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Diastolic Dysfunction in Normotensive Patients with Diabetes Mellitus- A Double Blind Randomised Prospective Multicentre Study in North India

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Results: In our Study, 72 % of the patients had diabetes for a duration of less than ten years and, 28 % of the patients had more than ten years. 20% had Body Mass Index within Normal Range but Impaired in remaining 80%.

Keywords: diabetes, hypertension, echocardiography, ventricle.

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Results: In our Study, 72 % of the patients had diabetes for a duration of less than ten years and, 28 % of the patients had more than ten years. 20% had Body Mass Index within Normal Range but Impaired in remaining 80%. On Echocardiography, E/A ratio that is Peak velocity of early mitral flow/ Peak velocity of late mitral flow was less than 1 in 85 % of cases where as it was between 1 to 2 in the remaining 15 % of cases. IVRT that is Isovolumetric Relaxation Time was greater than 100 millisecond in 65% of cases where as it was between 60 and 100 in the remaining 35% of cases. Moreover, Deacceleration Time of E (Peak velocity of early mitral flow) was greater than 200 milliseconds in 69 % of cases, whereas it was between 150 and 200 milliseconds in the remaining 31 %.

Conclusion: Left Ventricular Diastolic Dysfunction in normotensive patients with Diabetes without evidence of coronary heart disease is higher than previously suspected especially, in North India. Conventional echocardiography is a simple, economical test for detecting Left Ventricular dysfunction in these patients.

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I. INTRODUCTION

The term Diabetes mellitus which in Greek means "to run through" or "Siphon," was first coined by Arataeus of Cappadocia in 2nd century AD as a generic description for conditions causing increased urine output. Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and, protein metabolism associated with an absolute or relative deficiency in insulin secretion and insulin action, which is modulated by genetic and environmental factors resulting in micro and macroangiopathy. Important differences in the types and frequency of Diabetes mellitus and its complications have been reported between countries as well as ethnic and cultural groups.¹ Indians are genetically more susceptible to Diabetes mellitus compared to other races. India will have the largest number of diabetic subjects in the world by 2025 and one out of 5 diabetic subjects in the world will be an Indian. India is going to be the "Diabetic capital of the world".^{1,2}

Subclinical abnormalities of left ventricular function are recognized in both Type 1 and Type 2 diabetes mellitus. Studies using Doppler echocardiography have confirmed the findings of abnormal diastolic function as an early indicator of cardiac involvement in asymptomatic patients with Type 1 or Type 2 diabetes mellitus.³ The term 'diabetic cardiomyopathy' has been introduced for this condition. It has been suggested that microangiopathic lesions of the myocardium, altered composition and, fibrosis of myocardial interstitium and accumulation of lipids in myocardial cells are involved in the pathogenesis of diabetic cardiomyopathy.⁴ In 2001, Nichols et al. reported on the close link between diabetes and heart failure.⁵

II. MATERIAL AND METHODS

Our was a prospective study conducted across four centers in different states in North India. The present study was approved by the ethical committee of the Department of Cardiology, Hindu Rao Hospital, North Delhi Municipal Corporation medical college, New Delhi. 2500 Patients diagnosed as suffering from

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Diabetes Mellitus (either type 1 or type 2), who, were normotensive but older than 18 years were selected randomly without awareness of both the clinician and the patient (double-blind). Diabetes was diagnosed as per ADA guidelines 2018. Patients age less than 18 years who were either Hypertensive or suffering from Congestive Heart Failure/Coronary Heart Disease or Chronic Kidney Disease or Hypo/Hyperthyroidism thyroid or Cardiomyopathy causing drugs like Donorubicin, bleomycin, adriamycin, etc.) were excluded from the study. After comprehensive history and examination, all patients underwent baseline tests like Fasting blood sugar, Post prandial blood sugar, Glycated haemoglobin, Kidney function test, Complete blood count, Chest radiograph, Electric Cardio Gram (ECG), Echocardiography, Urine routine and microscopy, Urine sugar and ketones. Also, Tread Mill Test (TMT), Thyroid profile, and Lipid profile were done in indicated cases. Echocardiography gives a detailed picture of diastolic dysfunction. The study was conducted in accordance with "Recommendations guiding physicians in biomedical research involving human subjects," adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964.

a) 2D echocardiography

M-mode, and color Doppler examination were done by Agilent Image Point machine with 2.5 to 5 MHz probes. All recordings were done with patients in supine and left lateral position. The transducer was placed in the left parasternal, apical, and subcostal areas of the chest, and the parasternal long axis and short axis were taken to record various dimensions and measurements.

b) Echocardiographic Measurements

Diastolic function of the left ventricle is best assessed by evaluating the mitral inflow velocity curves (MIVC) by Echo-Doppler techniques. In this study, the following parameters were considered to evaluate LV diastolic dysfunction.

- a) Mitral 'E' velocity (Peak velocity of early mitral flow)
- b) Mitral 'A' velocity (Peak velocity of late (atrial) mitral flow)
- c) Mitral E/A ratio (Normal 1-2)
- d) Isovolumic relaxation time (IVRT) (Normal 60-100 msec)
- e) Deceleration time of mitral 'E' curve (DT of E) (Normal 150-200 msec). Mitral flow velocities were measured by pulsed wave Doppler with sample volume placed between the leaflet tips. It is necessary to keep it between the leaflet tips as Doppler parameters are dependent on the sample volume location.

III. RESULTS

2500 Patients were analyzed and compared on various parameters. Figure 1 shows the demographics of the patients involved in the study. 55.4 % were Males, 44.4 % were Females, and 0.2 % were not otherwise specified. The mean age of patients was 48.8yrs.

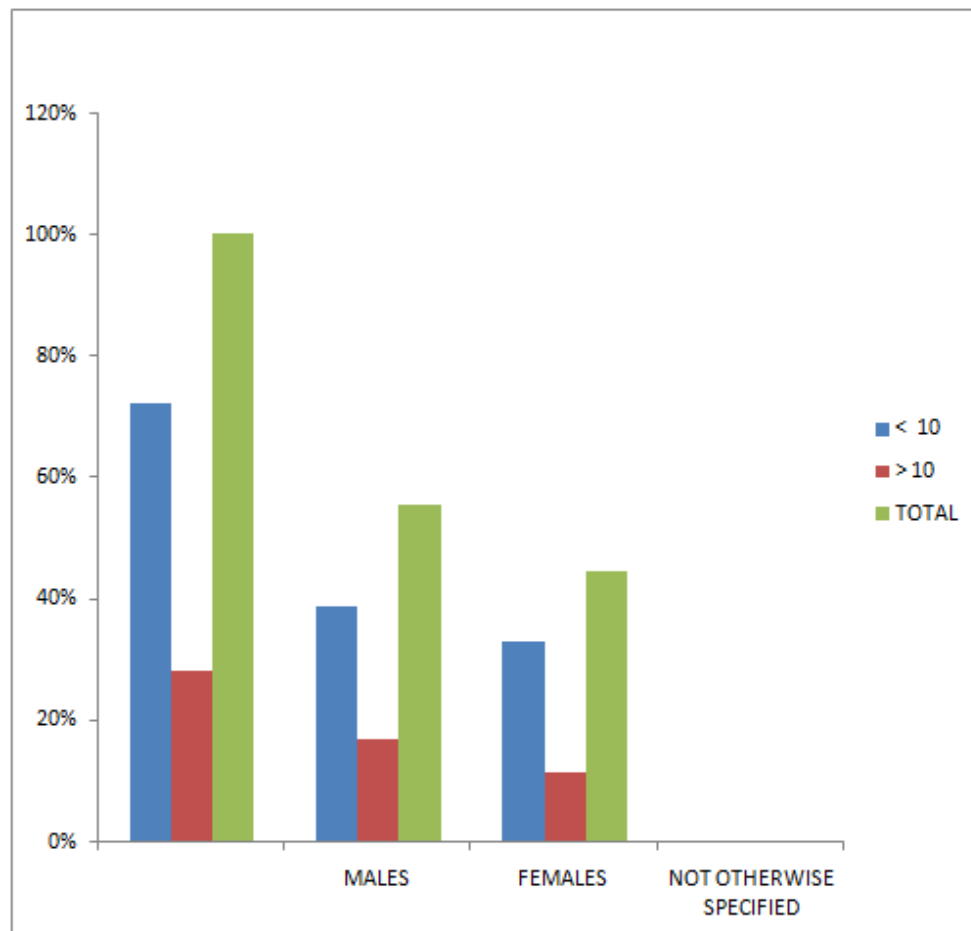


Figure 1: Gender wise distribution of patients

The majority of the patients belong to the duration of less than ten years of diabetes (Figure 2). The mean duration of diabetes of patients was 8.54yrs with a standard deviation of 3.21.

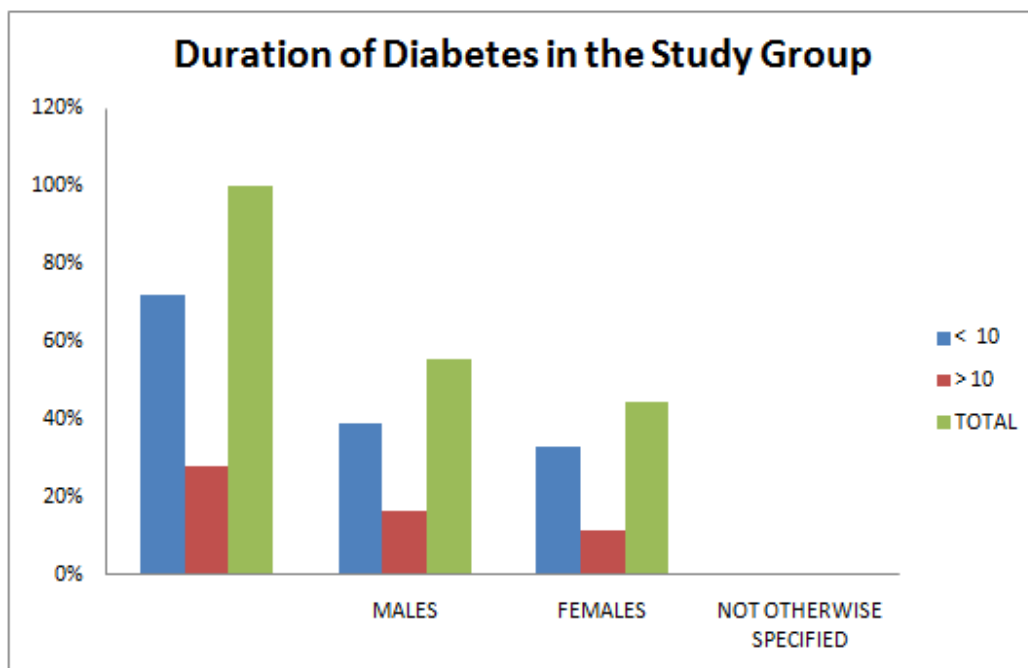


Figure 2: Duration of diabetes in the study group

All the patients in the study were also evaluated for Body Mass Index, and it was found that around 80 % were either overweight or obese. Details are clearly shown in Figure 3.

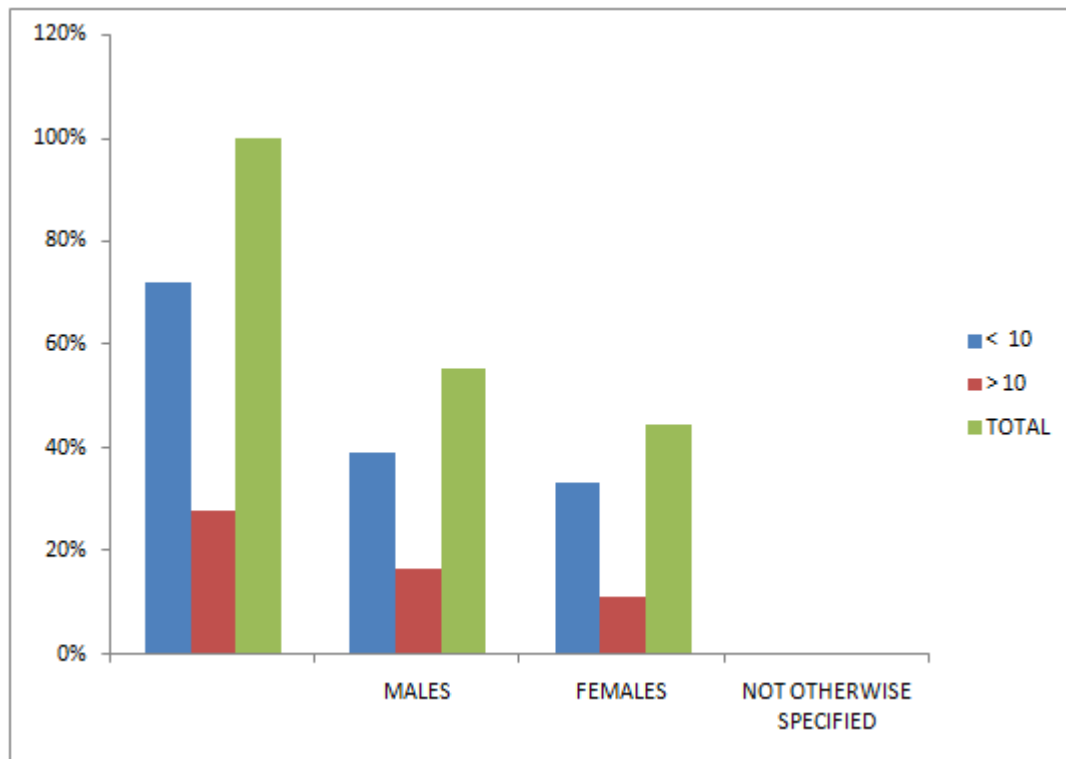


Figure 3: Distribution of body mass index values in the study population

Echocardiography was done in all patients. E/A ratio that is Peak velocity of early mitral flow/ Peak velocity of late mitral flow was less than 1 in 85 % of cases where as it was between 1 to 2 in the remaining 15 % of cases (Figure 4). E/A ratio is the most specific and sensitive indicator of diastolic dysfunctions.

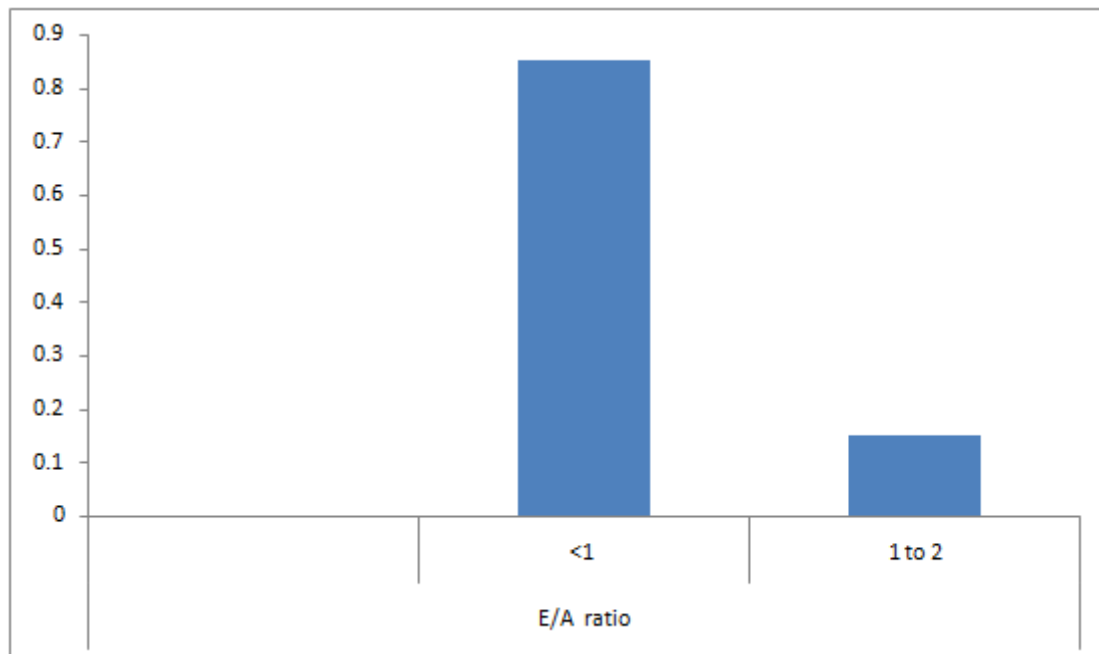


Figure 4: E/A ratio in the study group

IVRT that is Isovolumetric Relaxation Time was higher than 100 millisecond in 65% of cases where as it was between 60 and 100 in the remaining 35% of cases (Figure 5).

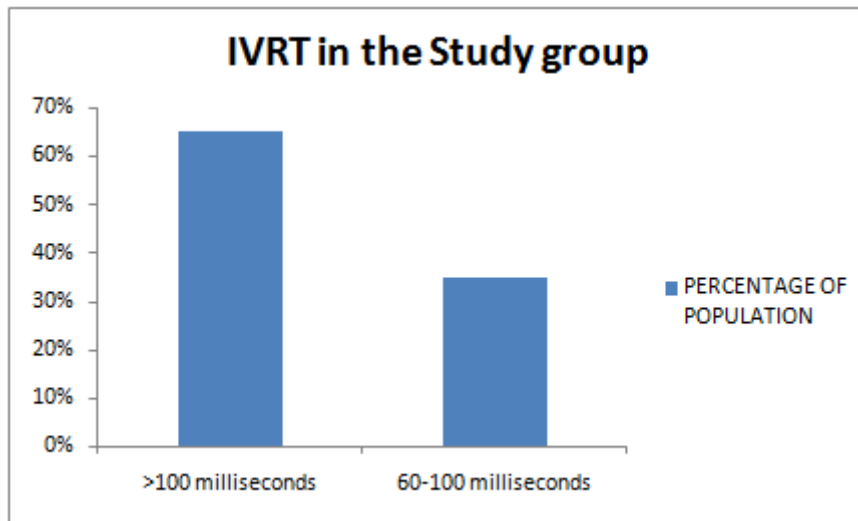


Figure 5: IVRT in the study group

Moreover, Deacceleration Time of E (Peak velocity of early mitral flow) was higher than 200 milliseconds in 69 % of cases whereas it was between 150 and 200 milliseconds in remaining 31 % (Figure 6).

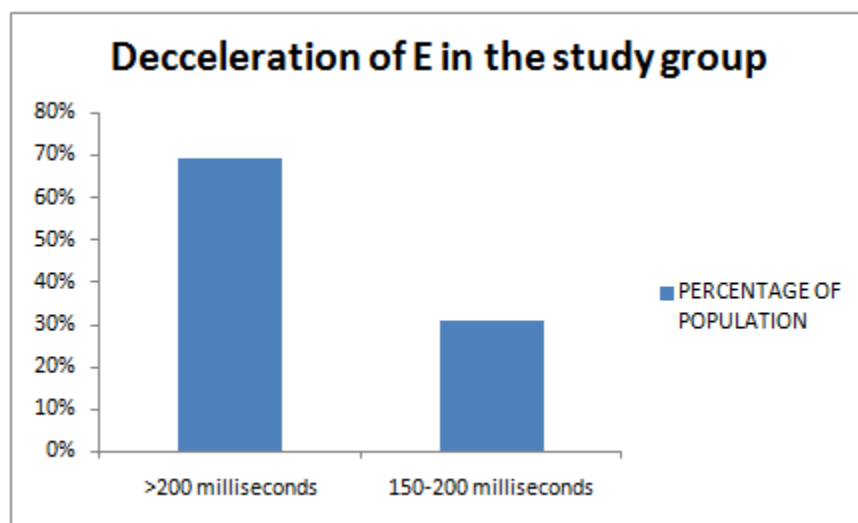


Figure 6: Deacceleration of E in the study group

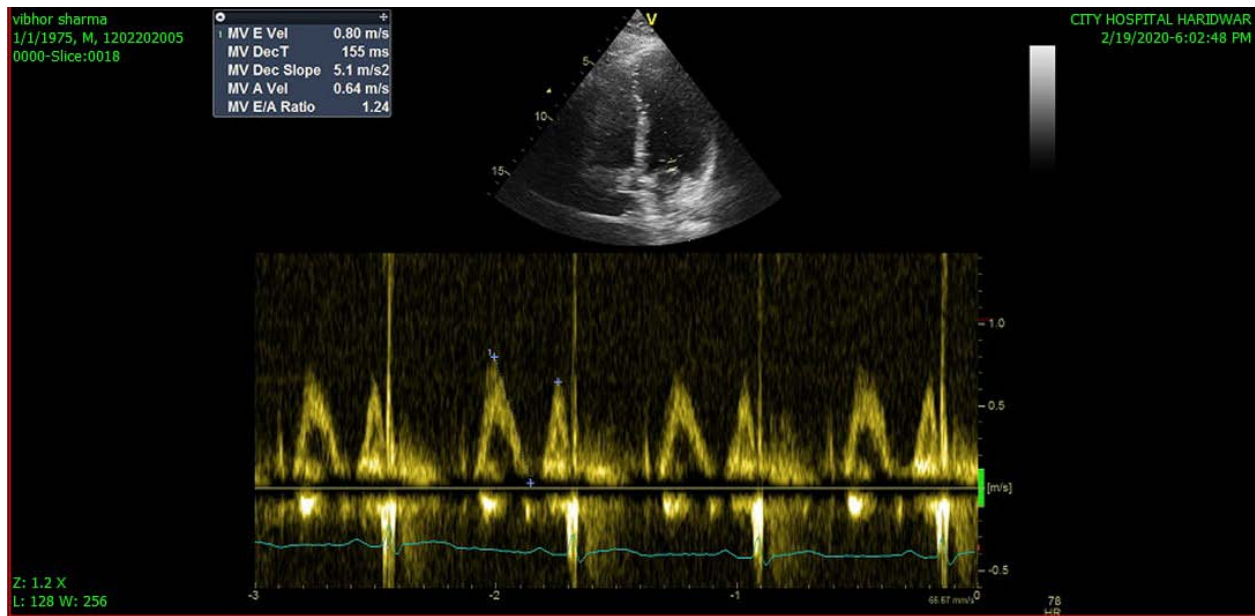


Figure 7: Normal mitral inflow pattern. E>A, E-early inflow wave: A-atrial contraction

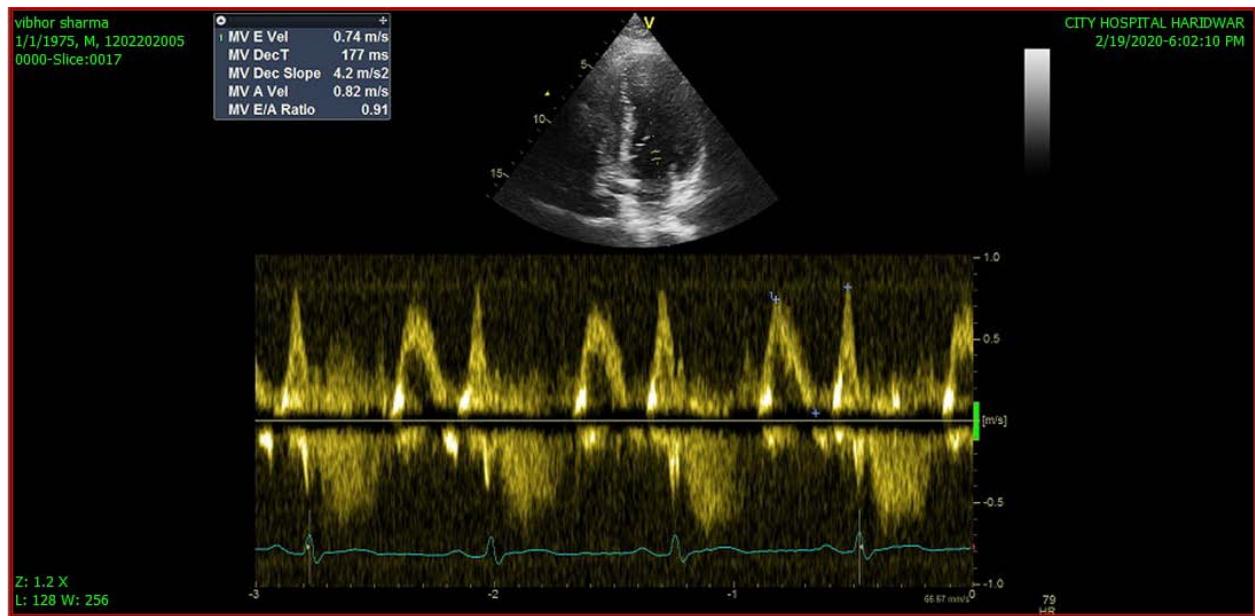


Figure 8: Delayed relaxation abnormality. Reversed E/A ratio (E/A<1)

IV. DISCUSSION

Diabetic cardiomyopathy has been proposed as an independent cardiovascular disease, and left ventricular diastolic dysfunction may represent the first stage of diabetic cardiomyopathy. It has been related to an increase in left ventricular wall thickness and myocardial mass and, early in the process, signs of myocardial diastolic dysfunction occur.⁶ There is experimental and clinical evidence of enhanced cellular apoptosis with myocyte loss as a consequence of oxidative stress induced by hyperglycaemia.⁷ Sanderson et al. suggested that impairment of the diastolic function of the left ventricle, i.e., its filling abnormalities are far more common than systolic dysfunction.⁸ The present

study reports left ventricular dysfunction by m-mode, 2-D echo, and color Doppler studies.

We can easily infer that the late atrial filling wave (A) was significantly increased, probably due to elevated LV filling pressure secondary to impaired relaxation among diabetic individuals. The diastolic abnormalities in diabetic patients most likely indicate reduced LV compliance secondary to small vessel disease, infiltrative myocardial process, metabolic derangement, or a combination of the three. Hence, our study clearly outlines the ongoing cardiac damage in diabetic patients even when the blood pressure stays within the normal range.

V. CONCLUSION

Though invasive procedures like Coronary Angiography and Scintigraphy are Gold Standard in demonstrating the Cardiovascular Compromise in suspected patients, Echocardiography serves as a gold standard screening tool in detecting early functional changes in heart, especially in diabetic patients. We strongly recommend it to be included in routine investigations leading to the work of diabetic patients.

Conflict of Interest: NIL

Funding: No funding required to carry out the present research work.

Ethical Clearance: Study was conducted in accordance with WMA (World Medical Association) Declaration of Helsinki, June 1964.

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