Original Article

ASSOCIATION OF HYPERTENSION AND DIASTOLIC DYSFUNCTION WITH TYPE-2 DIABETES MELLITUS

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ABSTRACT

Objective: To evaluate the prevalence of hypertension and diastolic dysfunction (LVDD) with normal ejection fraction in type-2 diabetes mellitus.

Method: Two hundred twelve diabetic patients (98 females and 114 males) from January 2005 to June 2006 were enrolled in this study. Their ages ranged from 35 to 65 years with mean age of 55 years. Patients with Diabetes Mellitus Type-2, Hypertension: BP³140/90 (with or without medication) Body Mass Index³30, Waist-Hip ratio>0.90. Left Ventricular Diastolic Dysfunction (LVDD) and Serum Triglyceride and HDL Cholesterol were included.

Result: Out of 212 patients, 104(49%) were found to be hypertensive (both systolic and diastolic) and 12 patients (5.6%) were found to be suffering from isolated systolic hypertension. Hence total number of hypertensive patients was 116 (54.6%). Thirty two patients were found to be suffering from diastolic dysfunction.

Conclusion: Hypertension and Diabetes are interlinked and show how micro and macrovascular complications of diabetes are increased when two conditions occur together. The LVDD is much more prevalent than previously suggested in patients with type-2 diabetes mellitus. Hence LVDD is an early marker of diabetic cardiomyopathy.

KEYWORDS: Diabetes Mellitus Type-2, Hypertension, Diastolic dysfunction.

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INTRODUCTION

Diabetes Mellitus is a cardiovascular disease. Two out of three diabetic patients die of cardiovascular disease or its complications.[1] According to the international diabetic federation the number of diabetic patients worldwide was estimated as 150 million in 2000, a figure that is said to rise to 300 million in 2025.[2] The implications are enormous, both in terms of personal suffering and cost to health-care systems, which are increasingly faced with treating the serious macro-vascular complications of diabetes mellitus.

Hypertension frequently co exists with diabetes, there is an increased prevalence of hypertension among diabetic patients[3] but there is also high propensity among hypertensive patients to develop type-2 diabetes.[4,5] When occurring together the two disease entities appear to aggravate one another worsening both the diabetes and cardiovascular end points.[6]

Data from UK Prospective Diabetes Study (UKPDS) revealed that every 10mm.Hg reduction in the level of systolic BP is associated with a nearly 12% lower incidence in myocardial infarction, down to a systolic BP level of <120mm.Hg.[7] Progressive lower diastolic BP also reduces CV risk progressively. The Hyper-

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tension Optimal Treatment (HOT) trial showed that number of major cardiovascular events dropped in line with increasing astringent target diastolic BP-target.[8] These findings are reflected in the BP-target for diabetic patients of < 130/80mm of Hg as now recommended by European Society of Hypertension,[9] JNC7 report[10] and American Diabetes Association.[11]

Hypertension is the most important preventable cause of premature death in various countries. The ASCOT study (AngloScandanavian Cardiac Outcomes Trial) demonstrated both control of blood pressure and reduction in risk of strokes, heart attacks and other related diseases such as diabetes.[12]

Regarding diastolic dysfunction the most common feature of diabetic heart is abnormal early left-ventricular diastolic filling, suggesting reduced compliance or prolonged relaxation[13] because diabetes affect diastolic functions before systolic function,[14] left ventricular diastolic dysfunction may be an early marker of diabetic cardiomyopathy. Hypertension is also associated with impaired diastolic filling.[15]

PATIENTS AND METHODS

A total of 212 patients (98 females and 114 males) of Diabetes Mellitus, 35 to 65 years of age (mean age was 55 years), from Ziauddin Medical University Hospital and its consultation clinic (Kaemari Campus) were enrolled in this study during January 2005 to June 2006. Prevalence of Hypertension and left ventricular diastolic dysfunction was carried out by means of cross-sectional study and all the patients were selected on random sample basis. The inclusion criteria was: Diabetes Mellitus Type-2, Hypertension: BP ≥140/90 mm Hg. (with or without medication) Body Mass Index^{3}30 Waist-Hip ratio>0.90.

Diastolic Dysfunction (Normal Systolic function LV ejection fraction ≥50% no segmental wall motion abnormalities and no evidence of significant coronary valvular, infiltrative pericardial or pulmonary disease) and serum Triglyceride and HDL Cholesterol.

Patient on insulin therapy, those with history of angina pectoris or myocardial infarction, Diabetic complications like Nephropathy, Neuropathy, and Retinopathy as well as valvular and congenital heart disease were excluded.

BP was measured with a random zero mercury sphygmanometer. The mean of 6 measurements (3 while lying and 3 while standing) of systolic and diastolic BP was used on different occasions. As regards the assessment for obesity, BMI was calculated as weight in Kgs. divided by the square of height in meters. Waist circumference was calculated as an average of 2 measurements taken after inspiration and expiration at the mid-point of the lowest rib and iliac crest.

Waist-Hip ratio was defined as waist-girth divided by the hip-circumference measured at greater trochanter. For assessment of blood sugar, HbA1c and dyslipidaemia, the patients were asked to fast 12 to 14 hours. Then the blood samples were analysed. The reading of fasting blood glucose level, serum triglyceride, HDL, LDL Cholesterol plasma glucose concentration were measured by a glucose oxidase method and HbA1C was measured by an affinity binding assay, serum cholesterol, triglyceride and HDL were analyzed enzymatically. The reading of fasting blood glucose level, serum triglyceride, HDL, LDL cholesterol and HbA1c were recorded. For the assessment of effect on the CV system, ECG, chest X-ray and echocardiography were carried out.

Echocardiography was recorded by means of a 2-dimensional, M-mode and Doppler method. Patients were examined on the left lateral decubitus position using standard parasternal, short axis and apical views. Left ventricular diastolic dysfunction (LVDD) was evaluated. All Doppler measurements were assessed at the end of expiration.

From the transmitted recording, the measurements were carried out. Peak E- velocity in cms/sec. (Peak early transmitted filling velocity during early diastole). Peak A velocity in cms/sec (peak transmitted Atrial filling Velocity during late diastole) and declaration time in milliseconds. (Time elapsed between peak E-velocity and the point where the extrapolation of

the declaration slope of the E-velocity crosses the zero base line). No subject had echocardiographically detectable regional wall motion abnormalities and each subject had normal ejection fractions. All the cardiac valves were examined to rule out significant valvular disease.

RESULT

A total of 212 patients were screened and diagnosed with DM Type-2, their mean fasting blood sugar level was 140mg/dl. On average basis HBA1C was proved to be >8. Their mean age was calculated as 55 years. Mean duration of DM was 10 years. Out of 212 patients, 104(49%) patients were found to be hypertensive (both systolic and diastolic) and 12(5.6%) patients were suffering from systolic hypertension. Thus there were 116 hypertensive patients (54.6%). Among them both systolic and diastolic hypertension, there were 58 males and 46 females. Among systolic hypertensive patients 7 were males and 5 were females.

Serum Cholesterol was increased by 220mg/dl (mean). Serum Trigyceride was found to be 210mg/dl (mean). Overall Body Mass Index was found to be 30 and waist-hip ratio was 0.92.

Table-I: Characteristic of 212 diabetic patients

Age in years (mean)	55
	SD±6
Male	114
Female	98
Hypertension	116(54.7%)
BMI (Kg/m2) (mean)	30
	SD±2.8
Fasting blood sugar (mean)	140m/dL
	SD±12.9
HbA1C% (mean)	8
	SD±0.95
Blood cholesterol (mean)	220mg/dL
	SD±20.40
Blood triglycerides (mean)	210mg/dL
	SD±19.5
HDL (mean)	44mg/dL
	SD±7.8
Waist-hip ratio	0.92
	SD±0.06

Note: SD *(Standard deviation)*

Table-II: Hypertension and diastolic dysfunction ratio in Diabetes Mellitus

Sex	*Total No. of patients*	*Hypertension*	*Diastolic dysfunction*
	n=212	n=116	n=32
Male	114	65 (57%)	20(17.5%)
Female	98	51 (52%)	12(12.2%)

P-Value = 0.468 =0.283

Diastolic dysfunction was carried out by means of 2-D (2 Dimensional) colored Doppler, and M-Mode echocardiography was performed. Only 32(15%) patients had shown isolated diastolic dysfunction having ejection fraction ≥50. There were no ECG changes in the heart. All chest X-rays of patients were normal, so patients had Diabetes Mellitus Type-2 hypertension and diastolic dysfunction.

Thirty two out of 212 patients showed diastolic dysfunction with normal ejection fraction; subjects with impaired relaxation showed lower E-wave velocity compared with subjects with normal diastolic function. A-wave velocity was higher in patients with impaired relaxation compared with patients with normal diastolic dysfunction. Hence E:A ratio showed an inverse proportion or less than one. Most cases of diastolic dysfunction with normal ejection fraction were found in elderly age groups. There was no correlation between the E:A ratio and lipid profile, E:A ratio and HbA1C, E:A ratio and fasting blood glucose, E:A ratio and fasting blood glucose, E:A ratio and left ventricular mass.

Table-III: Involvement of different age groups

Ages (yrs)	*Diabetes Mellitus*	*Hypertension*	*Diastolic dysfunction*
35-45	20	6	2
46-55	94	52	13
56-65	98	58	17
Total	212	116	32

DISCUSSION

According to the WHO estimates, there were >5.2 million Diabetics in the year 2000 and it will be 13.9 million by the year 2030. Pakistan is 6th in the world ranking.[16] Hence according to the DCCT and UKPDS, poor HbA1C control will be progressively worsening complications. Every 1% decrease in mean HbA1C (%) yields significant reduction in complications.[17] Hypertension is a common finding in patients with type-2 diabetes mellitus, when present it is an ominous sign that double the already elevated risk of future cardiovascular events.

Lowering BP has repeatedly shown to benefit hypertensive diabetic patients in terms of both macro and micro vascular disease. The fact that anti-hypertensive treatment reduces diabetic and CV end points in diabetes underlines the necessity to integrate rigorous BP control with glycaemic control in the management of diabetes.

In this study 212 diabetes mellitus patients were selected, out of which 116 patients (54.6%) proved to be hypertensive. Among them 12 patients were those who had systolic hypertension. They belonged to ≥60 years of age. FRAMINGHAM study revealed that on long term follow-up stroke and CHD are respectively 4 and 5 times more common in patients with systolic hypertension.[18] Both JNC-VII and WHO: (International Society of Hypertension) sub-committee guidelines have strongly recommended treating systolic hypertension at 140mm Hg. or even lower in diabetics. This isolated systolic hypertension is due to arterial stiffness, which results in an increased PWV (pulse wave velocity) and therefore reflects high pulse pressure.

There is a doubling of cardiovascular events when hypertension and diabetes mellitus coexist.[19] With each disease patient has abnormalities in central and peripheral characteristics of cardiovascular structure and function that precedes the clinical manifestation of cardiovascular disease, including increased left ventricular mass and wall thickness, left ventricular diastolic filling abnormalities impaired endothelial functions and increased arterial stiffness. The most common feature of the diabetic heart is abnormal early left ventricular diastolic filling, suggesting reduced compliance and prolonged relaxation.[13] Diabetes affects diastolic function before systolic function; left ventricular diastolic dysfunction (LVDD) may be an early marker of diabetic cardiomyopathy. Hypertension is also associated with impaired diastolic filling.[20]

In our study there were 32 cases of diastolic dysfunction with EF ≥50%. This study shows inverse EA ratio, prolonged relaxation of left ventricle during M-Mode, 2-D and Doppler echocardiography though the number is small but it signifies alarming situation of diabetic heart in adults without any myocardial ischemia, congestive cardiac failure and any valvular heart disease.

As the age increases, there is a decrease in EA ratio. This progression of LVDD with aging seems markedly accelerated by diabetes. Hence increasing numbers of cases are found in elderly people in this study. Therefore LVDD can occur in individuals with well-controlled diabetes and without vascular complication. This diabetic cardiomyopathy may happen due to arterial stiffness, inflammation, obesity and endothelial dysfunction.[21]

CONCLUSION

The evidence described clearly shows how closely Diabetes and hypertension are interlinked and how micro and macro vascular complications of Diabetes increase when the two conditions co-exist. The LVDD is much more prevalent than previously thought in patients with type 2 Diabetes Mellitus who are free of clinically detectable heart disease. Hence this study unmasks the significant number of LVDD. For prevention one should adopt life style modifications to control blood sugar level and a Dietary Approach to Stop Hypertension (DASH) eating plans.[22] (diet rich in fruits, vegetables and low fat dietary products with a reduced content of saturated and total fat.)

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