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# Assessment of Left ventricular diastolic dysfunction in patients with or without hypertension of Type II Diabetes Mellitus

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**Abstract** **Original Research Article**

***Background:*** 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. Non-invasive assessment of diastolic filling by Doppler echocardiography provides important information about left ventricular status. ***Objective:*** To assessment of left ventricular diastolic dysfunction in patients with or without hypertension of Type II Diabetes Mellitus. ***Materials and Methods:*** A prospective observational study was carried out at Department of Cardiology, Sher-E-Bangla Medical College, Barishal, Bangladesh from February 2019 to January 2020. We had studied left ventricular function of 102 randomly selected Diabetes Mellitus patients by echocardiography. These patients were divided into two groups, in one group comprising of 51 patients with Type II Diabetes Mellitus without hypertension (DM) were studied & in another group 51 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 are avoided or delayed with a proper diet, doing physical activity, medication and regular screening and treatment for complications.

**Keywords:** Echocardiography, Diabetes Mellitus, Hypertension, Left ventricular diastolic dysfunction.



## 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. The recurrence of diabetes mellitus is enormously expanding on the planet about 40% of patients with diabetes present with diastolic dysfunction and pervasiveness of diabetes in grown-ups overall was assessed to be 4% in 1995 and to ascend to 5.4% continuously 2025 and will be a 42% expansion in diabetic patients in the created nations and 70% expansion in the creating nations constantly 2025 [1]. Diastolic dysfunction is related with low mortality

which represents roughly 8% however high horribleness, in this manner the death rate hazard is expanded by two to four folds [2]. Aging, corpulence, diabetes mellitus, cardiovascular ischemia, hypertension, aortic stenosis, myocardial illnesses, endomyocardial clutters, pericardial emission and constrictive pericarditis are different normal reasons for left ventricular diastolic dysfunction [3]. The higher predominance of diastolic dysfunction and cardiovascular breakdown with saved discharge part (HFpEF) in type-2 diabetes patients appears to show the effect of diabetes in the improvement of these conditions and is related with changes in heart digestion, structure, work and the instruments adding to myocardial dysfunction in diabetes incorporate hyperglycemia, lipotoxicity, insulin obstruction and weight is a high hazard marker, an increment in weight, moreover associate with diabetes, hypertension, hyperlipidemia and impacts heart capacity and structure with developing age [4]. Diastolic dysfunction is one of the most widely recognized cardiovascular issue which prompts clinical crisis, the mass of left ventricle is thickened with insufficient filling of ventricles raising the weight inclination of blood in the aspiratory vessels which brings about the transudate liquid spillage into the lung alveoli causing pneumonic edema which lessens the degree of oxygen in blood creating brevity of breath and even passing if not identified and treated promptly [5]. Diastole is the period during which the myocardium does not have its capacity to deliver power and continues to an unstressed measurement and quality bringing about deficiency of these courses causing diastolic dysfunction and the progressions in diastolic capacity can be available without cardiovascular breakdown with or without systolic function [6]. 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.

## MATERIAL AND METHODS

A prospective observational study was carried out at Department of Cardiology, Sher-E-Bangla Medical College, Barishal, Bangladesh from February 2019 to January 2020 which included 102 randomly selected patients of Type II DM. These patients were divided into two groups; in one group 51 patients with Type II Diabetes Mellitus without hypertension (DM) were studied & in other group 51 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. Patients were divided into two groups; in one group 51 patients with Type II Diabetes Mellitus without hypertension (DM) were studied & in other group 51 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

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 an Esaote (SAMSUNG S-40) machine by experienced physician trained in the field. The built-in 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 (Table 1). 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.

## RESULTS

In our study, among DM group, diastolic function was normal in 45.09% cases, 29.41% cases had Grade 1 diastolic dysfunction, 17.64% cases had Grade 2 diastolic dysfunction & 7.84% cases had Grade 3 or 4 diastolic dysfunction. In DM+HTN group diastolic function was normal in 19.60% cases, 33.33% cases had Grade 1 diastolic dysfunction, 29.41% cases had Grade 2 diastolic dysfunction & 17.64% cases had Grade 3 or 4 diastolic dysfunction (Table 2).

**Table 2: Association of Diastolic Dysfunction Grading in Two Groups (N=102)**

| DD Grading | DM Group | DM+HTN Group | Total no. of cases |
|---|---|---|---|
| Normal | 23 (45.09%) | 10 (19.60%) | 33 |
| Grade 1 | 15 (29.41%) | 17 (33.33%) | 32 |
| Grade 2 | 9 (17.64%) | 15 (29.41%) | 24 |
| Grade 3 or 4 | 4 (7.84%) | 9 (17.64%) | 13 |

The p-value is 0.046. The result is significant at p <0.05.

In our study, DM group had 62.75% Male patients and 37.25% were Female. In DM+HTN group 64.70% were Male and 35.30% were Female. Among males, diastolic function was normal in 36.36% cases, 27.27% cases had Grade 1 diastolic dysfunction whereas 19.69% cases had Grade 2 diastolic dysfunction & 16.66% cases had Grade 3 or 4 diastolic dysfunction. Among females, diastolic function was normal in 25% cases, 38.88% cases had Grade 1 diastolic dysfunction whereas 30.55% cases had Grade 2 diastolic dysfunction & 5.55% cases had Grade 3 or 4 diastolic dysfunction (Table 3).

**Table 3: Diastolic Dysfunction in Relation to Sex Distribution (N=102)**

| 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 | 15(22.72%) | 9(13.63%) | 7(10.60%) | 11(16.66 %) | 5(7.57%) | 8(12.12%) | 5(7.57% ) | 6(9.09%) | 66 |
| 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 | 21 | 12 | 14 | 18 | 10 | 14 | 6 | 7 | 102 |
| | DD absent in 33 cases | | Grade 1 DD in 32 eases | | Grade 2 DD in 24 cases | | Grade 3 or 4 DD in 13 Cases | | |

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 5.14% cases, 21.42% cases had Grade 1 diastolic dysfunction whereas 21.42% 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 35.29% cases, 32.35% cases had Grade 1 diastolic dysfunction whereas 20.58% cases had Grade 2 diastolic dysfunction & 11.76% cases had Grade 3 or 4 diastolic dysfunction. Among 51-60 years age group, diastolic function was normal in 25% cases, 30.55% cases had Grade 1 diastolic dysfunction whereas 27.77% cases had Grade 2 diastolic dysfunction & 16.66% cases had Grade 3 or 4 diastolic dysfunction. Among 61-70 years age group, diastolic function was normal in 22.22% cases, 38.88% cases had Grade 1 diastolic dysfunction whereas 22.22% cases had Grade 2 diastolic dysfunction & 16.66% cases had Grade 3 or 4 diastolic dysfunction (Table 4).

**Table 4: Diastolic Dysfunction in Relation to Age Distribution (N=102)**

| 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 | 8(23.52%) | 4(11.76%) | 3(8.82%) | 8(23.52%) | 2(5.88%) | 5(14.70%) | 1(2.94%) | 3(8.82%) | 14+20=34 |
| 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 | 22 | 11 | 14 | 18 | 9 | 15 | 6 | 7 | 102 |
| | DD absent in 33 cases | | Grade 1 DD in 32 eases | | Grade 2 DD in 24 cases | | Grade 3 or 4 DD in 13 Cases | | |

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 31.37% cases had diabetes duration of 3years to 5 years, followed by 27.45% in newly detected cases & in diabetes of duration of more than 5years lastly 13.72% cases who had diabetes of duration of 6 months to3 years. In DM+HTN group, 45.09% cases had diabetes duration of more than 5years followed by 29.41% cases for duration of diabetes between 3 years to 5 years; 19.60% cases had diabetes duration of 6months to 3 years, whereas 6% patients had newly detected diabetes (Table 5).

**Table 5: Case Distribution Depending Upon Duration of Diabetes (N=102)**

| Duration of Diabetes | No. of cases (DM Group) | No. of cases (DM+HTN Group) |
|---|---|---|
| Newly Detected | 14 (27.45%) | 3 (5.88%) |
| 6 months to 3 years | 7 (13.72%) | 10 (19.60%) |
| 3 years to5 years | 16 (31.37%) | 15 (29.41%) |
| More than 5 years | 14 (27.45%) | 23 (45.09%) |

The p-value is 0.02. The result is significant.

In our study**,** among DM group 19.60% patients had chest pain, 23.52% patients had dyspnea on exertion & 56.86% were asymptomatic. Among DM+HTN group 33.33%patients had chest pain, 37.25% patients had dyspnea on exertion & 29.41% were asymptomatic (Table 6).

**Table 6: Association of symptoms with diastolic dysfunction (N=102)**

| Symptoms | DM group | DM+HTN group |
|---|---|---|
| Chest pain | 10 (19.60%) | 17 (33.33%) |
| Dyspnea on Exertion | 12 (23.52%) | 19 (37.25%) |
| Asymptomatic | 29 (56.86%) | 15 (29.41%) |

The p-value is 0.03. The result is significant.

In our study, among DM group 27.45% patients had mild retinopathy, 15.68% patients had moderate retinopathy, 1% patients had severe retinopathy & 54.90% were without retinopathy. Among DM+HTN group 33.33% patients had mild retinopathy, 29.41% patients had moderate retinopathy, 5% patients had severe retinopathy & 27.46% were without retinopathy (Table 7).

**Table 7: Association of retinopathy with diastolic dysfunction (N=102)**

| Retinopathy | DM Group | DM+HTN Group |
|---|---|---|
| Absent | 28 (54.90) | 14 (27.45%) |
| Mild Retinopathy | 14 (27.45%) | 17 (33.33%) |
| Moderate Retinopathy | 8 (15.68%) | 15 (29.41%) |
| Severe Retinopathy | 1 (1.96%) | 5 (9.80%) |

The p-value is .028. The result is significant at $p<0.05$.

## DISCUSSION

Left Ventricular Diastolic dysfunction is a risk factor for the development of congestive heart failure. In our study, we demonstrated that in a community diabetes and hypertension have an independent positive impact on LV diastolic function. We showed that diabetes and hypertension were independently associated with a higher E/E′ ratio, an index of LV end-diastolic pressure. The finding of a higher LV end-diastolic pressure when diabetes and hypertension coexist, compared with either condition alone, could explain in part the additional risk of developing heart failure in patients with combined diabetes and hypertension compared with patients with hypertension alone [10]. 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 102 patients of Type II Diabetes Mellitus with or without hypertension. These patients were divided into two groups, 51 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 45.09% cases, 29.41% cases had Grade 1 diastolic dysfunction, 17.64% cases had Grade 2 diastolic dysfunction & 7.84% cases had Grade 3 or 4 diastolic dysfunction. Among diabetes & hypertension group diastolic function was normal in 19.60% cases, 33.33% cases had Grade 1 diastolic dysfunction, 29.41% cases had Grade 2 diastolic dysfunction & 17.64% 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. 62.75% patients were Male and 37.25% were female. Among diabetic and hypertensive group, maximum patients were observed in 41- 50 years age group, 64.70% patients were Male and 35.30% 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 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. In our study, diabetic patient group has 31.37% patients who had diabetes of duration 3 years to 5 years, 27.45% patients had duration of more than 5 years, 14% patients had duration 6 months to 3 yrs & 27.45% patients had newly detected diabetes. Among diabetes with hypertension patients, 45.09% patients are in more than 5 yrs group, 29.41% patients in duration of 3 years to 5 years, 19.60% patients in 6 months to 3 years duration & 5.88% 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 27.45% patients had mild retinopathy, 15.68% patients had moderate retinopathy, 1% patients had severe retinopathy & 54.90% were without retinopathy. Among diabetes & hypertension group 33.33% patients had mild retinopathy, 29.41% patients had moderate

retinopathy, 9.80% patients had severe retinopathy & 29.41% were without retinopathy. LM Ruta *et al*, [20] showed that 60% patients had presence of retinopathy among diabetic patients.

## 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 are avoided or delayed with a proper diet, doing physical activity, medication and regular screening and treatment for complications. 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 are avoided or delayed with a proper diet, doing physical activity, medication and regular screening and treatment for complications.

## REFERENCES


1. Hameedullah, F., M, Khan., S. B. & Hafizullah, M. (2010). Prevalence of asymptomatic left ventricular diastolic dysfunction in normotensive type 2 diabetic patients. JPMI, 24(3), 188-192.
2. Biering-Sørensen, T., Biering-Sørensen, S. R., Olsen, F. J., Sengeløv, M., Jørgensen, P. G., Mogelvang, R., ... & Jensen, J. S. (2017). Global longitudinal strain by echocardiography predicts long-term risk of cardiovascular morbidity and mortality in a low-risk general population: the Copenhagen City Heart Study. *Circulation: Cardiovascular Imaging*, *10*(3), e005521.
3. Laflamme, D. (2018). *Cardiology: A Practical Handbook*. CRC Press.
4. Paulus, W. J., & Tschöpe, C. (2013). A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. *Journal of the American College of Cardiology*, *62*(4), 263-271.
5. Nasir, M., Hyder, S. N., & Hassan, A. (2016). Frequency of Left Ventricle Diastolic Dysfunction in Asymptomatic Type II Diabetic Patients. *Pakistan Journal of Medical & Health Sciences*, *10(3)*, 905-908.
6. Josephson, M. E. (2015). *Josephson's clinical cardiac electrophysiology*. Lippincott Williams & Wilkins.
7. Levy, D., Larson, M. G., Vasan, R.S., Kannel, W.B., & Ho, K. K. (1996). The progression from hypertension to congestive heart failure. J Am Med Assoc, 275, 1557–1562.
8. Palmieri, V., Bella, J. N., Arnett, D. K., Liu, J. E., Oberman, A., Schuck, M. Y., ... & Devereux, R. B. (2001). Effect of type 2 diabetes mellitus on left ventricular geometry and systolic function in hypertensive subjects: Hypertension Genetic Epidemiology Network (HyperGEN) study. Circulation, 103(1), 102-107.
9. Oh, J.K., Seward, J.B., & Tajik, A.J. (2006). Assessment of diastolic function and diastolic heart failure. The Echo Manual. 3rd edition, New Delhi: Wolters Kluwer Health (India) Pvt. Ltd; p120-142.
10. Sohn, D. W., Chai, I. H., Lee, D. J., Kim, H. C., Kim, H. S., Oh, B. H., ... & Lee, Y. W. (1997). Assessment of mitral annulus velocity by Doppler tissue imaging in the evaluation of left ventricular diastolic function. *Journal of the American College of Cardiology*, *30*(2), 474-480.
11. Dikshit, N. M., Wadia, P. Z., & Shukla, D. K. (2013). Diastolic dysfunction in diabetes mellitus. *Natl J Med Res*, *3*(July-September (3), 249-252.
12. Shrestha, N. R., Sharma, S. K., & Karki, P. (2009). Echo evaluation of Diastolic function in Asymptomatic type 2 Diabetes, a Cross sectional study. *Journal Nepal Medical Association*, *48*(173), 20-3.
13. Vinereanu, D., Nicolaides, E., Tweddel, A. C., MÄDLER, C. K., Holst, B., Boden, L. E., ... & Fraser, A. G. (2003). Subclinical left ventricular dysfunction in asymptomatic patients with Type II diabetes mellitus, related to serum lipids and glycated haemoglobin. *Clinical Science*, *105*(5), 591-599.
14. Nagabhushana, S., Kumar, A., Ranganatha, M., & Aravindh, C. L. (2014). STUDY OF DIASTOLIC FUNCTION IN ASYMPTOMATIC HYPERTENSIVES IN TERTIARY CARE CENTRE. *Journal of Evolution of Medical and Dental Sciences*, *3*(4), 907-921.
15. Galderisi, M. (2011). Diagnosis and management of left ventricular diastolic dysfunction in the hypertensive patient. *American journal of hypertension*, *24*(5), 507-517.
16. Jain, K., Palange, A. A., LalKakrani, A., & Dhanorkar, A. S. (2018). Left ventricular diastolic dysfunction in asymptomatic type 2 diabetes mellitus patients. *Int J Res Med Sci*, *6*(1), 240-246. https://doi.org/10.18203/2320-6012.ijrms20175727
17. Kosmala, W., Kucharski, W., Przewlocka-Kosmala, M., & Mazurek, W. (2004). Comparison of left ventricular function by tissue Doppler imaging in patients with diabetes mellitus without systemic hypertension versus diabetes mellitus with systemic hypertension. *The American journal of cardiology*, *94*(3), 395-399.
18. Patil, V. C., Shah, K. B., Vasani, J. D., Shetty, P., & Patil, H. V. (2011). Diastolic dysfunction in

asymptomatic type 2 diabetes mellitus with normal systolic function. *Journal of cardiovascular disease research*, *2*(4), 213-222. https://doi.org/10.4103/0975- 3583.89805

19. Bourne, R. R., Stevens, G. A., White, R. A., Smith, J. L., Flaxman, S. R., Price, H., ... & Vision Loss Expert Group. (2013). Causes of vision loss worldwide, 1990–2010: a systematic analysis. *The lancet global health*, *1*(6), e339-e349. doi:10.1016/S2214-109X(13)70113-X
20. Ruta, L. M., Magliano, D. J., Lemesurier, R., Taylor, H. R., Zimmet, P. Z., & Shaw, J. E. (2013). Prevalence of diabetic retinopathy in Type 2 diabetes in developing and developed countries. *Diabetic medicine*, *30*(4), 387-398.