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Study of cardiac co-morbidities in newly diagnosed type 2 diabetes mellitus patients with help of 2D echocardiography

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Abstract

Background: Diabetes mellitus is one of the leading cause of multisystem involvement resulting in significant comorbidities. Various cardiac disorders such as dilated cardiomyopathy, left ventricular diastolic dysfunction and myocardial infarction have been frequently associated with diabetes mellitus. Present study was aimed to study cardiac co-morbidities in newly diagnosed type 2 diabetes mellitus patients with help of 2D echocardiography.
Material and Methods: A prospective observational study was conducted in patients, 18-70 years, of either gender, newly diagnosed Diabetes mellitus type 2 based on Fasting blood sugar/ Post prandial blood sugar/HbA1c, willing to participate in the study.
Results: Out of 175 patients, 74 patients belonged to age group 51-60, which is the most commonly affected age group. Out of 175 patients, 109 (62%) patients were male and 66 (38%) patients were females. Most of the patients had HbA1c` in the range of 7-10%, 139 patients (79%), whereas the least number of patients were in the 6.5-7% group, 5 patients (3%) Most of the patients had normal cardiac diastolic function, whereas only 15 (8%) patients restrictive filling (grade 3 diastolic dysfunction). Grade 2 and 3 diastolic dysfunction was more common in a higher age range i.e. 51-60 and >60 years whereas it was absent in less than 40 year. Diastolic dysfunction was more common in patients having proteinuria >200 mg/dl, higher serum cholesterol levels, hba1c levels > 10% and in patents having E/e' ratio higher than 14. 47 patients were systolic dysfunction <50% with hba1c less than 10%, whereas only 3 patients had EF <50% with hba1c >10%.
Conclusion: Cardiac diastolic dysfunction is observed in patients of diabetes mellitus 2 more frequently as compared to systolic dysfunction.

Keywords: Cardiac diastolic dysfunction, type 2 diabetes mellitus, Hba1c, 2D echocardiography

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Introduction

Diabetes mellitus is one of the leading cause of multisystem involvement resulting in significant comorbidities [1]. Cardiovascular involvement is significant resulting in several cardiac complications. 2D echo cardiography stands to be an important imaging modality for assessing cardiac function.

Various cardiac disorders such as dilated cardiomyopathy, left ventricular diastolic dysfunction and myocardial infarction have been frequently associated with diabetes mellitus [2]. Cardiac diastolic dysfunction seems to be the most common manifestation in asymptomatic patients of diabetes mellitus type [2].

Correlation of diastolic dysfunction with HBA1C and various other parameters suggestive of poor glycemic control points to association of diabetes mellitus with diastolic dysfunction which if not looked at an early stage can progress to diabetic cardiomyopathy which is an irreversible form of cardiac dysfunction that includes both systolic and diastolic dysfunction [3, 4]. Present study was aimed to study cardiac co-morbidities in newly diagnosed type 2 diabetes mellitus patients with help of 2D echocardiography.

Material and Methods

A prospective observational study was conducted over a period from 1st June 2017 to 30th October 2019 at L.G hospital, Ahmedabad.

Inclusion criteria

- Patients, 18-70 years, of either gender, newly diagnosed Diabetes mellitus type 2 based on Fasting blood sugar/Post prandial blood sugar/HbA1c, willing to participate in the study.

Exclusion criteria

1. Patients who do not give valid consent.
2. Known case of diabetes mellitus type 2-previously diagnosed, treated or untreated.
3. Patients having ischemic heart disease and/or known systolic cardiac systolic or diastolic dysfunction.
4. Patients with cardiac valvular disease and cardiac rhythm abnormalities.

Study was explained to patients & a written informed consent was taken for participation. Demographic data (age, sex and residence), clinical history, family history & detailed medical history including history of past medical conditions were recorded. General & systemic examination done. Routine investigations including urine routine and microscopy, fasting, post prandial blood sugar, fasting lipid profile, HbA1c and urine protein (quantitative) were done. A 2D echocardiographic evaluation of every patient was done when they were found to have diabetes mellitus type 2 for the first time.

Their history and relevant clinical, biochemical and radiological data were noted in preformed questionnaire. The data was further systematically arranged in a Microsoft excel sheet- master chart and the data was further analysed by SPS software and inferences drawn.

Results

Out of 175 patients, 74 patients belonged to age group 51-60, which is the most commonly affected age group. Out of 175 patients, 109 (62%) patients were male and 66 (38%) patients were females.

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Table 1: Age & gender distribution

Age distribution	Male	Female	Total
<40	9 (5.14%)	0	9 (5.14%)
41-50	30 (17.14%)	12 (6.86%)	42 (24%)
51-60	41 (23.43%)	33 (18.86%)	74 (42.29%)
>60	29 (16.57%)	21 (12%)	50 (28.57%)
Total	109 (62.29%)	66 (37.71%)	175

In our study, most of the patients had HbA1c` in the range of 7-10%, 139 patients (79%), whereas the least number of patients were in the 6.5-7% group, 5 patients (3%)

Table 2: HbA1c on diagnosis of Type 2 DM

Hba1c	Number	%
6.5-7%	5	3.00%
7 - 10%	139	79.00%
>10%	31	18.00%

In our study, most of the patients had normal cardiac diastolic function, whereas only 15 (8%) patients restrictive filling (grade 3 diastolic dysfunction).

Table 3: Cardiac diastolic dysfunction

Cardiac Dysfunction	Number	%
Normal	104	59.43%
Impaired Relaxation (Grade 1)	40	22.86%
Pseudonormal (Grade 2)	16	9.14%
Restrictive Filling (Grade 3)	15	8.57%

In our study, most of the patients, 145 (83%), had normal early mitral inflow velocity, i.e. >50 cm/s. 122 (70%) patients had >7cm/s mitral annular early diastolic velocity, which is normal.

Table 4: Early mitral inflow velocity & mitral annular early diastolic velocity

Parameters	Number	%
Early Mitral Inflow Velocity(E)		
<50 Cm/S	30	17%
>50 Cm/S	145	83%
Mitral Annular Early Diastolic Velocity		
< 7 cm/s	53	30%
≥ 7 cm/s	122	70%

Grade 2 and 3 diastolic dysfunction was more common in a higher age range i.e. 51-60 and >60 years whereas it was absent in less than 40 year

Table 5: Relation of cardiac diastolic dysfunction with age

Cardiac Dysfunction	<40	41-50	51-60	>60
Normal	9 (5.14%)	28 (16%)	39 (22.29%)	30 (17.14%)
Impaired Relaxation (Grade 1)	0	11 (6.29%)	19	14 (8%)
Pseudonormal (Grade 2)	0	2 (1.14%)	7 (4%)	7 (4%)
Restrictive Filling (Grade 3)	0	1 (0.57%)	9 (5.14%)	6 (3.43%)

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Diastolic dysfunction was more common in patients having proteinuria >200 mg/dl, whereas it was absent in patients having proteinuria <160 mg/dl. (P value <0.00001). Cardiac diastolic dysfunction was more common in patients having proteinuria >300mg/dl as compared to those having proteinuria <300mg/dl. (P value < 0.00001).
Cardiac diastolic dysfunction was significantly related to higher serum cholesterol levels. (p value-0.03.). Cardiac diastolic dysfunction was significantly higher in patients with hba1c levels > 10% and it was low in patients with hba1c levels <10%. Cardiac diastolic dysfunction was observed in patents having E/e' ratio higher than 14 and it was very low in patients having this ratio <14. Cardiac diastolic dysfunction was observed in patients having Left atrial volume > 34 ml and significantly lower in patients having LA volume <34 ml.

Table 6: Correlation of cardiac diastolic dysfunction with various parameters

Cardiac Diastolic Dysfunction	Normal	Impaired Relaxation	Pseudonormal	Restrictive Filling
Fasting Blood Sugar		(Grade 1)	(Grade 2)	(Grade 3)
<200mg/dl	78 (44.57%)	8 (4.57%)	2 (1.14%)	1 (0.57%)
>200 mg/dl	26 (14.86%)	32 (18.29%)	14 (8%)	14 (8%)
Albuminuria				
<300mg	102 (58.29%)	20 (14.43%)	1 (0.57%)	3 (1.71%)
>300mg	2 (1.14%)	20 (11.43%)	15 (8.57%)	12 (6.86%)
Total Cholesterol				
<200	85 (48.57%)	34 (19.43%)	9 (5.14%)	14 (8%)
>200	19 (10.86%)	6 (3.43%)	7 (4%)	1 (0.57%)
HbA1c				
<7%	5 (2.86%)	0	0	0
7-10%	99 (56.57%)	40 (22.86%)	2 (1.14%)	4 (2.29%)
>10%	0	0	14 (8%)	11 (6.29%)
Ratio of early mitral inflow velocity and mitral annular early diastolic velocity				
<14	104 (59.43%)	40 (22.86%)	2 (1.14%)	1 (0.57%)
>14	0	0	14 (8%)	14 (8%)
LA volume				
<34 ml	104 (59.43%)	21 (12%)	2 (1.14%)	0
>34 ml	0	19 (10.86%)	14 (8%)	15 (8.57%)

47 patients were systolic dysfunction <50% with hba1c less than 10%, whereas only 3 patients had EF <50% with hba1c >10%. (p value: 0.19, not significant)

Table 7: Correlation of cardiac systolic dysfunction with HBA1C.

Cardiac systolic function	Hba1c < 10%	Hba1c >10%
<50%	47	3
>50%	103	15

Discussion

Cardiac diastolic dysfunction is an earliest marker for diabetes induce cardiomyopathy. This condition can further progress to cardiac failure. Hence, it is important to detect diastolic dysfunction at the earliest to prevent its progression to overt heart failure.
Diastolic dysfunction occurs far earlier in patients of diabetes mellitus as compared to systolic dysfunction unless it is not associated with primary cardiac condition like ischemic heart disease, valvular heart disease, and cardiac rhythm abnormalities. Therefore, in our study patients having above conditions were excluded. Patients having significant systolic dysfunction (i.e. <40%) were also excluded from our study.
In our study, out of 175 patients the age group from 51-60 years was most commonly

affected, whereas patients belonging to age group <40years were least affected. In study by Dhar *et al*., [5] most commonly affected age group was 31 to 60 years, in which 48% males and 30% females developed diabetic cardiomyopathy. In a similar study done by Perumal *et al*., [6] found that patents with age between 31 to 50 have 28% chances to get LVDD while patients with age between 31 to 40 have 45% chances to get LVDD.

In present study, cardiac diastolic dysfunction was observed in 40% patients. Whereas, 60% patients had normal diastolic function. In previous study like Tarumi *et al*., [7] who reported LVDD in 36% patients and Antonio Nicolino A *et al*., [8] reported LVDD from 32-40%.

Paul Poirier *et al*., [9] in their study found LVDD in 60% of patients of whom 28% had pseudo normal pattern and 32% had impaired relaxation. However, systolic function was in normal all subjects and there was no correlation between LVDD and extent of metabolic control. Hba1c, lipid profile, and duration of diabetes did not correlate with diastolic dysfunction in their study. Rajesh Rajput *et al*., [10] found diastolic dysfunction in 63% of patients and all of them had impaired relaxation. Pseudo normal pattern or restrictive filling was not observed at all.

Present study findings correlates with the study of Paul Poirier *et al*., [9] and N.H. Anderson *et al*., [11] But does not correlate with results of study performed by Rajesh Rajput *et al*., [10] The discrepancy in the results can be explained by the fact that above studies were performed taking patients with long standing diabetes into consideration, whereas our study was based on evaluation of patients having recently diagnosed diabetes mellitus type 2.

Nichols G.A. *et al*., [12] studied 9,591 type 2 DM (T2DM) patients & revealed diastolic dysfunction in 11.8% of diabetic subjects at baseline, with an additional 7.7% of patients developing diastolic dysfunction during a 30-month period of observation.

Diastolic dysfunction: the primary and early functional consequence of various morphological alterations is LV diastolic function [13]. Early reports showed lower transmitral E/A ratios among patients with DM [14], followed by lower mitral annular early diastolic velocity assessment [15], greater E/E' [16], and larger left atrial (LA) volume [17]. Subclinical LV diastolic dysfunction increased mortality independent of HTN, CAD, or other echocardiographic parameters [18].

Meena *et al*., [19] concluded that among diabetic cases 9.09% cases with HbA1C range 6-7%, 33.33% of cases with HbA1C range 7.1-8%, 100% of cases with HbA1C range >8.1% were showing diastolic dysfunction which was statistically significant ($p<0.0001$). Similar findings were noted in present study.

Celentano *et al*., [20] also studied subjects with normal glucose tolerance, with impaired glucose tolerance, and with type 2 DM and found early signs of diastolic dysfunction (assessed by E/A mitral flow ratio), not only in patients with diabetes but also in those with impaired glucose tolerance, independent of the confounding role of ischemia, body weight, and blood pressure [21]. Holzmann *et al*., showed in a middle-aged population without previously diagnosed DM a continuous relationship between concentrations of fasting plasma glucose, HbA1C and LVDD [21]. Study done by Shreshta *et al*., in 100 asymptomatic type 2 Diabetes Mellitus, LVDD was found in 71 subjects of whom 60 had impaired relaxation and 11 had a Pseudo normal pattern of ventricular filling detected by Doppler Echo which included Valsalva maneuver [22].

The strong heart study concluded that albuminuria is independently associated with LV systolic and diastolic dysfunction in type 2 DM; this may explain in part the relationship of albuminuria to increased cardiovascular (CV) events in the DM population. Screening for albuminuria identifies individuals with high CV risk and possible cardiac dysfunction.

Many researchers found a strong correlation between the development of diabetic cardiomyopathy and increased level of HbA1c. Mean of HbA1C (%) was found higher in group with LVDD (7.67±0.90) as compared to group without LVDD (7.24±0.64). [23, 24]. This concludes that HbA1C is strongly associated with presence of LVDD ($p=0.0057$). Perumal *et*

al., [24] noted that patients with HbA1c between 6.5 to 8 have 17% chances to get LVDD with significant P value of 0.03. Patients with HbA1c between 8 to 10 have 35% chances to get LVDD with significant P value of 0.02. Patients with HbA1c 6.5 to 8 have double the chances when compared to HbA1c 6.5 to 8 with significant association statistically. Female patients with HbA1c 8 to 10 have 15% chances of having LVDD with significant association statistically (P value 0.02). Male patients with HbA1c between 6.5 to 8 have 36% chances to get LVDD without significant P value of 0.279.

Systolic function was also evaluated in our study. It was found that there was no significant association between higher values of hba1c and systolic dysfunction. A probable explanation to above findings and results can be given as, patients included in the study were all recently diagnosed diabetics and all those subjects were selected such that none of them had pre exiting underlying heart condition that could act as confounding factor for our results. Moreover, patients included in our study belongs to low socio-economic class and has lower awareness for regular health checkups, one of the reasons these patients might have presented with overt diabetes mellitus at the time of diagnosis causing detectable and significant amount of diastolic dysfunction.

However, systolic dysfunction is also a manifestation of diabetic cardiomyopathy but that seems to follow a long-standing uncontrolled diabetes mellitus along with many other comorbid cardiac conditions as well as other comorbidities that can lead to cardiac dysfunction, major one of them being systemic hypertension. The patients in our study had significant diastolic dysfunction but systolic dysfunction was not a prominent feature. This finding suggests that if diastolic dysfunction is picked up at an early stage in diabetics, it may be possible to avoid irreversible diabetic cardiomyopathy and systolic dysfunction by maintaining strict control of hyperglycemia.

Conclusion

Cardiac diastolic dysfunction is observed in patients of diabetes mellitus 2 more frequently as compared to systolic dysfunction. Moreover, the diastolic dysfunction correlates with the severity of diabetes and relative duration of diabetes as observed with higher value of Hba1c on diagnosis of DM 2 associated with higher incidence of diastolic dysfunction. Hence, early diagnosis of LV diastolic dysfunction is imperative to prevent progression to irreversible diabetic cardiomyopathy.

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