

Echocardiographic Evaluation of Diastolic Dysfunction in Type 2 Diabetes Mellitus and It's Correlation to Microvascular Complication Nephropathy

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Abstract

Introduction: In diabetic patients, incidence of heart failure is high, even in the absence of hypertension and coronary artery disease. Although heart disease in diabetes is primarily due to macrovascular origin, but growing evidence from different observations suggests the possibility of microvascular pathogenesis also.

Aim: To assess the diastolic dysfunction in asymptomatic, normotensive type 2 diabetic patients and to correlate it with the microvascular complication nephropathy .

Methodology: 60 Diabetic (type 2) patients from Jawaharlal Nehru medical college and associated hospital Ajmer were enrolled in our cross-sectional study. Diabetic nephropathy was assessed by a 24 hour urine albumin measurement. 2D echocardiography was done to assess left ventricular diastolic dysfunction.

Results: Among the 60 patients enrolled in our study, 34 were male patients and 26 were female patients. Maximum number of patients was in the age group 50 -

59 years (18 patients). The mean age in our study was 49.3 ± 10.4 . The overall prevalence of nephropathy was 66.67%(40). Among the 60 patients of type 2 diabetes, 34 of them had evidence for diastolic dysfunction. Out of 40 patients with nephropathy, 32 of them had diastolic dysfunction accounting for 80% (p value= <0.001).

Conclusion: In our study. diastolic dysfunction is strongly associated with nephropathy. Hence it's strongly supports microvascular origin of pathogenesis of diastolic dysfunction . Hence cardiac disease in diabetes is no longer only a macrovascular disease, but also microvascular changes do play a role.

Keywords: diastolic dysfunction, nephropathy, diabetes mellitus

Introduction

Type 2 diabetes mellitus is an established risk factor for cardiovascular events and the development of congestive cardiac failure, through its association with hypertension and coronary artery disease. The existence of myocardial dysfunction in diabetic subjects even in

the absence of ischemic, valvular and hypertensive heart disease was proposed by Rubler *et al.* in 1972¹ and subsequently abnormalities in both systolic and diastolic functions have been demonstrated. Diastolic dysfunction has been described as an early sign of diabetic heart muscle disease preceding the systolic damage. The impact of isolated diastolic dysfunction in diabetes concerns exercise tolerability. The influence of diabetic complications on diastolic dysfunction has been investigated in several studies. Sampson *et al.*(1990)⁴⁶ found a significantly higher proportion of abnormal diastolic dysfunction in the group of diabetes with proteinuria. The pathogenesis of diastolic dysfunction in type 2 diabetic patients is not completely elucidated. The relation of microvascular complications with diastolic dysfunction in type 2 diabetics suggests that diabetic microangiopathy is a background factor.

Materials and Methods

Study Design: Cross sectional study

Sample: Diabetic patients from Jawaharlal Nehru medical college and associated hospital Ajmer were enrolled in the study. 60 patients were enrolled for the study after informed consent from all patients.

Inclusion Criteria

- Known case of type 2 diabetes mellitus patients
- Newly diagnosed type 2 diabetes mellitus patients
- Age group >30 years.

Exclusion Criteria

- Pregnant women
- Hypertensive patients
- Known coronary artery disease patients
- Known valvular heart disease, arrhythmias
- Other co morbidities(COPD, pre-existing renal disease, thyroid disorders)

Methodology

Measurement of Microalbuminuria

Diabetic nephropathy was assessed in the patient by measuring the renal parameters (blood urea and serum creatinine). Urine routine and cultures were done to exclude a urinary tract infection. Proteinuria was assessed in all patients. Ultrasonogram of kidneys was done when required. Microalbuminuria is estimated by a 24 hour urine collection. excretion of 30- 299 mg/day is considered as microalbuminuria. Values more than 300 indicate overt nephropathy or macroalbuminuria.

Causes for false positive tests:

Transient increases in urine albumin excretion may occur in a setting of

1. Short term hyperglycemia
2. Fever
3. Urinary tract infections
4. Marked hypertension
5. Cardiac failure
6. Contamination with seminal or menstrual fluid
7. Following exercise
8. Dehydration

In our patients, microalbuminuria was estimated in a 24 hrs urine sample using photometric techniques by the method of fully automated immunoturbidometry. The above mentioned causes were excluded in the patient before estimating urine albumin excretion.

The following reference values were used:

Microalbuminuria:- 30-299 mg/24 hr

Macroalbuminuria:- >300mg/24hr

Assessment of Diastolic Dysfunction

All the patients enrolled in the study were subjected to Echocardiography. Transthoracic echocardiography was done after clinical evaluation. 2D echocardiography was done to assess the ventricular dimensions, presence of regional wall motion

abnormalities and left ventricular ejection fraction. The parasternal long axis and short axis views were used. The ejection fraction was obtained using Simpson's approach. Doppler echocardiography was done and using the apical four chamber view. The transmitral velocities were obtained by positioning the sample volume at the level of the tips of mitral leaflets. The early mitral inflow velocity (E) and late inflow velocity (A) was obtained and E/A ratio was calculated.

Data obtained by above methods was analysed statistically using

1. SPSS 15
2. Chi square test

Observation And Results

Sex Distribution: Among the 60 patients enrolled in the study, 34 were male patients and 26 were female patients

Age distribution: Only patients above the age of 30 years were included in the study. Patients were evenly distributed with respect to age characteristics. Maximum number of patients was in the age group 50 - 59 years (18 patients). 13 patients were above the age of 60 years. The mean age in our study was 49.3 ± 10.4 .

Duration of diabetes: With respect to duration of diabetes, patients were evenly distributed. Maximum number of patients was in the subcategory of 0-4 years duration (23 patients out of 60). Mean duration of diabetes in our study was $6.83 \text{ years} \pm 4.9$.

Nephropathy in diabetes: 40 patients out of 60 had evidence of nephropathy in the form of proteinuria. Microalbuminuria is present in 34 patients and overt nephropathy (macroalbuminuria) is present in 6 patients.

Table 1: Nephropathy in diabetes

Nephropathy	No. of patients (n=40)
Microalbuminuria	34
Macroalbuminuria	6

Table 2: Diabetes duration and nephropathy

Duration of diabetes	No. of patients with nephropathy (n=40)	
	Microalbuminuria	Macroalbuminuria
0-4 years	10	0
5-9 years	13	2
10 years and above	11	4

The prevalence of nephropathy was considerably higher when the duration of diabetes was more than 5 years. Nearly 62.5% of patients were had diabetes for more than 5 years. The overall prevalence of nephropathy was 66.67%. Microalbuminuria was present in 56.6% of cases.

Prevalence of diastolic dysfunction

Among the 60 patients of type 2 diabetes, 34 of them had evidence for diastolic dysfunction. 32 of these patients had Grade I diastolic dysfunction and 2 of them had Grade II diastolic dysfunction. Grade III and Grade IV dysfunction were not observed in our study. The mean E/A ratio in our study was 1.047 ± 0.356 . In patients with diastolic dysfunction the E/A ratio was much lower (0.7701 ± 0.09) than patients with normal function

Diastolic dysfunction and duration of diabetes

In our study, the prevalence was 88.3%, when the duration of diabetes was more than 10 years.

Table 3: Diastolic dysfunction and duration of diabetes

Duration of diabetes(n=60)	No. of patients with diastolic dysfunction (n=34)		% of patients of diastolic dysfunction
	Grade I	Grade II	
0 – 4 years (n= 23)	5	0	21.7%
5- 9 years(n= 20)	13	1	70.0%
10 years and above(n=17)	14	1	88.3%

By chi square test, **p value = 0.001****, significant at 1 % level

Diastolic dysfunction and Nephropathy

Among 40 patients with nephropathy, 32 of them had diastolic dysfunction accounting for 80%. The association with macroalbuminuria was significantly higher with all 6 patients developing diastolic dysfunction.

Table 4: Diastolic dysfunction and Nephropathy

Nephropathy	No. of patients with diastolic dysfunction (n=26)		% of patients of diastolic dysfunction
	Grade I	Grade II	
Microalbuminuria (n= 34)	25	1	76.5%
Macroalbumuria (n = 6)	5	1	100%
Total (n=40)	30	2	80.0%

Table 5: Diastolic dysfunction and Nephropathy

Nephropathy	No. of patients (n=60)		Total no. of patients
	Normal diastolic function	Diastolic dysfunction	
No nephropathy	18	2	20
Nephropathy	8	32	40

Chi square test value: p <0.001**

Discussion

Diastolic dysfunction in diabetes:

As per our study, 57 % of type 2 diabetes had diastolic dysfunction. **Khalil S I et al. (2007)⁵⁰** estimated that about 58% of diabetic patients had diastolic dysfunction of which majority of them were Grade I diastolic dysfunction. **Cosson et al (2003)⁵** demonstrated 69% of diabetics have abnormalities in diastolic filling.

Diastolic dysfunction and sex: Although our study demonstrates a higher prevalence among females, it was statistically not significant and underlying causes or mechanisms are not available to substantiate the discrepancy.

Duration of diabetes and diastolic dysfunction: High statistical significance (p = 0.001**) was observed for the association between duration of diabetes and diastolic dysfunction. Data from **Khalil S I et al (2007)⁵⁰** show that the prevalence of diastolic dysfunction increases with duration of diabetes. The study demonstrates a 100% prevalence of diastolic dysfunction when the duration of diabetes was more than 10 years. In our study, the prevalence was 88.3% in the same age group. In a study by Raev et al., diastolic dysfunction started at 8 years after the onset of diabetes.

Diastolic dysfunction and nephropathy: The prevalence of microalbuminuria in our study was 56.6%, compared to other Indian data, which report a prevalence of around 30%. A considerable number of patients with diabetic duration < 5 years had microalbuminuria (10 patients). However, the association between nephropathy and diastolic dysfunction is strong in our study (p<0.001**).

The association of diastolic dysfunction with microvascular complications strongly suggests the

possibility of a background microangiopathy. Since microalbuminuria is also marker of endothelial dysfunction, diastolic dysfunction indicates a widespread endothelial dysfunction. Zoneraich et al⁴⁹ demonstrated small vessel disease in 72% of diabetic patients. Microvascular changes include formation of microaneurysms and capillary membrane thickening.

Thus with available data from our study and supporting data, the existence of diastolic dysfunction in diabetics, who are normotensive and free from coronary artery disease is confirmed. Newer modalities of diabetic treatment targeting the pathogenic mechanisms like aldose reductase inhibitors, PKC pathway inhibitors, ACE inhibitors can reverse diastolic dysfunction and improve cardiovascular mortality.

Conclusion & Summary

As per our study performed on 60 patients with type 2 diabetes free of coronary artery disease and hypertension.

- Diastolic dysfunction is common in individuals with type 2 diabetes. Grade I diastolic dysfunction is more commonly encountered. Grade III and Grade IV diastolic dysfunction were not encountered. Diastolic dysfunction in our study was isolated and asymptomatic.
- Duration of type 2 diabetes positively correlates with diastolic dysfunction. Longer the duration of diabetes, greater is the prevalence of diastolic dysfunction. ,(p value = **0.001****)
- Obesity has a positive correlation with diastolic dysfunction. The association is strong when BMI values > 30 kg/m² .(p value= **0.002****)
- Cardiac disease in diabetes is no longer only a macrovascular disease, but microvascular changes do play a role.

- Our study recommends cardiac screening of diabetic patients, especially those with duration of diabetes > 5 years, obese individuals, old age and patients with microvascular complications even if they are asymptomatic for diastolic dysfunction.
- Heart disease in diabetes is primarily due to macrovascular disease, but growing evidence from different observations suggesting the possibility of a microvascular diabetic heart is gaining more importance. With diabetic therapies being targeted at molecular and cellular levels, cardiac dysfunction in diabetics can be curtailed if not prevented.

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