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Original Research Paper

"STUDY OF CORRELATION BETWEEN LEFT VENTRICULAR DIASTOLIC DYSFUNCTION WITH HbA1C AND DURATION OF DIABETES MELLITUS"

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ABSTRACT:

Diabetes Mellitus is a metabolic disease which affects various organs of the body like heart, kidney, and peripheral nerves. Myocardial dysfunction in diabetic patients in absence of ischemic, valvular or hypertensive heart disease is identified as diabetic cardiomyopathy. It is an early sign of diabetic heart muscle involvement which usually precedes systolic dysfunction. There are very few Studies are found to correlate the relation between the glycemic control and left ventricular diastolic dysfunction. Hence this study is an attempt to determine the proportion of diastolic dysfunction in patients with type 2 DM and to correlate the relation of LVDD withHbA1c levels and duration of DM. A total of 100 diabetic patients with minimum 5 years duration of diabetes were selected from Rajarajeswari medical college and hospital. Patients with minimum history of 5 years of type 2 diabetes were evaluated for Doppler echocardiography and HbA1c levels. **Results:** In the present study, 58 out of 100 patients had left ventricular diastolic dysfunction and was higher prevalence in HbA1c more than 8%. Patients who had diastolic dysfunction had diabetes duration of diabetes was more than 8 years. **Conclusion:** LVDD is strongly correlated with HbA1c levels and duration of diabetes mellitus. There was significant positive correlation of age, fasting blood sugars, cholesterol levels and triglyceride levels with LVDD.

Keywords: diastolic dysfunction, diabetes mellitus, HbA1c.

INTRODUCTION

Diabetes mellitus is a metabolic disorder with heterogeneous etiology which is characterized by chronic hyperglycaemia and disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. Chronic uncontrolled sugars and insulin resistance contributes various macro and microvascular complications. Myocardial dysfunction in the absence of other causes of heart failure is defined as diabetic cardiomyopathy.[1,2]The different synchronized pathological processes lead to myocardial fibrosis, which is considered the main cause of diastolic and systolic dysfunctions in the diabetic heart [3]. Left ventricular diastolic dysfunction (LVDD) the first manifestation of cardiac remodelling in DM[4]. DM and HF affect each other in a bidirectional manner in the form of cause and outcome. 1% increase level of HbA1c is associated with an 8% increased risk of HF, independently of other cardiovascular (CV) risks[5]. HF further worsens the quality of life and influences the therapeutic effect of hypoglycaemic agents. Hence it is been implicated strictly to perform early detection and management of myocardial dysfunction in the diabetic population before the development of overt HF[6].This study was performed to establish the relation between left ventricular dysfunction with HbA1c and duration of diabetes mellitus.

METHODS

Patient selection

A total of 100 type 2 diabetic patients with minimum 5 years duration of diabetes were selected from

RajaRajeswari Medical College and Hospital, Bangalore**.**

Objectives: **a.** To determine the proportion of diastolic dysfunction in patients with Type 2 DM.

b. To correlate the relation of LVDD with HbA1C levels and duration of DM.

Age group 30- 60 years independent of sex, Patients with a history of type 2 diabetes for minimum period of 5 years duration with clinically no evidence of cardiac disease and blood pressure < 130/80 mmofHg and normal resting ECG were included in the study.

Exclusion criteria: 1. patients with systemic hypertension 2.Patients with thyroid disease. 3. Patients with peripheral vascular disease and arteriosclerosis. 4. Patients with congenital heart disease. 5. Patients with past history of ischemic heart disease, renal failure, valvular heart disease, cardiomyopathy. 6. Patients on anti-hypertensive agent and/or ACE inhibitor, 7.patients with evidence of LVH on 2D Echo.

Study design:

a) It a descriptive study of patients with h/o of type 2 diabetes with a minimum duration of 5 years were subjected to detailed medical history and examination. After 12 hours of fasting, a venous blood sample was collected and sent to biochemistry lab for estimation of FBS, HbA1C, Lipid profile and PPBS after 2hours following meal. All patients who met with the inclusion criteria were subjected to Doppler Echocardiography

b) In Doppler study, following parameters will be obtained;

- E - Peak velocity of early mitral flow
- A - peak velocity of late mitral flow
- E/A ratio
- DT- Deceleration Time
- IVRT - Iso Volumetric Relaxation Time
- LA size LVDD is considered with following findings
- E/A ratio <1 or >2
- DT <150 or >220 ms
- IVRT <60 or >100 ms

c) Reduction in 'E' velocity over 'A' velocity with E/A ratio <1 and increase in LA size with preserved EF will be considered as the evidence of LVDD.

Institutional ethical clearence was obtained before the study.

Other investigations:

- **2D ECHO, ECG**
- **HbA1c, Complete haemogram**
- **FBS, PPBS**
- **Blood urea and serum creatinine**
- **Thyroid profile**

Immunoturbidometric method of estimating HbA1c: Total haemoglobin and HbA1c concentrations are determined after haemolysis of the anticoagulated whole blood specimen. Total Hb is measured calorimetrically.HbA1c is determined immune turbidimetrically. The ratio of both concentrations yields the final percent HbA1c results.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance.

Statistical software:

The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were

used for the analysis of the data and Microsoft word and Excel have been used to

generate graphs, tables etc**.**

RESULTS AND ANALYSIS:

In our study, out of 100 patients, 53% were in the age group of 51- 60 years, 41-50 (37%) and 10% in 30 – 40 years age group. In the present study, mean Age was 50.40±6.38. 57% out of 100 patients were male and 43% were female. In our study, mean FBS was 197.57±71.31. and mean PPBS was 277.06±89.93.In the present study, mean HbA1C was 9.06±1.76. In this study a total of 82 patients had duration of diabetes was between 6–12 years. 12 patients had duration of diabetes less than 6 years. 4 patients had duration of diabetes between 12 –18 years, 2 patients had duration of diabetes greater than 18 years. In the present study, among 100 patients, 58 patients had LVDD. Out of 58 patients, 53 had LVDD Grade 1, 4 had LVDD Grade 2 and 1 patient had LVDD Grade 3. In 42 patients LVDD was absent. In our study, 82 patients had Duration of DM between 6-12 years, among them majority of patients had grade1 LVDD and LVDD was absent in 31 patients. The duration of DM in relation to LVDD was statistically strongly significant with p = <0.001. In our study, 38 patients had HbA1c between 8.1 – 9.5%, among whom 35patients had LVDD Grade 1, 3 patients had LVDD Grade 2, 1 patient had LVDD Grade. The study of HbA1c of patients in relation to LVDD was statistically strongly significant with p = 0.002. In the present study, mean FBS was 197.57±71.31. Mean FBS in LVDD Grade1 was 206.19±64.34, in LVDD Grade 2 was 269.50±92.48, in LVDD Grade 3 was243.00±0.00 and mean FBS in

LVDD absent patients was 178.76±73.41. The mean FBS of patients in relation to LVDD was statistically significant with p = 0.040. (table1). In the present study, mean PPBS was 277.06±89.93. Mean PPBS in LVDD Grade 1 was 289.51±80.38, in LVDD Grade 2 was 421.25±54.39, in LVDD Grade 3was 316.00±0.00 and mean PPBS in patients without LVDD was 246.69±88.93. The mean PPBS of patients in relation to LVDD was statistically strongly significant with p = 0.001. Mean FBS and PPBS was high with increase in grades of diastolic dysfunction. In the present study, mean HbA1c was 9.06±1.76. Mean HbA1C in LVDD Grade 1 was 9.44±1.76, in LVDD Grade 2 was 11.50±1.77, in LVDD Grade 3 was12.20±0.00 and mean HbA1C in patients without LVDD was 8.30±1.38, which was lower than patients with LVDD. The meanHbA1C of patients in relation to LVDD was statistically strongly significant with p =<0.001.In the present study, mean Duration of Type 2 DM was 7.85±2.87. Mean duration of Type 2 DM in LVDD Grade 1 was 8.26±1.81, in LVDD Grade 2 was11.50±2.65, in LVDD Grade 3 was 12.00±0.00 and mean Duration of Type 2 DM in without LVDD patients was 6.21±1.16. Patients with grade 3 diastolic dysfunction had duration of diabetes was more than other two grades. The mean duration of Type 2 DM in relation to LVDD was statistically strongly significant with p = <0.001.

Comparison of Sugar variables according to LVDD grading of patients studied

Variables	LVDD Grade				Total	p value
	Absent	1	2	3		
FBS (mg/dl)	178.76±73.41	206.19±64.34	269.50±92.48	243.00±0.00	197.57±71.31	0.040*
PPBS (mg/dl)	246.69±88.93	289.51±80.38	421.25±54.39	316.00±0.00	277.06±89.93	0.001**
HbA1c%	8.30±1.38	9.44±1.76	11.13±1.77	12.20±0.00	9.06±1.76	<0.001**
Duration Type IIDM	6.21±1.16	8.26±1.81	16.50±2.65	20.00±0.00	7.85±2.87	<0.001**

ANOVA test

In the present study, **(table 2)** mean peak velocity of early mitral flow (E) was74.71±13.35. The mean E value in relation to LVDD was statistically strongly significant with p = <0.001 **(table2).** In the present study, mean peak velocity of late mitral flow (A) was 75.98±13.06. The mean A value in relation to LVDD was statistically strongly significant with p = <0.001. In the present study, mean E/A was 1.02±0.27. E/A ratio is high in LVDD grade 3 patients. Mean E/A in relation to LVDD was statistically strongly significant with p = <0.001. In the present study, mean DT was 202.27±31.22.There is increase in deceleration time with increase in LVVD grade. The mean DT in relation to LVDD was statistically strongly significant with p = <0.001. In the present study, mean IVRT was 103.28±30.61. There is increase in isovolumetric relaxation time when there is increase in LVDD grade and was statistically strongly significant with p = <0.001. In the present study, mean LA size was 3.40±0.39. We observed there is increase in mean LA size in LVDD grade 3 patients when compared to grade 2 and grade1.The LA size in relation to LVDD was statistically strongly significant with p = <0.001.In the present study, mean EF size was 58.32±2.35. The mean EF in relation to LVDD was statistically strongly significant with p = <0.001.

Comparison of Echo cardiographic parameters according to LVDD grading of patients studied. (table2).

Variables	LVDD Grade				Total	p value
	Absent	1	2	3		
E	81.20±10.72	67.10±7.54	92.00±5.54	136.70±0.00	74.71±13.35	<0.001**
A	68.02±9.07	83.56±11.50	62.60±1.93	61.40±0.00	75.98±13.06	<0.001**
E/A Ratio	1.20±0.10	0.81±0.12	1.47±0.10	2.22±0.00	1.02±0.27	<0.001**
DT	175.86±10.47	226.96±18.66	175.00±19.51	112.00±0.00	202.27±31.22	<0.001**
IVRT	77.36±9.23	127.45±20.36	69.50±14.93	46.00±0.00	103.28±30.61	<0.001**
LA Size	3.16±0.28	3.53±0.33	3.94±0.03	4.87±0.00	3.40±0.39	<0.001**
EF	60.23±1.06	57.28±1.46	54.75±0.96	47.00±0.00	58.32±2.35	<0.001**

DISCUSSION:

Diabetic cardiomyopathy has been proposed as an independent cardiovascular disease and many mechanisms such as microvascular disease, autonomic dysfunction, metabolic dysfunction, metabolic disorder, interstitial fibrosis are considered as causative factors. Despite similar left ventricular systolic function, patients with diabetes have more pronounced heart failure symptoms, use more diuretics, and have an adverse prognosis compared with those without diabetes. This can be due to presence of diastolic dysfunction of the left ventricle in these patients. Hence left ventricular diastolic dysfunction represent the first stage of diabetic cardiomyopathy preceding changes in systolic function, reinforcing the importance of early examination of ventricular function in individuals with diabetes.[7,8] In our study we found higher prevalence of LVDD (58%) compared to studies done by Rajendhra dhar et al.,[9] and Abhay kumar et al.,[10] where it is 39% and 41% respectively. In our study, mean FBS in LVDD grade 1,2,3 was 206.19, 269.50, 243.0 respectively, which was high when compared to patients without LVDD. Similarly, Patil et al.,[11, 12] in their study also found that the patients with constantly increased mean fasting blood sugar have higher prevalence of developing LVDD as compared to patients with normal blood sugar levels. Perumal et al., in their study found that Mean FBS was higher in LVDD group (189.80±30.90) as compared to LVDD negative group (179±29.80).[13] In the present study it was found that mean HbA1c of patients was high in LVDD present group when compared to without LVDD group. We found HbA1c is strongly associated with presence of LVDD with p=<0.001. Also found that with increase in HbA1c, there was increase in incidence of LVDD. Patients with HbA1c >9.5%had higher grades of LVDD when compared with patients of HbA1c 8.1 -9.5% and6.5-8.0%. Rajendra Dhar et al.,[9] in his study on 100 type 2 diabetes patients found 39% patients had LVDD. He also observed 16% of patients with HbA1C less than 8% had LVDD, where 30% of patients had LVDD with HbA1C greater than 8%.[9,10] In the present study E/A ratio increased as grade of LVDD increased which was strongly significant with p= <0.001.The E/A ratio in Strong Heart Study was more decreased in patients having poor glycaemic control (as indicated by higher levels ofHbA1c and

fasting glucose) than in patients having well controlled of diabetic Status. Mehrdad et al.,[14] [15,16]showed a significant correlation of HbA1c with E/A ratio. In the present study there was increase in IVRT as grades of LVDD increased which was strongly significant with p=<0.001 and also it was found that DT was also increased with increase in LVVD grades which was strongly significant with
p=<0.001.

CONCLUSION:

Overall prevalence of diastolic dysfunction was 58% in the present study. LVDD is strongly correlated with HbA1c levels and increasing duration of diabetes since diagnosis. LVDD was more common in the patients with HbA1c of8.1-9.5%. HbA1c is a very good indicator of long term prognosis. Diastolic dysfunction in diabetic patients represents an early stage in the natural history of diabetic cardiomyopathy. Its timely recognition may help to avoid or significantly delay the onset of congestive heart failure. We conclude that early diagnosis and treatment for diastolic dysfunction in the form of ACE inhibitors, angiotensin II receptor blockers, aldosterone antagonists, diuretics etc., depending on clinical scenario, will reduce the morbidity and improve the outcome of diastolic heart failure.

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