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A study of Left Ventricular Diastolic Dysfunction by Echocardiography in patients of Type II Diabetes Mellitus with or without Hypertension.

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Abstract:
Background: *Noninvasive assessment of diastolic filling by Doppler echocardiography provides important information about left ventricular status. Our study aims the prevalence of Left Ventricular Diastolic Dysfunction (LVDD) by Echocardiography in Type II DM patients with or without hypertension and also to study the probable factors associated with it for early detection, prevention and treatment of heart failure.*
Materials and Methods*: We did a prospective study in Department of Medicine at Dr. D. Y. Patil Hospital, Kolhapur from May 2012 to August 2014. We had studied left ventricular function of 100 randomly selected Diabetes Mellitus patients by echocardiography. These patients were divided into two groups, in one group comprising of 50 patients with Type II Diabetes Mellitus without hypertension (DM) were studied & in another group 50 patients having Type II Diabetes Mellitus with hypertension (DM + HTN) were studied. The diagnosis of Type II DM was done according to the criteria laid down by American Diabetes Association 2012. A detailed clinical history was taken using a structured questionnaire prepared by us for left ventricular function evaluation by echocardiography.*
Results*: Both groups showed male preponderance. Our study showed diastolic dysfunction in 68% of patients. The occurrence of incidence of Grade 3 or 4 left ventricular diastolic dysfunction increases with coexisting diabetes mellitus with hypertension. Aging individuals, male population, duration of diabetes, presence of hypertension were determinants for the occurrence of diastolic dysfunction. There was correlation of diastolic dysfunction with retinopathy as well. Early diagnosis and treatment of diabetic cardiomyopathy may improve systolic and diastolic functions of heart.*
Conclusion: *Diastolic dysfunction seems to be a prognostic marker in diabetic patients who have no prior cardiac illness. Our study exhibits that coexisting hypertension and diabetes mellitus in a patient have positive impact on left ventricular diastolic dysfunction. Early detection may help in the risk stratification of hypertensive & diabetic patients. Diabetes and hypertension should be kept in controlled and its consequences be avoided or delayed with a proper diet, doing physical activity, medication and regular screening and treatment for complications.*

Key Word: ***Echocardiography, Diabetes Mellitus, Hypertension, Left ventricular diastolic dysfunction, Retinopathy***

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I. Introduction

Diabetes Mellitus (DM) is a global health problem due to increased prevalence of obesity and physical inactivity. It is common and a serious disease with chronic complications and constitutes a substantial burden for both patient and health care system. Diabetes occurs when the body cannot effectively utilize the insulin it produces, or pancreas does not produce sufficient insulin, resulting in hyperglycemia. Adults with diabetes mellitus are at 2-3-fold increased risk of developing ischemic heart disease, stroke and over time leads to serious damage to many organs of the body. Globally the number of people with diabetes mellitus rose from 108 million in 1980 to 422 million in 2014 that means prevalence rose from 4.7% to 8.5%. [1] According to International Diabetes Federation, in 2019 approximately 463 million adults (20-79 years) were living with diabetes; estimated that by 2045 this will rise to 700 million. [2] Almost half of all deaths attributable to high blood glucose occur before the age of 70 years. World Health Organization estimates that diabetes was the seventh leading cause of death in 2016. [3]

Diastolic dysfunction is common in cardiac disease and contributes to the signs and symptoms of heart failure. [4] Studies have reported that the diastolic heart failure is ominous and comparable to heart failure with reduced ejection fraction. However, the importance of this public health problem has been under-recognized as it is

undiagnosed in most of the patients, resulting in a lack of optimal treatment in the community. [5] Diastolic dysfunction is associated with future occurrence of heart failure, is a predictor of cardiovascular morbidity and mortality in the general population, [6] and is associated with a reduced exercise performance in asymptomatic subjects.

Hypertension also is the leading cause of death worldwide and one of the world's great public health problems. Especially in the elderly, diabetes is often associated with arterial hypertension, which is in turn associated impaired diastolic dysfunction and unfavorable cardiovascular outcome. [7] Also, hypertension and diabetes both share comorbidities and conditions, like obesity and LV hypertrophy, that can impact LV structure and mechanics. [8] Therefore, there is an urgent need to prevent DM and its complications. Although there are studies available reporting the prevalence of diastolic dysfunction among diabetics but there is a wide prevalence range noted from these studies. Also, early screening and intervention will aid reducing the disease burden. In view of the above facts this study is being done to evaluate the individual and synergistic role of diabetes and hypertension on LV diastolic function.

II. Material And Methods

We did a prospective study, from May 2012 to August 2014, in Department of Medicine at Dr. D. Y. Patil Hospital, Kolhapur which included 100 randomly selected patients of Type II DM. These patients were divided into two groups, in one group 50 patients with Type II Diabetes Mellitus without hypertension (DM) were studied & in another group 50 patients having Type II Diabetes Mellitus with hypertension (DM + HTN) were studied. The diagnosis of Type II Diabetes Mellitus was done according to the criteria laid down by American Diabetes Association 2012. Our study aims to evaluate the prevalence of LVDD by Echocardiography in Type II DM patients with or without hypertension and also to study the probable factors associated with LVDD for early detection, prevention and treatment of heart failure.

Study Design: Prospective observational study

Study Location: Department of Medicine at Dr. D. Y. Patil Hospital, Kolhapur.

Study Duration: May 2012 to August 2014.

Sample size: 100 patients.

Sample size calculation: The target population was randomly selected. Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL).

Subjects & selection method: Patients were divided into two groups, in one group 50 patients with Type II Diabetes Mellitus without hypertension (DM) were studied & in another group 50 patients having Type II Diabetes Mellitus with hypertension (DM + HTN) were studied. The diagnosis of Type II Diabetes Mellitus was done according to the criteria laid down by American Diabetes Association 2012.

Inclusion criteria:

1. Type II DM diagnosed patients without Hypertension
2. Type II DM diagnosed patients with Hypertension

Exclusion criteria:

1. Patients having clinical and ECG evidence of IHD (Cardiomyopathies, Valvular heart disease, Pericardial disease,
2. Type I diabetes mellitus,
3. Endomyocardial diseases,
4. Infiltrative (amyloidosis) and
5. Non infiltrative diseases (e.g., idiopathic and hypertrophic cardiomyopathy).

Procedure methodology

All selected patients were evaluated for left ventricular function by Echocardiography. The echocardiography was done using a Esaote (Model 2014) machine by experienced physician trained in the field. The inbuilt software in the machine was used to calculate LV ejection fraction (EF). Pulse wave doppler derived mitral inflow velocities (E and A) were obtained by putting sample volume at the tip of mitral leaflets. E wave deceleration time (DT), isovolumic relaxation time (IVRT) was also obtained at the same time. DD was diagnosed and graded according to the values mentioned in the table below. Additionally, TDI was used to assess DD by putting the sample volume at septal and lateral mitral annulus. [9]

Tissue Doppler early diastolic mitral annular velocity (E"), which is relatively non-load dependent in patients with cardiac disease, is generally thought to be the best non-invasive estimate of LV relaxation. The longer it takes for the LV to relax, the lower is the E" velocity. The resulting E/E" ratio, has been validated as a reasonably reliable non-invasive indicator of LV filling pressure in patients with preserved LVEF. [10]

Table 1: Echo based diastolic dysfunction was graded as follows				
Parameter	**Normal**	**Gr I DD Impaired myocardial relaxation**	**Gr II DD pseudo normal pattern**	**Gr III or Gr IV DD restrictive filling irreversible**
E/A	1.0-1.5	< 1.0	1.0 - 1.5	>1.5
IVRT	70-90 ms	> 90 ms	< 90 ms	< 70 ms
DT	160-240 ms	>240	160-200	<160
E/E" (TDI)	< 8	>15	>15	>15
E and A Peak velocity of blood during early diastolic filling (E) and atrial contraction (A); IVRT Isovolumetric relaxation time; DT Deceleration time; E" septal early diastolic mitral annular motion as measured by doppler tissue imaging.				

Statistical analysis

Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Chi-square test were performed to test for differences in proportions of categorical variables between two groups. The level $P < 0.05$ was considered as the cutoff value or significance.

III. Result

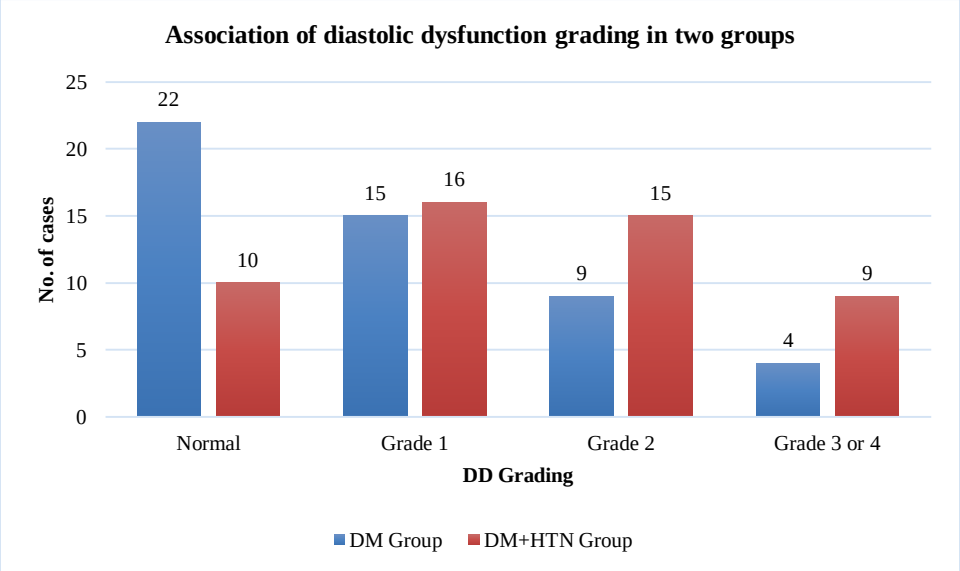
In our study, among DM group, diastolic function was normal in 44% cases, 30% cases had Grade 1 diastolic dysfunction, 18% cases had Grade 2 diastolic dysfunction & 8% cases had Grade 3 or 4 diastolic dysfunction. In DM+HTN group diastolic function was normal in 20% cases, 32% cases had Grade 1 diastolic dysfunction, 30% cases had Grade 2 diastolic dysfunction & 18% cases had Grade 3 or 4 diastolic dysfunction. (**Table 1**) (**Figure 1**)

Table 1: Association of diastolic dysfunction grading in two groups

DD Grading	DM Group	DM+HTN Group	Total no. of cases
Normal	22 (44%)	10 (20%)	32
Grade 1	15 (30%)	16 (32%)	31
Grade 2	9 (18%)	15 (30%)	24
Grade 3 or 4	4 (8%)	9 (18%)	13

The chi-square statistic is 7.9553. The p-value is .046944. The result is significant at p <0.05.

Figure 1: Association of diastolic grading in two groups

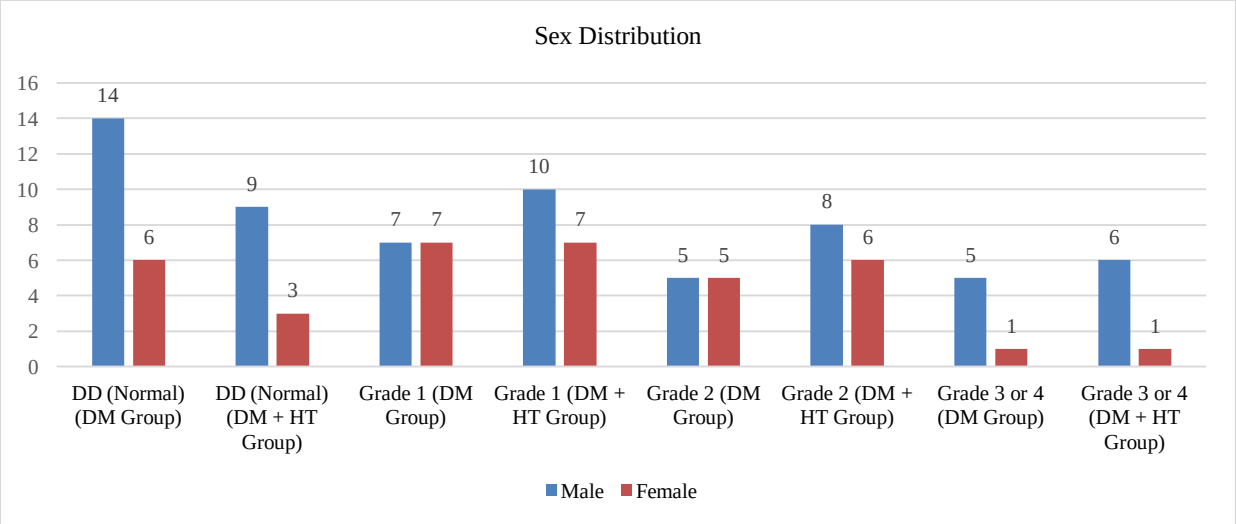


In our study, DM group had 62% Male patients and 38% were Female. In DM+HTN group 66% were Male and 34% were Female. Among males, diastolic function was normal in 36% cases, 26% cases had Grade 1 diastolic dysfunction whereas 21% cases had Grade 2 diastolic dysfunction & 17% cases had Grade 3 or 4 diastolic dysfunction. Among females, diastolic function was normal in 25% cases, 38% cases had Grade 1 diastolic dysfunction whereas 31% cases had Grade 2 diastolic dysfunction & 6% cases had Grade 3 or 4 diastolic dysfunction. (**Table 2**) (**Figure 2**)

Table 2: Diastolic dysfunction in relation to sex distribution

Sex	DD (Normal) (DM Group)	DD (Normal) (DM + HT Group)	Grade 1 (DM Group)	Grade 1 (DM + HT Group)	Grade 2 (DM Group)	Grade 2 (DM + HT Group)	Grade 3 or 4 (DM Group)	Grade 3 or 4 (DM + HT Group)	(DM Group) + (DM + HT Group) = Total
Male	14 (21.8%)	9 (14.06%)	7 (10.9%)	10 (15.6%)	5 (7.8%)	8 (12.5%)	5 (7.8%)	6 (9.3%)	64
Female	6 (16.66%)	3 (8.33%)	7 (19.4%)	7 (19.4%)	5 (13.88%)	6 (16.66%)	1 (2.7%)	1 (2.7%)	36
Total cases in each group	20	12	16	15	10	14	6	7	100
	DD absent in 32 cases		Grade 1 DD in 31 cases		Grade 2 DD in 24 cases		Grade 3 or 4 DD in 13 cases		

Figure 2: Diastolic dysfunction in relation to sex distribution

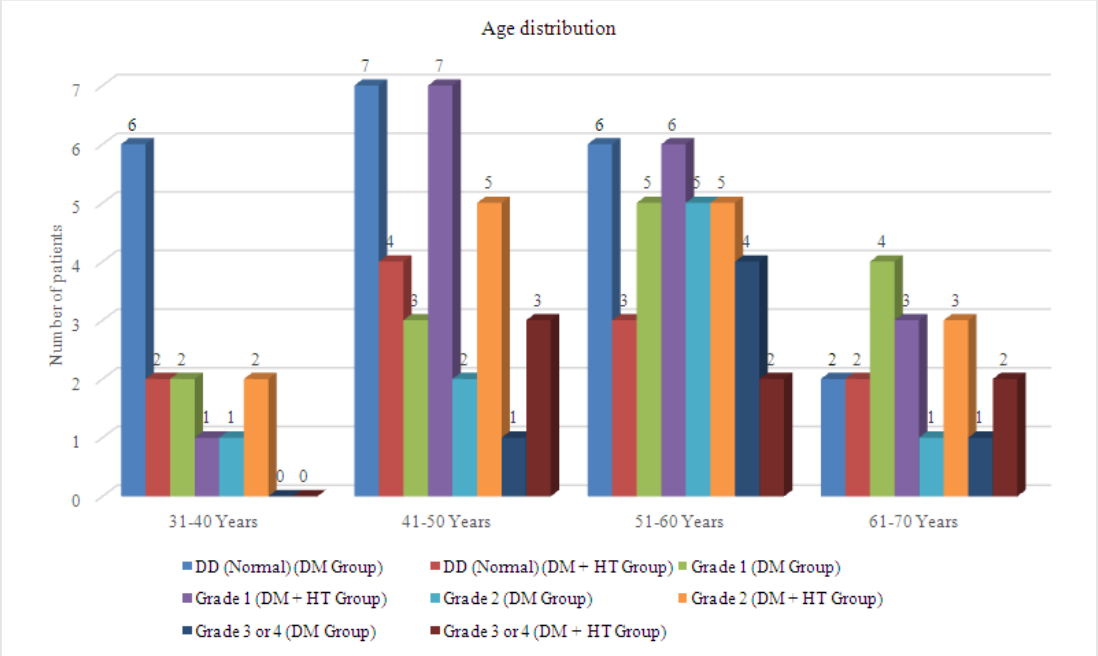


In our study, the minimum age was 31 years and the maximum age observed was 70 years. Maximum numbers of cases observed were in the 51-60 years age group in patients with Diabetes Mellitus. Patients with both Diabetes and hypertension had maximum cases among 41-50 years age group. Among 31-40 years age group, diastolic function was normal in 58% cases, 21% cases had Grade 1 diastolic dysfunction whereas 21% cases had Grade 2 diastolic dysfunction & no cases were seen in Grade 3 or 4 diastolic dysfunction. Among 41-50 years age group, diastolic function was normal in 35% cases, 31% cases had Grade 1 diastolic dysfunction whereas 22% cases had Grade 2 diastolic dysfunction & 12% cases had Grade 3 or 4 diastolic dysfunction. Among 51-60 years age group, diastolic function was normal in 25% cases, 31% cases had Grade 1 diastolic dysfunction whereas 27% cases had Grade 2 diastolic dysfunction & 17% cases had Grade 3 or 4 diastolic dysfunction. Among 61-70 years age group, diastolic function was normal in 22% cases, 39% cases had Grade 1 diastolic dysfunction whereas 22% cases had Grade 2 diastolic dysfunction & 17% cases had Grade 3 or 4 diastolic dysfunction. (**Table 3**) (**Figure 3**)

Table 3: Diastolic dysfunction in relation to age distribution

Age	DD (Normal) (DM Group)	DD (Normal) (DM + HT Group)	Grade 1 (DM Group)	Grade 1 (DM + HT Group)	Grade 2 (DM Group)	Grade 2 (DM + HT Group)	Grade 3 or 4 (DM Group)	Grade 3 or 4 (DM + HT Group)	(DM Group) + (DM + HT Group) = Total
31-40 Years	6 (42.8%)	2 (14.21%)	2 (14.21%)	1 (7.14%)	1 (7.14%)	2 (14.28%)	0	0	9 + 5 = 14
41-50 Years	7 (21.87%)	4 (12.5%)	3 (9.37%)	7 (21.85%)	2 (6.25%)	5 (15.62%)	1 (3.12%)	3 (9.37%)	13 + 19 = 32
51-60 Years	6 (16.66%)	3 (8.33%)	5 (13.88%)	6 (16.66%)	5 (13.88%)	5 (13.88%)	4 (11.11%)	2 (5.55%)	20 + 16 = 36
61-70 Years	2 (11.11%)	2 (11.11%)	4 (22.22%)	3 (16.66%)	1 (5.55%)	3 (16.66%)	1 (5.55%)	2 (11.11%)	8 + 10 = 18
Total cases in each group	21	11	14	17	9	15	6	7	100
	DD absent in 32 cases		Grade 1 DD in 31 cases		Grade 2 DD in 24 cases		Grade 3 or 4 DD in 13 cases		

Figure 3: Diastolic dysfunction in relation to age distribution



We have also classified patients in our study, as newly detected diabetes, patients having diabetes for 6 months to 3 years, patients having diabetes for 3 years to 5 years & patients having diabetes for more than 5 years. Among them, in DM group 30% cases had diabetes duration of 3years to 5 years, followed by 28% in newly detected cases & in diabetes of duration of more than 5years lastly 14% cases who had diabetes of duration of 6months to3 years. In DM+HTN group, 44% cases had diabetes duration of more than 5years followed by 30% cases for duration of diabetes between 3 years to 5 years; 20% cases had diabetes duration of 6months to 3 years, whereas 6% patients had newly detected diabetes. (**Table 4**) (**Figure 4**)

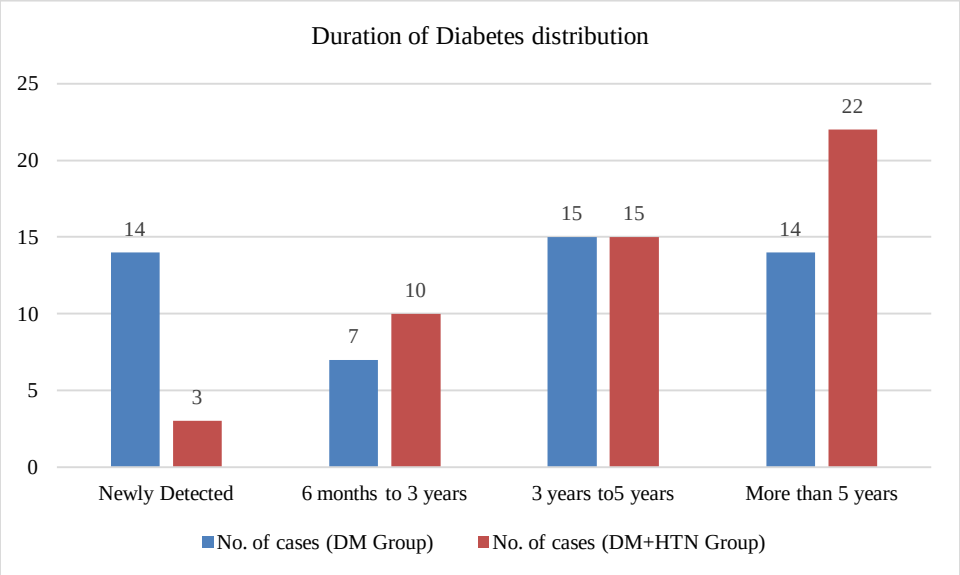
Table 4: Case distribution depending upon Duration of diabetes

Duration of Diabetes	No. of cases (DM Group)	No. of cases (DM+HTN Group)
Newly Detected	14 (28%)	3 (6%)
6 months to 3 years	7 (14%)	10 (20%)

3 years to5 years	15 (30%)	15 (30%)
More than 5 years	14 (28%)	22 (44%)

The chi-square statistic is 9.4248. The p-value is 0.024145. The result is significant

Figure 4: Case distribution depending upon Duration of diabetes



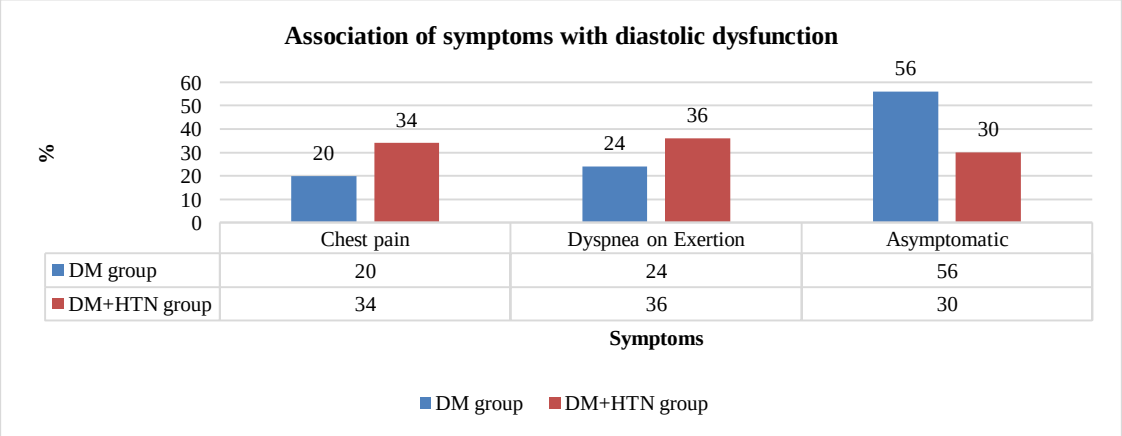
In our study**,** among DM group 20% patients had chest pain, 24% patients had dyspnea on exertion & 56% were asymptomatic. Among DM+HTN group 34%patients had chest pain, 36% patients had dyspnea on exertion & 30% were asymptomatic. (**Table 5**) (**Figure 5**)

Table 5: Association of symptoms with diastolic dysfunction

Symptoms	**DM group**	**DM+HTN group**
Chest pain	10 (20%)	17 (34%)
Dyspnea on Exertion	12 (24%)	18 (36%)
Asymptomatic	28 (56%)	15 (30%)

The chi-square statistic is 6.945. The p-value is .031039. The result is significant

Figure 5: Association of symptoms with diastolic dysfunction



In our study, among DM group 28% patients had mild retinopathy, 16% patients had moderate retinopathy, 6% patients had severe retinopathy&50% were without retinopathy. Among DM+HTN group 22%

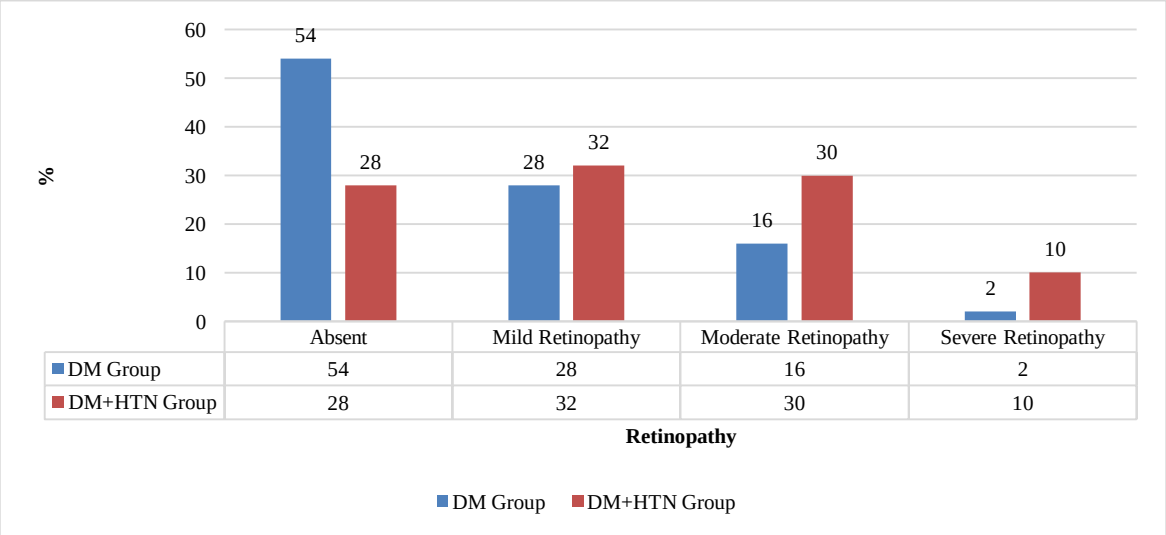
patients had mild retinopathy, 28% patients had moderate retinopathy, 8% patients had severe retinopathy&42% were without retinopathy. (**Table 6**) (**Figure 6**)

Table 6: Association of retinopathy with diastolic dysfunction

Retinopathy	DM Group	DM+HTN Group
Absent	27 (54%)	14 (28%)
Mild Retinopathy	14 (28%)	16 (32%)
Moderate Retinopathy	8 (16%)	15 (30%)
Severe Retinopathy	1 (2%)	5 (10%)

The chi-square statistic is 9.0524. The p-value is .028602. The result is significant at $p < .05$.

Figure 6: Association of retinopathy with diastolic dysfunction



IV. Discussion

It is well established that diabetes can lead to heart failure together with other micro vascular complications. Along with diabetes, hypertension is also important factor in development of heart failure. Left ventricular diastolic dysfunction represents the first stage of heart failure so it becomes very important to early examination of ventricular function in individual with diabetes mellitus and hypertension. We studied 100 patients of Type II Diabetes Mellitus with or without hypertension. These patients were divided into two groups, 50 patients in each group, (i)Type II Diabetes Mellitus without hypertension (DM) & (ii) Type II Diabetes Mellitus with hypertension (DM + HTN)

In our study, among diabetes group diastolic function was normal in 44% cases, 30% cases had Grade 1 diastolic dysfunction, 18% cases had Grade 2 diastolic dysfunction & 8% cases had Grade 3 or 4 diastolic dysfunction. Among diabetes & hypertension group diastolic function was normal in 20% cases, 32% cases had Grade 1 diastolic dysfunction, 30% cases had Grade 2 diastolic dysfunction & 18% cases had Grade 3 or 4 diastolic dysfunction. Nikhil M Dikshit *et al* [11] had 66% incidence of diastolic dysfunction in diabetic patients. Study by Shrestha NR & Sharma SK *et al* [12], Vinereanu D *et al* [13] had similar findings to our study. Study by Nagabhushana *et al* [14] showed 44% hypertensive patients having diastolic dysfunction. Study by Maurizio Galderisi *et al* [15] showed similar findings among diabetic and hypertensive groups.

In our study, diabetic group had maximum patients in the 51-60 years age group. 62% patients were Male and 38% were female. Among diabetic and hypertensive group, maximum patients were observed in 41-50 years age group, 66% patients were Male and 34% were female. Male preponderance was more among diabetic and hypertensive group.Study by Jain *et al*[16] in diabetes mellitus patients had 70% males and 30% females. Most of the subjects were between 51 – 60 years of age and comprised 40 % of sample size, similar to our study. Study of Wojciech Kosmala *et al*[17] showed 60% male population and 40% female population, most patients were observed in 50-55 years age group similar to ours.

In our study, diabetic patient group has 30% patients who had diabetes of duration 3 years to 5 years, 28% patients had duration of more than 5 years, 14% patients had duration 6 months to 3 yrs & 28% patients had newly detected diabetes. Among diabetes with hypertension patients, 44% patients are in more than 5 yrs group, 30% patients in duration of 3 years to 5 years, 20% patients in 6 months to 3 yrs years duration & 6% patients were in newly detected group. 56% patients had Stage 1 hypertension & 44% patients had Stage 2 hypertension. Patil VC *et al* [18] showed that most patients had duration of diabetes of more than 10 years. Whereas study by Nagabhushana *et al* [14] showed that average duration of hypertension was more than 3 years. 64% patients had Stage 1 hypertension & 36% patients had Stage 2 hypertension.

In our study, among diabetes group 20% patients had chest pain, 24% patients had dyspnea on exertion & 56% were asymptomatic. Among diabetes & hypertension group 34% patients had chest pain, 36% patients had dyspnea on exertion & 30% were asymptomatic. Maurizio Galderisi *et al*[15] had 50% asymptomatic patients. Commonest symptom was dyspnea.

Diabetic retinopathy is an important cause of blindness, and occurs as a result of long-term accumulated damage to the small blood vessels in the retina. Diabetes is the cause of 2.6% of global blindness.[19] In our study, among diabetes group 28% patients had mild retinopathy, 16% patients had moderate retinopathy, 6% patients had severe retinopathy & 50% were without retinopathy. Among diabetes & hypertension group 32% patients had mild retinopathy, 30% patients had moderate retinopathy, 10% patients had severe retinopathy & 28% were without retinopathy. LM Ruta *et al*[20] showed that 60% patients had presence of retinopathy among diabetic patients.

V. Conclusion

Myocardial involvement in diabetes may occur early in the course of disease, initially impairing early diastolic relaxation and when more extensive, it causes decreased myocardial contraction. More frequent incidence of heart failure in diabetics even in the absence of any other underlying heart disease, leads to presumption that Diabetes Mellitus unfavourably affects the heart muscle by its complications. Diastolic dysfunction seems to be a prognostic marker in diabetic and hypertensive patients who have no prior cardiac illness. In this study, prevalence of diastolic dysfunction was more among males. Grade 3 or 4 diastolic dysfunction was also more among males. Most of the newly detected Diabetic & hypertensive patients had normal diastolic function. Duration of diabetes & hypertension was directly proportional to prevalence of diastolic dysfunction. The combination of hypertension and diabetes exerts a synergistic effect on LVDD and results in higher LV filling pressure than either condition alone. Male predominance, aging individuals, duration of diabetes, presence and severity of hypertension were determinants for the occurrence of diastolic dysfunction There was correlation of diastolic dysfunction with retinopathy as well. However further study may through more light in this particular area. Early diagnosis and treatment of diabetic cardiomyopathy may improve systolic and diastolic functions of heart. So, Diabetes and hypertension should be kept in controlled and its consequences be avoided or delayed with a proper diet, doing physical activity, medication and regular screening and treatment for complications.

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