risk of clinical atherosclerotic disease. The relative impact was greatest for intermittent claudication (IC) and congestive heart failure (CHF) and least for CHD.

**Objective :**1. To study the prevalence of diastolic dysfunction in type 2 diabetes mellitus in normotensive patients. To study the correlation of the LVDD and long-term glycemic control using HbA1c.

**Methodology:** The data for the purpose of the study was collected in a predesigned and pretested proforma which include various socioeconomic parameters like age & gender as well as clinical parameters based on inclusion and exclusion criteria. About 50 cases were selected on the basis of the simple random sampling method. The analysis of data was made on the basis of the important statistical parameters like the mean, mode, standard deviation, standard error, the t-test and the proportion test. The study is a cross sectional study conducted among 50 diabetic patients. All the relevant biochemical investigations done and ECG and ECHO was done.

**Results :**Among the 50 study participants, of these 30 study participants with LVDD, Majority 53.3 % had Grade 2 LVDD and then 40 % were with Grade 1 LVDD, followed by which 6.7% participants were with Grade 3 LVDD association between age category and diastolic dysfunction, among study participants aged less than or equal to 50 years 50 % had diastolic dysfunction and among aged more than 50 years 70 % had diastolic dysfunction.

**Conclusion:** Persons with type 2 diabetes mellitus should be screened with echocardiography for subclinical diastolic dysfunction. Due to the epidemiological transition of the population towards aging and a more sedentary lifestyle, the prevalence of diabetes mellitus has been rapidly increasing and the prevalence of diabetic cardiomyopathy has been increased too. In the study conducted among 50 participants majority of the study participants that is 30 participants present with left ventricular diastolic dysfunction and hence screening the diabetic patients with ECHO would slow down the progression of diabetic cardiomyopathy and helps in appropriate management and cause significant reduction in the morbidity and mortality in patients with diabetes.

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### I. INTRODUCTION

Due to the epidemiologic transition of the population towards aging and more sedentary lifestyle related to urbanization during the past few decades, the prevalence of type 2 diabetes mellitus (T2DM) has been rapidly increasing and the age of onset becomes younger globally<sup>1</sup>. Many developing countries are currently suffering from the increasing burden of T2DM and comorbidities which used to predominantly burden developed countries.<sup>1</sup> Diastolic dysfunction may be the earliest marker for diabetes induced cardiac disease, which leads to the progressive cardiac failure. Thus, the importance of detecting diastolic dysfunction using tissue doppler echocardiography helps in preventing the progression of patients to symptomatic congestive cardiac failure.<sup>2</sup> Left ventricular diastolic dysfunction is characterized by impairment in early diastolic filling, prolongation of isovolumetric relaxation and increased atrial filling. The prevalence of diastolic dysfunction is due to myocardial fibrosis<sup>3</sup>, the most likely reason for this is due to the accumulation of advanced glycosylation products in the myocardium and receptor expression, increased cross linking of collagen and myocardial fibrosis.<sup>4-7</sup> Myocardial damage in patients with diabetes, affects diastolic function before systolic function. In patients with type 2 diabetes, cerebrovascular disease and peripheral artery disease are also types of cardiovascular disease (T2DM). In both kinds of DM, considerably contribute to morbidity and mortality. Cardiovascular disease is the leading cause of death among T2DM patients.<sup>8</sup> CHD is closely associated with T2DM. This strong relationship has been proved in different studies, beginning with the Framingham study.

This study, after 20 years of surveillance, had shown a 2-fold to 3-fold increased risk of clinical atherosclerotic disease. The relative impact was greatest for intermittent claudication (IC) and congestive heart failure (CHF) and least for CHD. The relative impact was substantially greater for women than for men. DM is also an independent risk factor for cerebrovascular disease and stroke, as for CHD.<sup>9,10</sup> Concerning the macrovascular complications of T2DM, this disease acts as an independent risk factor not only for ischemic disease and stroke but also for death.<sup>11-13</sup> Hyperglycemia also increases the myocardial content of free radicals and oxidants, which decreases nitric oxide levels, worsens endothelial function and induces myocardial inflammation. Lipotoxicity due to elevation of free fatty acids associated with hyperglycemia and insulin resistance may also be a factor because free fatty acids and their oxidation products may be directly toxic to the myocardium and contribute to the development of diabetic cardiomyopathy<sup>14,15</sup>.

## II. MATERIALS AND METHODS

**Study design:** Hospital based Cross sectional study,

**Study setting:** Government Vellore Medical College Hospital,

**Study period:** JANUARY 2021 to DECEMBER 2021

**Study population:** The study was conducted in Government Vellore Medical College and Hospital, 50 patients who are the known case of Type II diabetes Mellitus patients were selected, the age of the patient varied from 20 to 70 years. The data for the purpose of the study was collected in a predesigned and pretested proforma which include various socioeconomic parameters like age & gender as well as clinical parameters based on inclusion and exclusion criteria. About 50 cases were selected on the basis of the simple random sampling method. The analysis of data was made on the basis of the important statistical parameters like the mean, deviation, standard error, the t-test and the proportion test. Sample size:50

### Inclusion criteria:

1. Patients were aged between 30 to 70years
2. Patients were of duration of diabetes more than 1 year
3. Patients who are willing to voluntarily participate in this study after informed consent

### Exclusion criteria:

1. Patients with coronary artery disease excluded by clinical, ECG and Abnormal TMT
2. Clinical evidence of chronic respiratory disease
3. Evidence of valvular heart disease
4. Hypertensive patients (BP > 140/90mmHg)
5. Patients on Anti-Hypertensive agents (ACE inhibitors, ARBs)
6. Subjects with macro albuminuria
7. subjects with diabetic retinopathy
8. known case of thyroid disorders
9. patients with age > 60 years
10. subjects with poor transthoracic echo window

**Study procedure and Methodology:** Each of the participants will be asked pre-specified questions according to the Proforma. Blood samples will be collected for laboratory investigations, FBS, PPBS, HbA1c, TFT, blood urea, serum creatinine, serum lipid profile, urine albumin, chest X-ray, ECG, ECHO using tissue doppler other blood, urine routine and fundus examination were done. Data entry and analysis. Data collected was entered in Microsoft excel and analyzed using SPSS version 24.0

**Estimation of Diastolic Dysfunction:** This is done by Echocardiogram

**PROCEDURE:** After meeting the inclusion criteria and Exclusion criteria, patients with known diabetes mellitus were selected, in ECHO look for the presence of diastolic dysfunction. Parameters included are left atrial volume index >28 ml/m<sup>2</sup> or reduced lateral e' velocity. Age < 55 yrs: e' < 10 cm/s, Age 55-65 yrs: e' < 9 cm/s, Age > 65yrs

:e' < 8 cm/s

Normal	Grade 1	Grade 2	Grade 3
E/A Ratio >0.8 e' normal for age Normal LA volume	E/A <0.8 Reduced e' for age LA VI may be normal or >28 ml/m <sup>2</sup>	E/A >0.8 Reduced e' for age LA VI >28 ml/m <sup>2</sup>	E/A > 1.5 Reduced e' for age LA VI >28 ml/m <sup>2</sup> E-Wave DT < 140 ms

**Statistical Analysis:**

**Data entry-** The data were entered using Microsoft Excel 2019 software package and the data sheet was imported into SPSS version 23 for data analysis. **Data cleaning** – Before analyzing the data each variable was acquired to check for missing values, blank values and typing errors. The corresponding case numbers were used to trace the questionnaires and the information was rechecked and entered. **Descriptive statistics** - Initially, the frequency tables were obtained for all the variables such as socio-demographic characteristics, blood parameters and LV diastolic dysfunction. Quantitative data are expressed as mean and standard deviation, Qualitative data are expressed as frequency. **Test of significance-** Chi-Square Test was used to assess the association between independent and dependent variables.

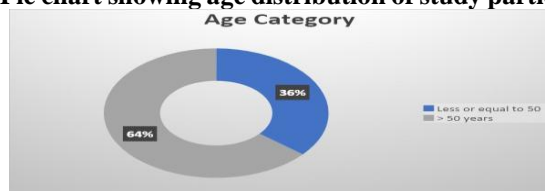
**III. RESULTS**

**Table 1: Age distribution of study participants.**

Age Distribution	Frequency (n)	Percent (%)
Less or equal to 50	18	36.0
> 50 years	32	64.0
Total	50	100.0

The mean age of study participants were 53.12 years  $\pm$  8.183, the minimum age of the study participants was 36 years and maximum were 70 years. Majority 64 % of participants were aged more than 50 years, followed by 36 % aged less than or equal to 50 years.

**Fig.1: Pie chart showing age distribution of study participants.**

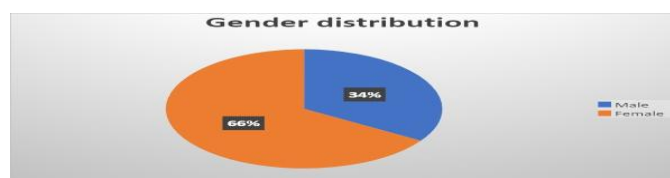


**Table 2: Distribution of study participants according to gender.**

Gender	Frequency (n)	Percent (%)
Male	17	34
Female	33	66
Total	50	100

Female were the majority study participants with 66% and followed by male participants with 34 %.

**Fig.2: Pie chart showing gender distribution of study participants.**

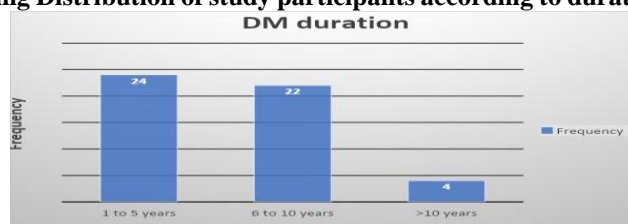


**Table 3: Distribution of study participants according to duration of diabetes mellitus.**

DM Duration	Frequency	Percent
1 to 5 years	24	48.0
6 to 10 years	22	44.0
>10 years	4	8.0
Total	50	100

Above table shows distribution of study participants according to the duration of diabetes mellitus, of them 48 % were between 1-5 years followed by 44 % of participants were between 6 to 10 years and remaining 8 % were more than 10 years duration.

**Fig.3: Bar chart showing Distribution of study participants according to duration of diabetes mellitus.**

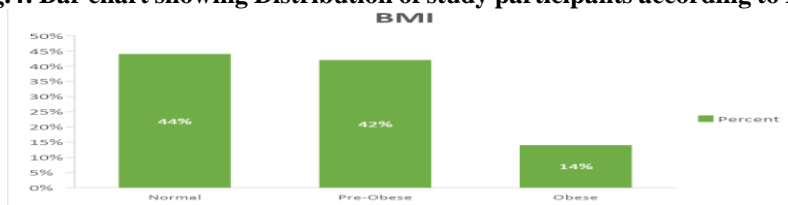


**Table 4: Distribution of study participants according to BMI**

BMI	Frequency	Percent
Normal	22	44.0
Pre-Obese	21	42.0
Obese	7	14.0
Total	50	100.0

Among 50 study participants, 44 % was with normal BMI and 42 % students were pre obese and remaining 14 % were obese.

**Fig.4: Bar chart showing Distribution of study participants according to BMI**

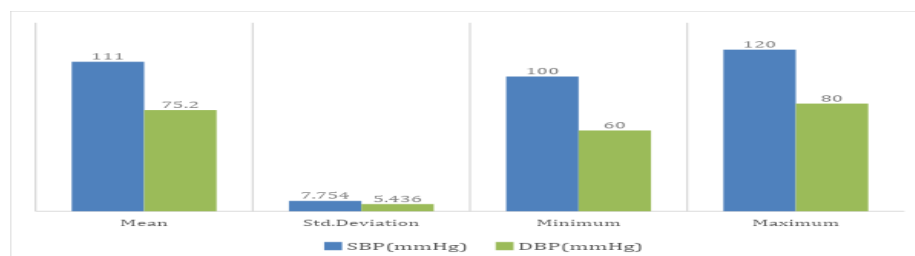


**Table 5: Distribution of study participants according to blood pressure**

Blood pressure	Mean	Std.Deviation	Minimum	Maximum
SBP (mmHg)	111.0	7.754	100	120
DBP (mmHg)	75.20	5.436	60	80

Out of 50 participants, the mean SBP was 111 mmHg ( $\pm 7.354$ ) while mean diastolic blood pressure was 75.20 mmHg ( $\pm 5.436$ ).

**Fig.5: Bar chart showing Distribution of study participants according to blood pressure**

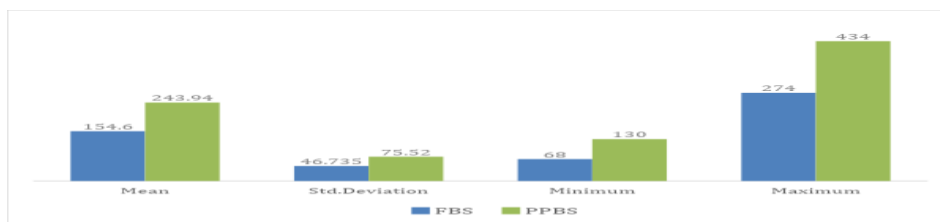


**Table 6: Distribution of study participants according to Blood Glucose Levels**

Blood Glucose	Mean	Std.Deviation	Minimum	Maximum
FBS	154.60	46.735	68	274
PPBS	243.94	75.520	130	434

Out of 50 study participants, the mean fasting blood sugars were 154.60 ( $\pm 46.735$ ) with minimum fasting blood sugars were 68 mg/dl and maximum were 274 mg/dl, while Post prandial blood sugars were 243.94 ( $\pm 75.520$ ) with minimum ppbs were 130 mg/dl and maximum were 434 mg/dl

**Fig.6: Bar chart showing distribution of study participants according to Blood Glucose Levels**

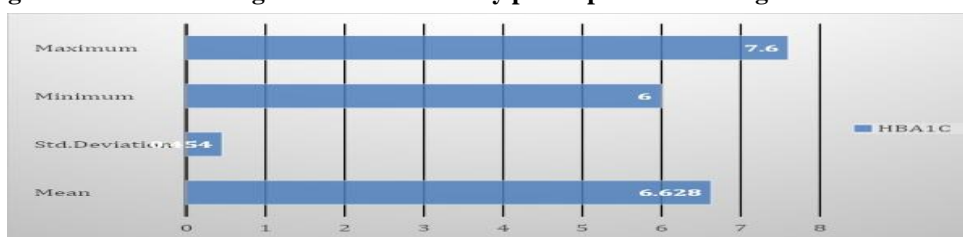


**Table 7: Distribution of study participants according to HbA1C**

HbA1C	Mean	Std.Deviation	Minimum	Maximum
HBA1C	6.628	.4540	6.0	7.6

Among 50 study participants, the mean HbA1C were 6.628 ( $\pm 0.4540$ ), with minimum 6 and maximum 7.6.

**Fig.7: Bar chart showing Distribution of study participants according to HbA1C**

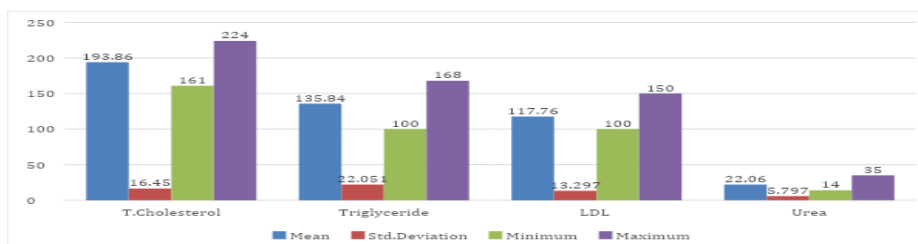


**Table 8: Distribution of study participants according to Blood Parameters**

Blood pressure	Mean	Std.Deviation	Minimum	Maximum
T. Cholesterol(mg/dl)	193.86	16.450	161	224
Triglyceride(mg/dl)	135.84	22.051	100	168
LDL (mg/dl)	117.76	13.297	100	150
Urea(mg/dl)	22.06	5.797	14	35

Among 50 study participants, the mean total cholesterol was 193.86 mg/dl ( $\pm 16.450$ ) with minimum cholesterol levels were 161 mg/dl and maximum cholesterol levels were 224 mg/dl, while the mean triglyceride levels were 135.84 mg/dl ( $\pm 22.051$ ) with minimum triglyceride levels were 100 mg/dl and maximum were 168 mg/dl. The mean LDL levels were 117.76 mg/dl ( $\pm 13.297$ ) with minimum 100 mg/dl and maximum were 150 mg/dl. The mean Urea levels were 22.06 mg/dl ( $\pm 5.797$ ) with minimum urea levels were 14 mg/dl and maximum were 35 mg/dl.

**Fig.8: Bar chart showing Distribution of study participants according to Blood Parameters**

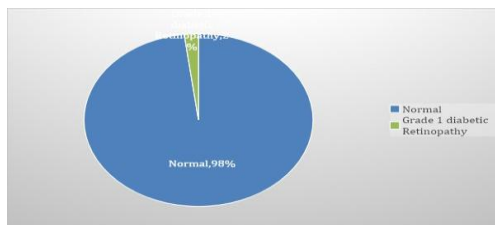


**Table 9: Distribution of study participants according to Fundus Examination**

Fundus Examination	Frequency	Percent
Normal	49	98.0
Grade 1 diabetic Retinopathy	1	2.0
Total	50	100.0

Among the study participants, 98 % had normal fundus, 2 % had grade 1 diabetic Retinopathy.

**Fig.9: Pie chart showing Distribution of study participants according to Fundus Examination**

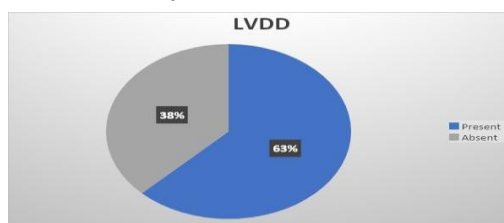


**Table 10: Distribution of study participants according to Left ventricular Diastolic Dysfunction.**

LVDD	Frequency	Percent
Present	30	62.5
Absent	18	37.5
Total	48	100.0

2 patients were excluded from the study because they presented systolic dysfunction.

**Fig.10: Pie chart showing Distribution of study participants according to Left ventricular Diastolic Dysfunction.**

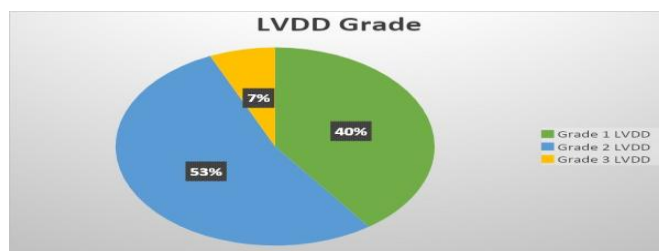


**Table 11: Distribution of study participants according to Left ventricular Diastolic Dysfunction grade.**

LVDD	Frequency	Percent
Grade 1 LVDD	12	40
Grade 2 LVDD	16	53.3
Grade 3 LVDD	2	6.7
Total	30	100.0

Among the 30 study participants with LVDD, Majority 53.3 % had Grade 2 LVDD and then 40 % were with Grade 1 LVDD, followed by which 6.7% participants were with Grade 3 LVDD.

**Fig.11: Pie chart showing Distribution of study participants according to Left ventricular Diastolic Dysfunction grade.**



**Table 12: Association between age category of study participants and diastolic dysfunction.**

Age category	DDF			Chi-square value ( $\chi^2$ )	df	P value
	Present	Absent	Total			
≤50 years	9 (50.0 %)	9 (50.0 %)	18 (100 %)	1.920	1	.166
>50 years	21(70.0 %)	9 (30.0 %)	30 (100 %)			

The above table shows association between age category and diastolic dysfunction, among study participants aged less than or equal to 50 years 50 % had diastolic dysfunction and among aged more than 50 years 70 % had diastolic dysfunction. This difference in diastolic dysfunction between age categories were statistically not significant.

**Table 13: Association between gender and diastolic dysfunction.**

Gender	DDF			Chi-square value ( $\chi^2$ )	df	P value
	Present	Absent	Total			
Male	8 (53.3 %)	7 (46.7 %)	15 (100.0 %)	0.782	1	0.376
Female	22 (66.7%)	11 (33.3 %)	33 (100.0 %)			

Out of 48 study participants who had diastolic dysfunction, 66.7 % female and 53.3 % male had diastolic dysfunction and this difference was not significant statistically.

**Table 14: Association between duration of diabetes of study participants and diastolic dysfunction.**

DM duration	DDF			Chi-square value ( $\chi^2$ )	df	P value
	Present	Absent	Total			
1 to 5 years	11 (45.8 %)	13 (54.2 %)	24 (100.0 %)	6.093	2	0.048
6 to 10 years	17 (77.7%)	5 (22.7 %)	22 (100.0 %)			
> 10 years	2 (100.0 %)	0 (0 %)	2 (100 %)			

The above shows association between duration of diabetes and diastolic dysfunction, among participants who had diabetes for more than 10 years 100 % had diastolic dysfunction. Among participants with diabetes duration between 6 to 10 years, 77.7 % had diastolic dysfunction and among participants with diabetes duration between 1 to 5 years, 45.8 % had diastolic dysfunction and this difference between three groups were statistically significant (p value 0.048).

**Table 15: Association between BMI categories of study participants and diastolic dysfunction.**

BMI	DDF			Chi-square value ( $\chi^2$ )	df	P value
	Present	Absent	Total			
Normal weight	13 (59.1 %)	9 (40.9 %)	22 (100.0 %)	1.891	2	0.389
Pre obese	11 (57.9 %)	8 (42.1 %)	19 (100.0 %)			
Obese	6 (85.7 %)	1 (14.3 %)	7 (100 %)			

Table 15 shows association between BMI and diastolic dysfunction, 85.7 % participants with obesity had diastolic dysfunction, 57.9 % with pre obesity had diastolic dysfunction and 59.1 % in normal weight had diastolic function. This difference in diastolic function between BMI categories was statistically not significant.

**Table 16: Association between HbA1c levels of study participants and diastolic dysfunction.**

Diastolic dysfunction	HbA1c				t	P value*
	N	Mean	Std. Deviation	Std. Error Mean		
Present	30	6.773	.3352	.0612	3.506	0.001
Absent	18	6.344	.5136	.1211		

\* p value based on independent sample t test.

The above shows association between diastolic dysfunction and HbA1c, participants with diastolic dysfunction had mean HbA1c of 6.773 ( $\pm 0.33$ ) and mean HbA1c of participants with no diastolic dysfunction was 6.344 ( $\pm 0.51$ ) and this difference was statistically significant with p value of 0.001.

#### IV. DISCUSSION

**Age and sex:** The mean age of study participants were 53.12 years  $\pm 8.183$ , the minimum age of the study participants was 36 years and maximum were 70 years. Majority 64 % of participants were aged more than 50 years, followed by 36 % aged less than or equal to 50 years. Female was majority study participants with 66% and followed by male participate with 34 %. **Duration of Diabetes Mellitus:** Regarding the duration of diabetes mellitus, 48 % were between 1-5 years followed by 44 % of participants were between 6 to 10 years and remaining 8 % were more than 10 years duration.

**Systolic and diastolic blood pressure:** Out of 50 participants, the mean SBP were 111 mmHg ( $\pm 7.354$ ) while mean diastolic blood pressure were 75.20 mmHg ( $\pm 5.436$ ).

**Blood sugar:** Out of 50 study participants, the mean fasting blood sugars were 154.60 ( $\pm 46.735$ ) with minimum fasting blood sugars were 68 mg/dl and maximum were 274 mg/dl, while post prandial blood sugars were 243.94 ( $\pm 75.520$ ) with minimum ppbs were 130 mg/dl and maximum were 434 mg/dl Among 50 study participants, the mean HbA1C were 6.628 ( $\pm 0.4540$ ), with minimum 6 and maximum 7.6.

**Lipid profile:** Among 50 study participants, the mean total cholesterol was 193.86 mg/dl ( $\pm 16.450$ ) with minimum cholesterol levels were 161 mg/dl and maximum cholesterol levels were 224 mg/dl, while the mean triglyceride levels were 135.84 mg/dl ( $\pm 22.051$ ) with minimum triglyceride levels were 100 mg/dl and maximum were 168 mg/dl. The mean LDL levels were 117.76 mg/dl ( $\pm 13.297$ ) with minimum 100 mg/dl and maximum were 150 mg/dl.

**Renal function test:** The mean Urea levels were 22.06 mg/dl ( $\pm 5.797$ ) with minimum urea levels were 14 mg/dl and maximum were 35 mg/dl.

**Fundus changes:** Among the study participants, 98 % had normal fundus, 2 % had grade 1 diabetic Retinopathy

**Diastolic dysfunction and association between risk factors and diastolic dysfunction**

Among the 30 study participants with LVDD, Majority 53.3 % had Grade 2 LVDD and then 40 % were with Grade 1 LVDD, followed by which 6.7% participants were with Grade 3 LVDD association between age category and diastolic dysfunction, among study participants aged less than or equal to 50 years 50 % had diastolic dysfunction and among aged more than 50 years 70 % had diastolic dysfunction. This difference in diastolic dysfunction between age categories were statistically not significant. Out of 48 study participants who had diastolic dysfunction, 66.7 % female and 53.3 % male had diastolic dysfunction and this difference was not significant statistically. Among participants who had diabetes for more than 10 years 100 % had diastolic dysfunction. Among participants with diabetes duration between 6 to 10 years, 77.7 % had diastolic dysfunction and among participants with diabetes duration between 1 to 5 years, 45.8 % had diastolic dysfunction and this difference between three groups were statistically significant (p value 0.048). In association between BMI and diastolic dysfunction, 85.7 % participants with obesity had diastolic dysfunction, 57.9 % with pre obesity had diastolic dysfunction and 59.1 % in normal weight had diastolic function. This difference in diastolic function between BMI categories was statistically not significant. In association between diastolic dysfunction and HbA1c, participants with diastolic dysfunction had mean HbA1c of 6.773 ( $\pm 0.33$ ) and mean HbA1c of participants with no diastolic dysfunction was 6.344 ( $\pm 0.51$ ) and this difference was statistically significant with p value of 0.001.



## V. CONCLUSION

Persons with type 2 diabetes mellitus should be screened with echocardiography for subclinical diastolic dysfunction. Due to the epidemiological transition of the population towards aging and more sedentary lifestyle, the prevalence of diabetes mellitus has been rapidly increasing and the prevalence of diabetic cardiomyopathy has been increased too. In the study conducted among 50 participants majority of the study participants that is 30 participants present with left ventricular diastolic dysfunction and hence screening the diabetic patients with ECHO would slow down the progression of diabetic cardiomyopathy and helps in appropriate management and cause significant reduction in the morbidity and mortality in patients with diabetes.

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