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A Study of Systolic and Diastolic Dysfunction in Normotensive Asymptomatic Patients with Type 2 Diabetes Mellitus

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Abstract

Various genetic and environmental factors influence the etiology and prognosis of diabetes. 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. Diabetes mellitus was formerly considered a disease of affluent. It has now become apparent that increase in Diabetes mellitus is due to demographic changes, cultural transition and population ageing, urbanization, increased consumption of refined foods, westernization, sedentary habits and over nutrition. In the present study fifty four type 2 diabetes patients who were normotensive and with no symptoms of cardiac disease, were selected for during the study . All patients were evaluated for left ventricular systolic and diastolic dysfunction by echocardiography. In the present study the E/A ratio <1 was seen in 22 (40.7%) of 54 individuals in the Study Group and 3 (5.5%) among the Control Group. The p value <0.001 and is statistically significant. Thus, 22 individuals in Study Group and 3 in Control Group had diastolic dysfunction.

Keywords: Systolic and Diastolic Dysfunction; Normotensive Asymptomatic Patients; Type 2 Diabetes Mellitus.

Introduction

Diabetes mellitus is a disease known to mankind for the past 2500 years. The word *diabetes* comes from Latin *diabētēs*, which in turn comes from Ancient Greek which literally means "a passer through; a siphon."Ancient Greek physician Aretaeus of Cappadocia (1st century CE) used that word, with the intended meaning "excessive discharge of urine", as the name for the disease. The word *mellitus* comes from the classical Latin word *mellītus*, meaning "mellite" (i.e. sweetened with honey). It was Thomas Willis who in 1675 added "mellitus" to the word "diabetes" as a designation for the disease, when he noticed the urine of a diabetic had a sweet taste (glycosuria) [1,2].

The Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency in insulin secretion and/or insulin action, which is modulated by genetic, HLA and environmental factors resulting in micro and macroangiopathy. It often runs in families. It is associated with decrease in insulin production or utilization, resulting in body's inability to utilize nutrients appropriately [3].

Various genetic and environmental factors influence the etiology and prognosis of diabetes. 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. Diabetes mellitus was formerly considered a disease of affluent. It has now become apparent that increase in Diabetes mellitus is due to demographic changes, cultural transition and population ageing, urbanization, increased consumption of refined foods, westernization, sedentary habits and over nutrition [1].

Diabetes mellitus has become a leading cause of premature death, disability and high health care costs. It is a silent killer disease. WHO estimates that 346 million people worldwide have diabetes. In 2004, an estimated 3.4 million people died from consequences of high blood sugar. More than 80% of diabetes deaths occur in low- and middle-income countries. WHO projects those diabetes deaths will double between 2005 and 2030 [4].

Indians are genetically more susceptible to Diabetes mellitus compared to other races. Indians settled abroad also show increased prevalence to Diabetes mellitus indicating that environmental factors also play a role in incidence of diabetes. 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". WHO has estimated that the number is likely to be 5.72 crores by 2025. The rapid increase in population, increased longevity and high ethnic susceptibility to diabetes, coupled with rapid urbanization and changes from traditional lifestyles will most likely trigger a Diabetes mellitus epidemic [1].

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. Diabetic subjects have been reported to develop congestive heart failure in the absence of coronary heart diseases, hypertension or any known structural heart disease [4].

The term 'diabetic cardiomyopathy' has been introduced for this condition and it was first coined by Rubler in 1972. It has been suggested that microangiopathic lesions of the myocardium, altered composition and fibrosis of myocardial interstitial and accumulation of lipids in myocardial cells are involved in pathogenesis of diabetic cardiomyopathy [5,6].

This study aims at to identify the systolic and diastolic dysfunction innormotensive asymptomatic type 2 diabetes mellitus patient to recognize the earlyinvolvement of heart in patients.

Methodology

In the present study fifty four type 2 diabetes patients who were normotensive and with no symptoms of cardiac disease, were selected for during the study . All patients were evaluated for left ventricular systolic and diastolic dysfunction by echocardiography.

Inclusion Criteria

- Patients with Type 2 Diabetes Mellitus satisfying ADA 2011 criteria.

Exclusion Criteria

- Patients with hypertension
- Patients with coronary artery disease.
- Patients with any other acquired or congenital heart disease causing systolic and diastolic dysfunction.
- Thyroid disorder.
- Overt renal disease.
- Patients with corpulmonale.
- Heart failure secondary to any cause.
- Any other disease/disorders interfering with the cardiac function like anaemia, vitamin deficiencies, toxin induced etc.,

With these exclusion criteria, out of 240 patients attending diabetic clinic 54 patients were selected. The relevant information were recorded in a pre-tested proforma. After taking detailed history, thorough clinical examination was done according to the proforma. BMI was calculated as weight (kilograms) divided by height (meters)squared.

Following investigations were done (All Biochemical parameters were done in a Semi-Autoanalyzer):

I. FBS & PPBS: was measured by a glucose oxidase method,

II. Blood urea: was measured by Modified Berthelot method,

III. Serum creatinine: was measured by Modified Jaffe's method,

IV. Fasting lipid profile: Total cholesterol and Triglycerides were measured by peroxidase method,

V. Glycatedhaemoglobin: was measured by Ion Exchange Resin method,

VI. Urine albumin: was evaluated by Micral-Test strips,

VII. ECG in all 12 leads,

VIII. Fundus examinations,

IX. Echocardiography.

Results

ECG had been taken in all the patients and were within normal limits

Table 1a: Showing Ejection Fraction (%) in Study and Control Group

	Group	Mean	SD	Minimum	Maximum	p-value
Ejection fraction	Study Group	65.14	3.68	60	74	<0.001
	Control Group	68.4	2.73	62	75	

Table 1b: Showing systolic dysfunction EF in Study and Control Group

	Ejection fraction < 50%	Ejection fraction > 50%
Study Group	0 (0%)	54
Control Group	0 (0%)	54
total	0 (0%)	108

In the present study, the mean EF of the Study Group was 65.14±3.68 and ranges from 60% to 74%. The mean EF of the Control Group was 68.4±2.73 and and ranges from 62% to 75%. A p-value of <0.001 which is statistically significant. But, systolic dysfunction was not seen in any of the individuals in the study as well as in the control group (Table 11a,b).

Table 2a: Showing Fractional Shortening (%) in Study and Control Group

	Group	Mean	SD	Minimum	Maximum
Fractional shortening	Study Group	33.5	3.82	39	25
	Study Group	36.09	3.48	42	28

Table 2b: Showing systolic dysfunction based on FS in Study and Control Group

		Study Group	Control Group	p-value
Fractional shortening	< 25%	0 (0%)	0 (0%)	<0.001
	> 25%	54 (100%)	54 (100%)	
	Total	54 (100%)	54 (100%)	

The mean fractional shortening in Study Group was 33.5±3.82 and ranges from 25-39%. The mean fractional shortening in Control Group was 36.09±3.48 and ranges from 28% to 42%. A p-value is <0.001, which is significant. However, none of the individuals in both study and control group had systolic dysfunction (Table 2a,b).

Table 3: Showing Diastolic Parameter (E/A ratio) in Study and Control Group

		Study Group	Control Group
E/A ratio	< 1.0	22 (40.7%)	3 (5.5%)
	≥ 1.0	32 (59.3%)	51(94.5%)
	Total	54 (100%)	54 (100%)

In the present study the E/A ratio <1 was seen in 22(40.7%) of 54 individuals in the Study Group and 3 (5.5%) among the Control Group. The p value <0.001 and is statistically significant. Thus, 22 individuals in Study Group and 3 in Control Group had diastolic dysfunction (Table 3).

In the Table 4 the study group has beenseparated on the basis of left ventricular diastolic dysfunction and the various physical and metabolic characteristics have been compared among them.

The inferences that can be derived from the above table are that:

The mean age of the cases with diastolic dysfunction was 54±4 years and that of the cases without diastolic dysfunction was 46±5 years. So, the mean age of patients with diastolic dysfunction

Table 4: Characteristics of the Study Group Separated on the Basis of Left Ventricular Diastolic Dysfunction:

Characteristics	Subjects with diastolic dysfunction	Subjects with Normal diastolic function	P value
n	22	32	
Age (years)	54±4	46±5	<0.001
Diabetes duration (years)	6.9	6.5	0.298
BMI (kg/m2)	24.5±2.0	23.3±1.6	0.028
Systolic blood pressure (mmHg)	123±5.5	120±7.3	0.091
Diastolic blood pressure (mmHg)	79±3.6	76±5.8	0.056
HbA1c(%)	9.38±1.38	8.54±1.27	0.026
Fasting glucose (mg/dl)	169±15	163±13.5	0.006
Post prandial glucose (mg/dl)	247±34	222±33	0.010
Total cholesterol (mg/dl)	194±17	186±16	0.100
Triglycerides (mg/dl)	125±14	122±15	0.501
HDL Cholesterol (mg/dl)	37.5±3.4	37.7±3.7	0.860

was greater than that of the patients without diastolic dysfunction. The p-value is <0.001 which is statistically significant.

The mean duration of diabetes among the cases (6.9 years) with diastolic dysfunction was higher than that of the cases without diastolic dysfunction (6.5 years) but the p-value was not significant.

The mean systolic blood pressure of the cases with diastolic dysfunction (123±2.0) was higher than the cases without diastolic dysfunction (120±7.3) but this was not statistically significant (p-value 0.091).

The mean diastolic blood pressure of the cases with diastolic dysfunction (79±3.6) was higher than the cases without diastolic dysfunction (76±5.8) but this was not statistically significant (p-value 0.056).

The mean fasting blood glucose of the cases with diastolic dysfunction (169±15) was higher than the cases without diastolic dysfunction (163±13.5) and this was also statistically significant (p-value 0.006).

The mean post-prandial blood glucose of the cases with diastolic dysfunction (247±34) was higher than the cases without diastolic dysfunction (222±33) and this was also statistically significant (p-value 0.010).

The mean HbA_{1c} (%) of the cases with diastolic dysfunction (9.38±1.38) was higher than the cases without diastolic dysfunction (8.54±1.27) and this was statistically significant (p-value0.026).

The lipid profile of the patients with diastolic dysfunction was higher than the patients without diastolic dysfunction but they were not statistically significant.

Discussion

In the present study, LV systolic function was assessed by measuring ejection fraction and fractional shortening as important parameters through m-mode and 2D echocardiography. In the present study mean EF of the Study Group was 65.14±3.68. The present study is comparable to that of Poirier P et al. [7] Abdul Khaliq M.H. et al. [8] Boyer J.K et al. [9] and Rajput R et al. [10] who showed mean ejection fraction of 65%, 58%, 64% and In the present study mean Fractional Shortening was 33.5±3.82. The present study is comparable to that of Abdul Khaliq M.A. et al.,[2] John K. Boyer [9] and Rajput R et al. [10] who showed mean fractional shortening of 33.0±8.6 and 32.7±5.32 and 29.06±9.2 respectively.

In the present study, 22 patients had E/A ratio of < 1 constituting 40.7% of study group and 32 patients (59.2%) had E/A ratio > 1. thus diastolic dysfunction was seen in 22 patients (40.7%) as, E/A < 1 is very sensitive and specific indicator of LV diastolic dysfunction.

In the present study in comparison the other studies the diastolic dysfunction was found in relatively lesser no of patients. This is mainly because conventional Doppler has limited value in the clinical settings of elevated end diastolic pressure were there can be apparent normal transmitral flow velocity with pseudonormalisation of E/A ratio. In the present study an attempt was made to exclude pseudonormalisation by looking at IVRT and hepatic doppler. However, it would have been better if values of Doppler during Valsalva maneuver or tissue Doppler imaging would have been considered. Thus, since in the present study these variables were not taken there could have been underestimation of diastolic dysfunction. The values obtained in the present study are comparable with that of Poirier P et al. [7] wherein before considering for the pseudonormal pattern the percentage diastolic dysfunction was is seen in only 38% of cases. However on using valsalva maneuver and pulmonary venous recordings an additional 28%of cases had diastolic dysfunction.

Zabalgoitia et al. [15] conclude that diastolic dysfunction in type 2 DM patients is often found despite adequate metabolic control and freedom for clinically detectable heart disease. The Valsalva maneuver can unmask an additional 17% of patients with subclinical abnormal LV filling pattern who otherwise would be classified as having a normal diastolic physiology.

But, even with this limitation a significant number of patients had diastolic dysfunction in comparison with the Control Group. In the present study 22 cases (40.7%) had LV diastolic abnormalities and this was inspite of relatively normal LV systolic function and absence of cardiac symptoms. Even in the related studies done by Poirier P et al. [7] Gani Bajraktari (2005) [11], Cosson S et al. (2003) [12], a significant percentage of normotensive asymptomatic Type 2 Diabetic patients had diastolic dysfunction.

In the present study the diastolic dysfunction (E/A ratio <1) was also seen in 3 (5.5%) of normal subjects and all these individuals belonged to a higher age group. Thus, this observation is most probably due to the influence of age on diastolic function as described earlier.

In the present study a statistically significant (p-value <0.05) difference was found in the age, glycemic status (FBS, PPBS and $HbA_{1c)}$ and BMI among the subjects with and without diastolic dysfunction.

In the present study, it was found that subjects with normal diastolic function were younger (46±5 years) than the subjects with diastolic dysfunction (54±4 years).

In the present study indices of glycemic status (blood sugar and glycated haemoglobin) were higher in the subjects with diastolic dysfunction than in those without diastolic dysfunction. A similar observation was made by Hiramatsu K et al. (1992) [13], Uusitupa M et al. (1983) [14]. In all these studies it was also observed that there was an improvement in cardiac function after adequate treatment and control of diabetes.

Hiramatsu K et al. [13] found that left ventricular diastolic filling is impaired in mildly hyperglycemic patients with Type 2 diabetes mellitus without severe complication, the abnormality being more intense in patients with retinopathy. A short term glycemic control resulted in marked decrease in the abnormalities of left ventricular function in patients without retinopathy but not in those with it [13].

However, there was no differences among groups in diabetes duration, systolic and diastolic blood pressure and fasting lipid profile.

Conclusion

The asymptomatic involvement of the heart in diabetic patients is a common condition. It mainly manifests as diastolic dysfunction. A direct correlation between diastolic dysfunction and glycemic control is seen and a poor glycemic status worsens the diastolic dysfunction. Conventional echocardiography is found to be a simple & economical test for detecting LV dysfunction and that alteration of E/A ratio < 1 is a sensitive and specific indicator of early diastolic dysfunction. Therefore, echocardiography in type 2 diabetes mellitus patients irrespective of symptoms may be considered as a screening procedure for early detection of cardiac dysfunction. Also, a good glycemic control is one of the remedial measures for diabetic cardiomyopathy.

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