

Relation between Diabetes mellitus and Ejection fraction in elderly Egyptians without ischemic heart disease

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Abstract

Background: Diabetes mellitus (DM) can lead to heart failure. This is partly related to the presence of hypertension or dyslipidemia in association with DM or the occurrence of ischemic heart diseases.

Aim: To study the relation between DM and ejection fraction (EF) in elderly not known to have hypertension or ischemic heart disease.

Methods: 190 elderly patients were included in the study. They were divided into cases and controls according to the presence or absence of DM. Echocardiography was done and blood samples were collected to measure glycated hemoglobin (HbA1c) and lipid profile.

Results: EF was lower in cases Both HbA1c and duration of DM showed an inverse correlation with EF (P value < 0.001)

Conclusions: DM is associated with reduced EF & the occurrence of heart failure which is related to both the control and the duration of DM.

Keywords: Diabetes mellitus- heart failure - ejection fraction- elderly- Egyptians

Background

Heart failure (HF) and type 2 DM are considered nowadays two epidemic diseases.^{1,2} Although DM is considered a risk factor for the occurrence of heart failure and greatly increases the risk of worse outcomes, morbidity and mortality once heart failure develops.^{3,4} the mechanism is less well understood. Heart failure can be described as a state of insulin resistance but the underlying mechanisms are not clear yet.⁵ Diabetic cardiomyopathy can be defined as myocardial disease in patients having DM that cannot be related to any other known cardiovascular disease (CVD), such as hypertension and coronary heart disease. Many changes can affect the structure and function of the heart in patients with diabetic cardiomyopathy. Therefore patients with diabetes are liable to develop heart failure even early in the course

of the disease.⁶ The spectrum of disease varies, ranging from subclinical left ventricular (LV) diastolic and systolic dysfunction, to overt systolic dysfunction in advanced disease.⁷ Rubler and colleagues published the earliest report about diabetic cardiomyopathy, after performing a postmortem study in patients with DM and HF without an evidence of hypertension or coronary heart disease.⁸ Many studies confirmed the relation between DM and HF; however no studies were conducted in Egypt studying either cardiac function in patients with DM without hypertension or ischemic heart disease, the effect of diabetes duration or diabetes control.

Methods

A case control study included 190 patients 60 years old and above recruited from Ain-shams University

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hospitals during the period between May and August 2015 after agreement to participate in the study. Patients were classified as cases and controls according to the presence or absence of DM. Cases and controls were matched for age. Patients were considered to have DM if they had fasting blood sugar ≥ 126 mg/dl on two occasions, HbA1c ≥ 6.5 or were on anti-diabetic medications. History was taken regarding the duration of DM and the number of anti-diabetic drugs taken. Transthoracic echocardiography was done by experienced cardiologist to measure EF using Simpson's and 2 D methods.

Patients having hypertension or ischemic heart disease were excluded from the study. In order to measure HbA1c, a 3ml blood sample was collected by venipuncture in EDTA containing tube to detect control of DM during the previous three months. Samples were refrigerated for 24-48hours before centrifugation. Venous blood samples were collected after 12 hour fasting to measure serum lipids.

Statistical Analysis

Analysis of data performed by using SPSS package version 15.0.

Description of data in the form of mean (M) and standard deviation (SD) for all quantitative variables and frequency and percentage for all qualitative variables. Comparison of qualitative variables was done using chi-square test (X²). Significance levels measured according to P value (probability) P>0.05 insignificant, P<0.05 significant, P<0.01 highly significant.

Results

The study included 190 patients, 98 cases and 92 controls. Mean age of the study population was 67 as shown in Table 1. Female patients were 102, and male patients were 88. Forty percent of cases were smokers, however only 20% of controls used to smoke. Diabetes duration ranged from 2-13 years and patients received in average from one to three anti-diabetic medications including insulin. Table 2 shows that EF was lower in cases (Mean 50.22 +/- 10.76) than controls (53.15 +/- 9.95). Lipid levels didn't differ significantly between cases and controls except for triglycerides (TG), that were significantly higher in cases (P value 0.024). When HbA1c was measured as shown in Table 3, it was negatively correlated with EF indicating that worse control of DM is associated with lower EF and can lead to heart failure (P value < 0.001). Also increased diabetes duration and the use of higher number of anti-diabetic drugs were associated with lower EF (P value

< 0.001, 0.008) respectively. Serum lipids level didn't correlate with EF.

Table 1: Demography of the study population

		Cases N=98	Controls N=92
Sex	Male	44 (45%)	44 (48%)
	Female	54 (55%)	48 (52%)
Age	Mean \pm SD	67 \pm 5.9	67.5 \pm 5.9
Smoking (n)	Smokers	40 (41%)	20 (22%)
	Non smokers	58 (59%)	72 (78%)
DM duration	Mean \pm SD	7.939 \pm 5.2	-----
Number of anti-diabetic medications	Mean \pm SD	1.83 \pm 0.7	-----

Table (2): Comparison of Ejection fraction and lipid profile between cases and controls

	Cases N = 98	Controls N= 92	P value
EF %	50.22 \pm 10.76	53.15 \pm 9.95	0.05*
Total cholesterol (mg/dl)	152.87 \pm 53.87	144.49 \pm 53.50	0.28
TG (mg/dl)	146.39 \pm 55.01	129.12 \pm 50.05	0.024*
HDL (mg/dl)	42.28 \pm 5.58	43.58 \pm 5.76	0.114
LDL (mg/dl)	99.38 \pm 22.44	96.05 \pm 20.84	0.289

EF= ejection fraction TG = triglycerides HDL=high density lipoproteins LDL= low density lipoproteins

Table (3): Correlation between ejection fraction and HbA1c, diabetes duration, number of anti-diabetic medications and serum lipid levels in cases

	r	P value
HbA1c	-0.522	<0.001*
Diabetes duration	-0.695	<0.001*
Number of Anti-diabetic medications	-0.266	<0.008*
Total cholesterol	0.038	0.355
TG	0.131	0.197
HDL	0.072	0.479
LDL	0.014	0.892

Discussion

Diabetes is associated with reduction in left ventricular ejection fraction as reported by Niklas et al.⁹ Although the difference in the study is slight between diabetic and non-diabetic, others found a significant reduction in EF in patients with DM.^{10, 11} It can be related to diabetic control. The U.K. Prospective Diabetes Study (UKPDS) including a large number of patients showed that an increase in HbA1c was associated with increasing the incidence of heart failure (2.3–11.9 per 1000 patient/year) over 10 years of follow-up. Research has shown that people with type 2 diabetes who reduce their HbA1c level by 1% are 19% less likely to suffer cataracts, 16% less likely to suffer heart failure and 43% less likely to suffer amputation or death due to peripheral vascular disease.¹² Many theories tried to explain the mechanisms responsible for decreased myocardial contractility in the diabetic patients. Hyperglycemia, the main metabolic disturbance in diabetes, is considered an important factor that increases the risk for the development of heart failure in those patients. In addition to hyperglycemia, type 2 DM is a combination of insulin resistance with increased insulin levels, lipotoxicity (increased non-esterified fatty acids), oxidative stress and the formation of advanced glycation end products (AGEs) responsible for many of complications.^{13,14} All these changes can alter calcium handling in the myocardium and can also promote apoptosis, fibrosis and myocyte hypertrophy, leading to structural and functional alterations of the myocardium.¹⁵ Patients with longer duration of DM showed lower EF, indicating the effect of disease duration on the occurrence of complications and on the pathogenesis of diabetic cardiomyopathy. Bauters et al., 2003 reported that a longer duration of DM, which is difficult to control, is more closely related to the development of HF than diabetes control.¹⁶ Also the use of more drugs for treating DM was associated with the reduction of EF. This may indicate poorer glycemic control. However, Scirica with his colleagues found that dipeptidyl peptidase 4 inhibitors (DPP-4) like saxagliptin increased the rate of hospitalization for heart failure.¹⁷ Whether anti-diabetic drugs are protective or harmful needs further study. This study didn't find a relation between dyslipidemia and EF, ensuring that there is a relation between DM and HF irrespective of the presence of dyslipidemia, hypertension or coronary artery disease (CAD). Kannel and colleagues also reported in the Framingham study, an increased risk of HF in type 2 diabetic subjects despite adjustment for CAD, hypertension, age, sex, cholesterol level and body weight.¹⁸

Conclusion:

DM is associated with reduced EF & the occurrence of heart failure. Heart failure can be largely related to the duration and the control of DM with better cardiac

function in patients with good control of DM and lower HbA1c values irrespective of the presence of hypertension or CAD.

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