PREVALENCE OF ASYMPTOMATIC LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN NORMOTENSIVE TYPE 2 DIABETIC PATIENTS

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ABSTRACT

Objective: *To determine the frequency of asymptomatic left ventricular diastolic dysfunction in normotesive type 2 diabetic patients.*

Material and Methods: *This descriptive case series study was conducted on 80 normotesive Type 2 diabetic patients at Cardiology Department, PGMI Lady Reading Hospital Peshawar from March 2007 to March 2008. Detailed history and physical examination was performed on every patient. . The glycemic status was defined on the basis of HbA1c. Exercise tolerance test was performed on every patient to exclude major ischemia. Echocardiography was performed in left lateral position. Main outcome measure was Left ventricular diastolic dysfunction.*

Results: *We enrolled 80 normotesive Type 2 diabetic patients in the study that fulfills the inclusion criteria. Left ventricular diastolic dysfunction was found in 53% (43/80). There were 20 (47%) males and 23 females (53%) among subjects presenting with diastolic dysfunction. Subjects with diastolic dysfunction the mean age were 55±15 years. Patients having no Left ventricular diastolic dysfunction mean age were 52.5±7 years.*

Conclusion: *There is a high prevalence of asymptomatic left ventricular diastolic dysfunction in normotensive type 2 diabetic patients.*

Key Words: *Type 2 diabetes mellitus, Left ventricular diastolic dysfunction.*

INTRODUCTION

Prevalence of diabetes in adult worldwide was estimated to be 4.0% in 1995 and to rise to 5.4% by the year 2025. It is higher in developing countries. The number of adults with diabetes in the world will rise from 135 million in 1995 to 300 million in the year 2025. The major part of this numerical increase will occur in developing countries. There will be a 42% increase, from 51 to 72 million, in the developed countries and a 170% increase, from 84 to 228 million, in the developing countries. Thus by the year 2025, >75% of people with diabetes will reside in developing countries. There are more women than men with diabetes, especially in developed countries. In the future, diabetes will be increasingly concentrated in urban areas[1].

Pakistanis are an ethnic group having an inherent predilection to develop diabetes. Increase in life expectancy and major changes in diet and lifestyles that are a part of urbanization and social development further contribute to the existing trend[2].

National diabetes survey of Pakistan documented prevalence of diabetes and Impaired Glucose Tolerance in four provinces. Diabetes and IGT was present in 22-25% of the subjects examined. In the urban areas, overall prevalence of diabetes ranged from 10.8% in Baluchistan to 16.5% in Sindh, whereas in the rural areas, prevalence of diabetes ranged from 13.9% in Sindh, 7.5% in Baluchistan to 6.39% in Punjab[3].

Rubler et al. first proposed the existence of a diabetic cardiomyopathy in 1972 on the basis

of postmortem finding[4]. Subsequently, abnormalities in both systolic and diastolic performance in diabetic subjects have been demonstrated in animal and human studies[5]. Diastolic dysfunction has been described as an early sign of the diabetic cardiomyopathy before systolic dysfunction[6].

As compared to age matched non diabetic patients there is high incidence of congestive heart failure in diabetic patients[7]. Several mechanisms were proposed for diabetic cardiomyopathy including microangiopathy, autonomic nervous dysfunction, defecting cellular calcium transport as well as structural changes in myocardial intracellular proteins and accumulation of collagens leading to increased stiffening of the ventricular wall[7]. Diabetic cardiomyopathy is associated with increased cardiovascular mortality[8].

Diastolic dysfunction comprises about 30 to 50% of patients admitted in hospital for heart failure[9]. Elderly patients admitted in hospital for heart failure is largely attributed to this condition[9]. Considering diastolic dysfunction diabetes mellitus is an important independent factor[10].

The most useful clinical tools for the assessment of left ventricular diastolic function is Conventional Doppler Echocadiography[11]. Not only utilized for the diagnostic purposes but also for establishing prognosis and evaluating the effect of treatment[11]. Tissue Doppler imaging has provided useful insight in the study of diastolic function[11]. Accurate assessment of diastolic dysfunction is possible with Tissue Doppler imaging and is relatively insensitive to the effects of pre-load compensation[11,12].

The first stage of diabetic cardiomyopathy is the development of Left ventricular diastolic dysfunction, reinforcing the importance of early detection of diastolic dysfunction in individual with diabetes[13]. It has been shown that intervention such as aerobic exercise could beneficially influence diastolic function, the early and accurate detection of left ventricular diastolic dysfunction might have therapeutic implication[13].

Therefore, this study was conducted to determine the frequency of asymptomatic Left ventricular diastolic dysfunction in normotensive Type 2 diabetic patients. This study highlights the problem of left ventricular diastolic dysfunction to be taken in consideration while treating patients with Type 2 diabetes mellitus who were free from symptoms of heart failure. Because it has been shown that poor control of diabetes leads to early development of microvascular complication and left ventricular dysfunction initially in the form of left ventricular diastolic dysfunction[6]. Studies showed correlation between glycemic control and left ventricular diastolic dysfunction with associated improvement in cardiac function after adequate treatment. Diastolic function correlated with improved glycemic control both in patients with and in patients without evidence of ischemic heart disease[14].

MATERIAL AND METHODS

This study was conducted from March 2007 to January 2008. All normotensive Type 2 diabetic patients free from complications of diabetes, consenting to participate, presenting in out patient department (OPD) of Lady Reading Hospital were included. Complete history and full physical examination was done on every patient included in the study. Patients with history of CAD, congestive heart failure, valvular heart disease, hypertension, connective tissue diseases, thyroid dysfunction and renal diseases were excluded from the study.

Blood Pressure less than 130/85 mmHg is defined as normotensive according to JNC 7 guidelines[15].

Diabetic status was defined on the basis of HbA1c level. Resting ECG and Exercise tolerance test was performed on every patient to exclude ischemia. The study patients underwent echocardiography (using Acuson CV70 Siemens system equipped with TDI technology). All patients were examined in the left lateral position. Measurements of the different chambers of the heart were done according to the recommendations of the American Society of Echocardiography.

From apical four-chamber view pulse wave Doppler Mitral inflow velocities were recorded by placing sample volume at the tips of the Mitral valve. The transmitral peak early diastolic velocity (E), peak late diastolic velocity (A), E wave deceleration time (DT) and E/A ratio were measured. Isovolumic relaxation time (IVRT) was recorded from apical 5- chamber view by simultaneously recording of the mitral and aortic flows.

Tissue Doppler Imaging was performed by activating the TDI function. To assess the diastolic function, two velocities, peak early diastolic velocity (Em) and peak late diastolic velocity (Am) at Mitral annulus was determined. Four different sites on the mitral annulus i.e. Lateral, Anterior, Septal and Inferior were selected. For lateral and septal sites apical 4-chamber view and for anterior and inferior sites apical 2-chamber views were utilised. Mean values from above four sites were used to assess global diastolic left ventricular function.

The normal cut-off values for Doppler echocardiography and Tissue Doppler Imaging were predefined and adopted from the guidelines of American Society of Echocardiography.

Impaired relaxation on conventional Doppler echocardiography was defined as deceleration time >220msec, Isovolumic relaxation time > 100 msec, E/A < 1. Diastolic dysfunction on Tissue Doppler imaging was defined as mean early diastolic mitral annulus velocity <0.11m/sec.

Statistical analysis: Data were analysed using SPSS version 10. The variables were age, sex, duration of diabetes mellitus, Ejection fraction, Fractional shortening, Mitral inflow velocities, Isovolumic relaxation time and Mitral E wave deceleration time on Doppler Echocardiography and the Mean diastolic mitral annular velocities on TDI. Data were expressed as mean ± standard deviation and in percentage.

RESULTS

We enrolled 80 normotesive Type 2 diabetic patients that fulfill the inclusion criteria. The glycemic status was defined on the basis of HbA1c. The basic characteristics of the patients were shown in Table 1. Males were 36 in number i.e. 45.4% as compared to females 44 in numbers i.e. 54.6%. Fifty three percent (43/80) had left ventricular diastolic dysfunction. There were 20 males and 23 females among patients presenting with diastolic dysfunction. Patients with diastolic dysfunction the mean age were 55±15. Basic echocardiographic characteristics were normal in all patient as shown by mean values in Table 2. Conventional Doppler and TDI parameters of patients having Left ventricular diastolic dysfunction were determined and the mean values are presented in Table 3.

Table 1: Basic clinical characteristics of patients

Characteristics	Patients having Left ventricular diastolic dysfunction
Mean Age (In Years)	55±15
Sex	M=20, F=23
Mean Heart rate	74±5
Mean Systolic blood pressure	120±10 mmHg
Mean Diastolic blood pressure	80±5 mmHg
Mean Duration of diabetes	12.29±4.
Mean HbA1c Level	8±1

Table 2: Echocardiographic characteristics of patients

Characteristics	Patients having Left ventricular diastolic dysfunction
LVESD (cm)	2.9
LVEDD (cm)	4.3
IVS (cm)	0.81
PW (cm)	0.80
EF%	65
FS%	30
LA (cm)	4.1

Table 3: Conventional Doppler and Tissue Doppler Imaging parameters of patients

Characteristics	Patients having Left ventricular diastolic dysfunction
E wave (m/sec)	0.57
A wave (m/sec)	0.66
E/A ratio	0.89
IVRT (msec)	105
DT (msec)	217
Em wave (m/sec)	0.06

DISCUSSION

In this study, we noted higher frequency of left ventricular diastolic dysfunction among normotensive diabetic patients seen at outpatient department was 53%. There were more female subjects both with normal and abnormal diastolic dysfunction— due to the higher incidence of diabetes among females. The study was limited due to the small sample size after exclusion of patients due to co-morbidities and intake of medications, which could alter their hemodynamic status.

The diastolic dysfunction was more frequently seen in patients having diabetes for more than 10 years. Patients having duration of diabetes less than 10 years were more likely to have normal diastolic function. Majority of patients having age ≥ 55 years had develop Left ventricular diastolic dysfunction.

The presence of left ventricular diastolic dysfunction in a significant proportion of our patients—especially after eliminating patients with other co-morbid illnesses and concentrating on normotensive patients with normal electrocardiograms—emphasizes the need for more sophisticated baseline screening methods such as the echocardiogram.

Echocardiogram gives similar prognostic information in relation to mortality as radionuclide. Echocardiogram is simple to perform at our major centers, is sensitive and specific,

repeatable and acceptable to patients. We have yet to make it more cost effective to patients though.

Screening for a disease or a complication of the disease will only make sense if there was something we could do to prevent or reverse this.

Poor control of diabetes leads to early development of microvascular complication and left ventricular dysfunction initially in the form of left ventricular diastolic dysfunction[6]. Studies showed correlation between glycemic control and left ventricular diastolic dysfunction with associated improvement in cardiac function after adequate treatment[19]. Diastolic function correlated with improved glycemic control both in patients with and in patients without evidence of ischemic heart disease[16]. Improved myocardial energy substrate utilization is likely to be involved[16]. Endothelial dysfunction is aggravated by hyperglycemia[17]. Normoglycaemia and insulin improved myocardial diastolic function and perfusion in non-insulin dependent diabetes[16].

Left ventricular diastolic abnormalities reported in diabetes mellitus contain a component of reversibility and can be prevented by aggressive treatment[16]. Chronic hyperglycemia contributes to diabetic complications through the formation of advanced glycosylation end products, which are irreversibly formed biochemical end products of non enzymatic glycosylation[17]. AGEs play a key role in the pathogenesis of cardiomyopathy[17]. Diabetes produces myocardial stiffness before the development of myocardial fibrosis in association with increased formation of AGEs[17]. All these processes can be slow down with good glycemic control[17]. Early and accurate detection of left ventricular diastolic dysfunction in Type 2 diabetic patients might have therapeutic implication[14]. Documentation of diastolic dysfunction should result in the initiation of therapy to prevent advancement to heart failure.

Tight glycemic control as evidenced by an HBA1c <1% above normal and near normal fasting glucose levels. Blood pressure control, lowering lipid levels to target levels for diabetics, exercise, weight management aiming for the appropriate BMI and waist-hip index and discontinuing smoking all prevent, reduce or reverse complications of diabetes.

SOLVD-P showed that treatment with ace-inhibitors reduced progression of LV dysfunction to chronic heart failure from whatever cause. Hospitalization was reduced by more than one third. Initial hospitalizations were reduced by 36% and 12 multiple hospitalizations by 44%. Diabetes mellitus predisposes to non-cardiac causes of heart failure. Diabetic cardiomyopathy is typically of the mildly dilated variety with diastolic preceding systolic dysfunction[18].

Although this study was limited by its small sample size, as a preliminary study, this emphasizes the need for early detection of diastolic dysfunction as part of the preventive management in the treatment of our diabetics. The high incidence of morbidity and mortality due to heart disease in diabetics makes it imperative to use a screening test, which is readily available and affordable/cost effective for our patients like the echocardiogram.

CONCLUSION

There is a higher prevalence of asymptomatic diastolic dysfunction in normotensive type 2 diabetic patients in the outpatient department of Lady Reading Hospital Peshawar. Echocardiogram including conventional Doppler and Doppler tissue imaging is recommended in work-up of diabetics. This will allow to initiate early and aggressive treatment for the prevention of heart diseases in this particular population.

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