

## Prevalence of Hypertension and Diastolic Dysfunction in Patients with Type-2 Diabetes Mellitus

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### Abstract

**Background:** left ventricular diastolic dysfunction is common in patients with type 2 diabetes mellitus, but their prognostic importance in these patients remains unknown. Aim of this study is to detect the association of hypertension and diastolic dysfunction (LVDD) with normal ejection fraction in type-2 diabetes mellitus.

**Method:** A cross-sectional study of 164 diabetic patients visit diabetic clinic in marjan teaching hospital (76 females and 88 males) from January 2007 to February 2008 were enrolled in this study. Their ages ranged from 35 to 65 years with mean age of 55 years. The inclusion criteria were: diabetes mellitus type 2, hypertension (BP  $\geq$  140/90 mmHg) with or without medication, body mass index 30, and waist-hip ratio  $>$  0.90. In those patients we do blood sugar, HbA1C, lipid profile, ECG, CXR & ECHO to detect Left Ventricular Diastolic Dysfunction (LVDD).

**Result:** Out of 164 patients, 80(48.7%) were found to be hypertensive (both systolic and diastolic) and 9 patients (5.3%) were found to be suffering from isolated systolic hypertension. Hence, total number of hypertensive patients was 89 (54%). Twenty five out of 164 patients were found to be suffering from diastolic dysfunction with normal ejection fraction.

**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.

### الخلاصة

إن الأهمية من هذه الدراسة هي لتحديد العلاقة بين ارتفاع ضغط الدم و العطل الانبساطي لعضلة القلب اليسرى مع داء السكري من النوع الثاني. حيث تمت دراسة 164 مريض من مركز السكري في بابل من شهر كانون الثاني 2007 إلى شباط 2008، حيث تم اختيار هؤلاء المرضى المصابين بالنوع الثاني ممن لديهم ارتفاع في ضغط الدم، زيادة مؤشر كتلة الجسم (أكثر من 30) ونسبة الخصر إلى الورك (أكثر من 0,9). تمت دراسة العطل الانبساطي لعضلة القلب اليسرى من خلال فحص المرضى بالايكو. من 164 مريض وجد ثمانون مريض مصاب بارتفاع ضغط الدم الانقباضي مع الانبساطي، و تسعة مرضى مصابين بارتفاع الضغط الانبساطي فقط.

خمسة و عشرون مريض من اصل 164 كانوا مصابين بعطل عضلة القلب الانبساطي و بنسبة 15,2% من مجموع المرضى. تستنتج من هذه الدراسة إن اجتماع داء السكري من النوع الثاني مع ارتفاع ضغط الدم في نفس المريض تؤدي إلى زيادة مخاطر الإصابة بالاختلالات مع تصلب الشرايين. هذا بالإضافة إلى أن عطل عضلة القلب الانبساطي المرافق لداء السكري هو علامة مهمة و مبكرة لاعتلال عضلة القلب بسبب داء السكري.

### Introduction

Diabetes Mellitus is a cardiovascular disease. Two out of three diabetic patients die of cardiovascular disease or its complications, 70-80% of people with diabetes die from a macrovascular event<sup>(1)</sup>.

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<sup>(2)</sup>.

Hypertension frequently co exists with diabetes, there is an increased

prevalence of hypertension among diabetic patients but there is also high propensity among hypertensive patients to develop type-2 diabetes<sup>(3,4)</sup>. When occurring together the two disease entities appear to aggravate one another worsening both the diabetes and cardiovascular end points<sup>(5)</sup>.

Lowering blood pressure 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 cardiovascular end points in diabetes underlines the necessity to integrate vigorous blood pressure control with glycaemic control in the management of diabetes, data from UK Prospective Diabetes Study (UKPDS) revealed that every 10 mm 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 <120mmHg<sup>(6)</sup>. There is a doubling of cardiovascular events when hypertension and diabetes mellitus coexist, 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<sup>(7)</sup>.

The hypertension Optimal Treatment (HOT) trial showed that number of major cardiovascular events dropped in line with increasing astringent diastolic blood pressure target<sup>(8)</sup>. These findings are reflected in the blood pressure target for diabetic patients of < 130/80 mmHg as now recommended by European Society of Hypertension<sup>(9)</sup>, and American Diabetes Association<sup>(10)</sup>. In people with diabetes, the risk from hypertension is greater than from hyperglycemia<sup>(11)</sup>. Diastolic dysfunction occurs when there is abnormal relaxation of

the left ventricular, left atrial, and pulmonary venous pressure, this may occur in the diabetics even in the absence of significant coronary heart diseases and left ventricular hypertrophy<sup>(12)</sup>.

The most common feature of diabetic heart is abnormal early left-ventricular diastolic filling, suggesting reduced compliance or prolonged relaxation<sup>(13)</sup>; because diabetes affects diastolic function before systolic function of left ventricle so diastolic dysfunction may be an early marker of diabetic cardiomyopathy<sup>(14)</sup>. Hypertension is also associated with impaired diastolic filling with diastolic dysfunction of left ventricle<sup>(15)</sup>.

## Method

A total of 164 patients (76 females and 88 males) of Diabetes Mellitus, 35 to 65 years of age (mean age was 55 years), from Marjan Teaching Hospital in its consultation diabetic clinic were enrolled in this study during January 2007 to February 2008. 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 were: Diabetes Mellitus Type-2, Hypertension: BP >140/90 mm Hg (with or without medication), Body Mass Index > 30 kg/m<sup>2</sup> & Waist-Hip ratio>0.90.

Diastolic Dysfunction (normal systolic function, LV ejection fraction  $\geq$  50% with no segmental wall motion abnormalities and no evidence of significant coronary valvular, infiltrative, pericardial or pulmonary disease).

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.

Blood pressure was measured with a random zero mercury sphygmomanometer. 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 Kg 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 glucose, HbA1c and dyslipidaemia, the patients were asked to fast 12 to 14 hours. Then the blood samples were analyzed. The reading of fasting blood glucose level, serum triglyceride, HDL, LDL Cholesterol. Plasma glucose concentration was 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 of cardiovascular 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.

Through this echocardiography we detect the ratio of peak early filling velocity to late filling velocity (E/A ratio ; normal value 1.0), the deceleration time of the early filling curve (DT; normal value > 150 to 220 msec), & the isovolumic relaxation time (IVRT).

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.

T-test and Chi-square were used appropriately. Results were considered significant if the p value is less than 0.05.

## Result

As in table (1) A total of 164 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. Serum Cholesterol was increased by 210mg/ dl (mean), serum Triglyceride was found to be 200mg/dl (mean), overall Body Mass Index was found to be 30 and waist-hip ratio was 0.95. Their mean age was calculated as 55 years. Mean duration of DM was 10 years.

As shown in table (2) Out of 164 patients, 80(48.7%) patients were found to be hypertensive (both systolic and diastolic) and 9(5.3%) patients were suffering from systolic hypertension. Thus there were 89 hypertensive patients (54%). Among them both systolic and diastolic hypertension, there were 45 males and 35 females. Among systolic hypertensive patients 5 were males and 4 were females.

Diastolic dysfunction was detected in 25(15.2%) patients , those shown isolated diastolic dysfunction having ejection fraction > 50, 16 male & 9 female. 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.

Twenty five out of 164 patients showed diastolic dysfunction with normal ejection fraction; subjects with impaired relaxation show decrease in the deceleration time of the early filling curve (DT<150 msec)

& 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 table (3). There was no correlation between the E:A ratio with lipid profile, E:A ratio with HbA1c, E:A ratio with fasting blood glucose and E:A ratio with left ventricular mass.

## Discussion

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<sup>(16)</sup>.

In this study 164 diabetes mellitus patients were selected, out of which 89 patients (54%) proved to be hypertensive. Among them 9 patients were those who had systolic hypertension, they belonged to  $\geq 60$  years of age. hypertensive and diabetic patients showed a greater level of left ventricular hypertrophy when compared to non-diabetic hypertensive ones<sup>(17)</sup>. While the myocardial fibrosis seems to be related to the hyperglycemia, the left ventricular hypertrophy has been more related to the insulin-resistance syndrome<sup>(18)</sup>.

On other hand, hypertension is also associated with impaired diastolic filling<sup>(19)</sup>. The most common feature of the diabetic heart is abnormal early left ventricular diastolic filling, suggesting reduced compliance and prolonged relaxation, diabetes affects diastolic function before systolic function; left ventricular diastolic dysfunction (LVDD) may be an early marker of diabetic cardiomyopathy<sup>(13)</sup>.

In our study there were 25 cases of diastolic dysfunction with  $EF \geq 50\%$ . 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. Despite the rest-preserved systolic function, a considerable proportion of those patients showed diastolic changes at the Doppler-echocardiographic examination. Those findings are in accordance to the clinical observations by other authors who showed the diastolic diabetes mellitus<sup>(20)</sup>.

This diastolic compromising that precedes the systolic changes in the evolution of the functional changes in the diabetic heart has been observed even in the absence of coronary artery disease and left ventricular hypertrophy. Many reports have shown prevalence's from 30 to 60% of diastolic dysfunction in well-controlled hypertensive diabetic individuals[21]. There is also the possibility that myocardial interstitial changes, with the increase of collagen concentration, have taken part in the induction process of the diastolic function[22]. Finally, we regard as great importance the observation that hypertensive diabetic patients and without clinical signs of cardiac disease show suggestive changes of diastolic dysfunction, when compared to their non-diabetic controls.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<sup>(23)</sup>.

## 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. Those results reinforce the need for similar additional studies, searching

to clarify the physiopathology, the ways of prevention and the treatment of such dysfunction. For prevention one should adopt life style modifications to control blood sugar level and a Dietary Approach to Stop Hypertension (DASH) eating plans, (diet rich in fruits, vegetables and low fat dietary products with a reduced content of saturated and total fat).

Table 1. Characteristic of 164 diabetic patients

Age in years (mean)	55 SD±6
Male	88
Female	76
Hypertension BMI(Kg/m2)(mean)	89(54%) 30 SD±2.8
Fasting blood sugar (mean)	140m/dL SD±12.9
HbA1C% (mean)	8 SD±0.95
Blood cholesterol (mean)	210mg/dL SD±20.5
Blood triglycerides (mean)	200mg/dL SD±18.4
HDL(mean)	44mg/dL SD±7.8
Waist-hip ratio	0.95 SD±0.05
Note: SD (Standard deviation)	

Table 2. Hypertension and diastolic dysfunction ratio in Diabetes Mellitus

<i>Sex</i>	<i>Total No. of patients</i>	<i>Hypertension</i>	<i>Diastolic dysfunction</i>
	<b>n=164</b>	<b>n=89</b>	<b>n=25</b>
<b>Male</b>	<b>88</b>	<b>50(56%)</b>	<b>16(64%)</b>
<b>Female</b>	<b>76</b>	<b>39(44%)</b>	<b>9(36%)</b>

**P-Value = 0.468 =0.283**

Table 3. Involvement of different age groups

<i>Ages (yrs)</i>	<i>Diabetes Mellitus</i>	<i>Hypertension</i>	<i>Diastolic dysfunction</i>
35-45	16	5	2
46-55	73	40	10
56-65	75	44	13
Total	164	89	25

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