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Correlation between diabetes mellitus and left ventricular hypertrophy

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Abstract

Left ventricular hypertrophy (LVH) is a strong predictor of cardiovascular disease and is common among patients with diabetes (DM), it is an independent risk factor for myocardial ischemia, cardiac arrhythmia, sudden death, and heart failure. The aim of this cross-sectional study is to see if there is any relationship between LVH diabetes in regarding to type of DM, its duration, type of treatment, HbA1c level, lipid profile, Body mass index (BMI), age of patients. A total 101 patients recruited from inpatient outpatient of internal medicine clinic, in Imam Al Hussein Medical City in Karbala during period from May 2016 to May 2017. Different parameters were studied including patients age, BMI, BSA. Blood pressure (BP) was measured with mercury sphygmomanometer. Investigations were done including: CBC, ECG, HbA1c, blood urea creatinine, lipid profile. Echocardiography was used to measure left Ventricular (LV) dimension doppler study to assess the diastolic function. Females number was 56, males 45. Thirty-six patients had type1DM, 64 type 2 and 1 had gestational DM. Duration of DM range from < 1 year to > 20 years. Nearly 34 patients used insulin, 40 Oral hypoglycemic agents (OHA), 12 combination of both, 15 without treatment. From echo study, 60.40% of patients had normal LVM, 39.60% had increased LVM. Diastolic function assessment revealed that 37.6% of patients had diastolic dysfunction (DD). There was no significant correlation between LVH DM characteristics, but it was more incidence in patients with older age in those with higher BSA, BMI.

Keywords: Diabetes; Left ventricle mass; ECG; Echocardiography

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Introduction

Diabetes mellitus is a chronic metabolic disease characterized by increased plasma glucose levels as a result of insulin deficiency, impaired action of insulin due to insulin resistance, or a combination of both abnormalities [1]. Despite all the treatments now available, the outcome for patients with DM remains disappointing, long-term complications of DM still cause significant morbidity mortality [2]. Cardiovascular disease (CVD) is a major contributor to morbidity mortality among patients with DM. Concomitant risk factors in patients with DM, such as hypertension, obesity, dyslipidemia, also contribute to the development of CVD should be identified early through screening [1]. One of the most common presentation of CVD in DM is LVH. LVH is an abnormal increase in the mass of the left ventricular myocardium caused by a chronically increased workload on the heart. This most commonly results from the heart pumping against an elevated after load, as in hypertension and aortic stenosis. Another notable cause is increased filling of the left ventricle (i.e., diastolic overload), which is the underlying mechanism for LVH in patients with aortic or mitral regurgitation and dilated cardiomyopathy [3]. A key component in the development of LVH is myocardial fibrosis, which compromises cardiac function. The fibrosis is initially manifested by diastolic dysfunction although systolic dysfunction also occurs with progressive disease. The development of myocardial fibrosis appears to be pathophysiologic ally linked to the renin-angiotensin-aldosterone system [4]. It can present as shortness of breath, fatigue, chest pain, often after exercising, sensation of rapid fluttering or pounding heartbeats (palpitations, dizziness or fainting [5]. LVH can be assessed by electrocardiography (ECG), echocardiography or cardiac magnetic resonance imaging (MRI). ECG is the simplest, cheapest and most readily available of the three tests for LVH. It is highly specific but low sensitive. Common ECG criteria of LVH include Cornell voltage criteria, Sokolow-Lyon voltage criteria, Romhilt-Estes point score system [6]. Echocardiography is the test of choice to assess for LVH. It is much more sensitive than ECG and help in detect other abnormalities such as left ventricular dysfunction and valvular disease. It can do by either transthoracic or transesophageal ultrasonography to measure the LV end-diastolic diameter, posterior wall thickness, and inter ventricular septum thickness. From these parameters and the

patient's height and weight, the LVM and LVMI can be calculated [7]. The aim of the study is to see if there is any relationship between LVH and DM characteristics.

Patients and Method

In our cross-section study,101 patients were recruited from inpatient and outpatient internal medicine clinic in Imam Al- Hussein medical city during period from May 2016 to May 2017. Inclusion criteria include: Type 1 and 2 DM, gestational DM. Exclusion criteria include; hypertension, ischemic heart disease, heart failure, stroke, hypertrophic cardiomyopathy, valvular and congenital heart disease, renal failure, athletes, anemia. Parameters studied -Including patients age, gender, height, weight, BSA, BMI and BP were measured. Investigations including CBC, ECG, HbA1c, serum urea and creatinine, lipid profile and echocardiography was done. BP was measured with mercury sphygmomanometers and cuffs of appropriate size. Hypertension was defined as a BP recording 140/90 mm Hg or higher or patients with normal BP on medications and the mean of three seated BP measurements, separated by a minimum interval of five minutes, was obtained [8]. ECG: A resting 12-lead ECG was recorded for each subject at10 mm/mV and 25 mm/s with the subject lying supine. There have been multiple ECG criteria proposed for diagnosing LVH (Sokolow, Cornell, and Romhiltestes criteria).

Echocardiography: M-mode and pulsed doppler echocardiography were done according to the recommendations of the American Society of Echocardiography (ASE) using a commercially available ultrasound system (3.5 MHz transducer; VIVD-9 General Electric) in the supine and left lateral decubitus position under supervision of 2-seniors of echo, LV dimensions were measured from 2D-guided, M-mode echocardiograms at the level of mitral leaflet tips or the papillary muscle using the parasternal view. The following equation provides a reasonable determination of LVM in grams:

LVM = 0.8 (1.04 ([LVID+PWT+IVST]3− [LVID]3)) + 0.6g. where LVID is the left ventricle internal dimension, PWT is the posterior wall thickness, IVST is the inter ventricular septal thickness, 1.04 is the specific gravity of the myocardium, and 0.8 is the correction factor. All measurements were made at end-diastole in centimeters [9]. The upper limit of LVM was 162 g in females and 224 g in males. The upper limit of the LVMI was 95 g/m2 in female and 115 g/m^2 in males [10].

LV EF was calculated using the two-dimensional directed M-mode method and sometime modified Simpsons method. Systolic dysfunction was defined by evidence of

regional wall motion abnormalities and/or an EF of <50%. Diastolic function was assessed by Doppler measurements of the mitral inflow and sometime doppler tissue imaging of the mitral annulus using the early diastolic septal annular velocity [9].

Statistical analysis

Data of the patients were entered and analyzed using the statistical package for social sciences (SPSS) version 24, IBM, US, 2016. Descriptive statistics presented as frequencies, proportions (%), mean and standard deviation according to the variable type. Analytic statistics performed using appropriate statistical tests; Chi square and Fisher's exact tests were used alternatively to compare frequencies. Student's t test and ANOVA test were used to compare means. Level of significance was set at ≤ 0.05 to be significant difference or correlation.

Results

There were 101 patients enrolled in the study, the mean age of the patients was 42.8 ± 18.2. Male patients were 45 (44.6%), female 56 (55.4%). Thirty-six patients (35.6%) had type 1 diabetes mellitus (DM) and 64 (63.4%) had type 2 DM while only one-woman patient had gestational DM. The duration of DM ranged from < 1 year to more than 10 years, 19 patients (18.8%) had duration less than one year, 63.4% duration between 1-10 years and 17.8% of patients had duration more than 10 years. On the other hand, 33.7% of patients used Insulin in treatment of their DM, 39.6% used OHA and 11.9% used a combination of Insulin and OHA, the remaining 15 patients (14.9%) did not use any treatment for DM. Only 2 patients were underweight while 46.5% had normal BMI, 28.7% overweight, 19.8% obese and 3% were morbidly obese. The mean body surface area (BSA) was 1.68 ±0.22 (range: 1.20 – 2.20) m^2. On the ECG study only 4 patients (4%) had LVH criteria, 2 patients had Sokolow criteria and 2 patients had Cornell criteria. According to the LVM, patients were divided into two groups, patients who had normal LVM were the percentage was 60.40% and patients who had abnormal LVM (increased), were the percentage was 39.60%, as shown in figure 1.

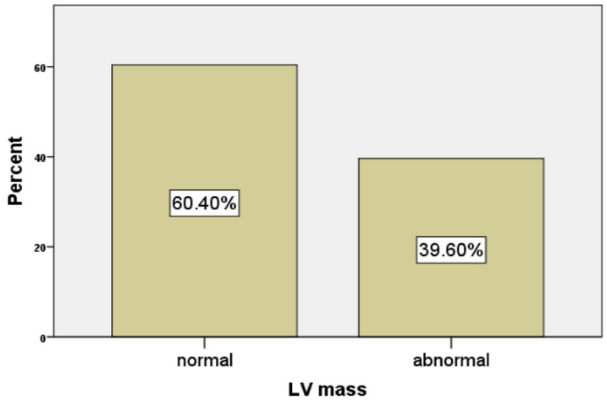

Figure 1.

Percentage of patients who had normal &abnormal LVM

Regarding to the distribution of patients according to the LVMI, nearly similar results, 59.41% has normal LVMI, 40.59% had abnormal LVMI. There was no significant correlation between LVM and type of DM, P- value was 0.25. No significant correlation between LVM and duration of DM, P-value was 0.018. No significant correlation between LVM and type of treatment, P-value was 0.51. No significant correlation with HbA1c, P-value 0.973. LVM not significantly correlated with lipid profile, P-value was >0.05. But was significantly correlated with increased age, P-value was 0.010 as shown in figure 2.

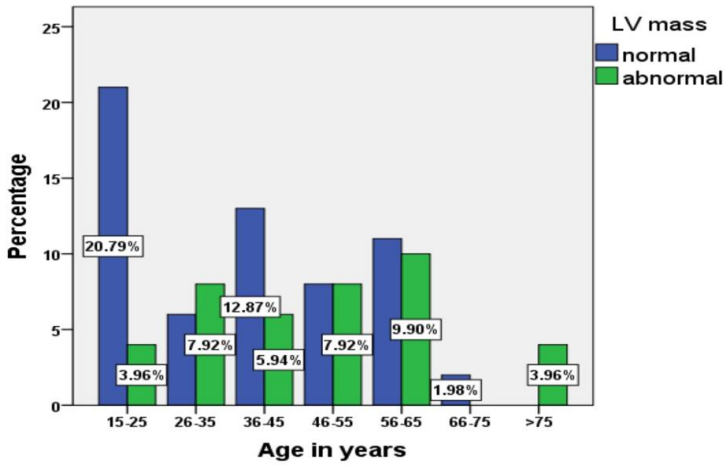

Figure 2

Relationship between LVM and age.

The relationship between LVM and BSA was near the significant, P-value was 0.05, as shown in figure 3.

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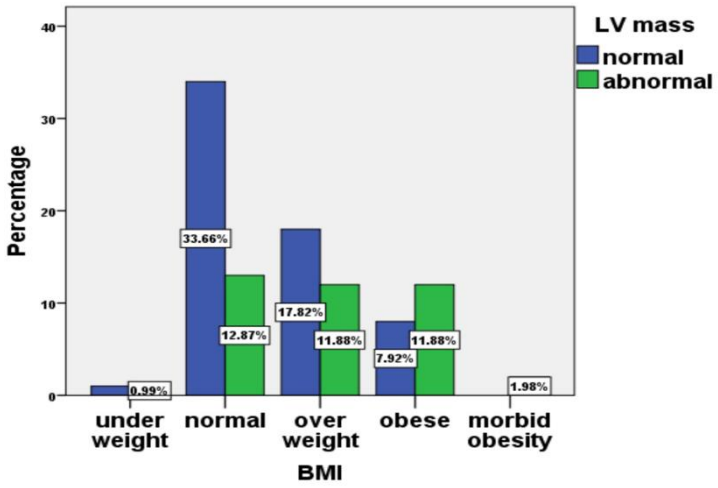

Figure 3.

Relationship between LVM and BMI

There was significant correlation between LVM and BSA, P-value was 0.011, as shown in figure 4.

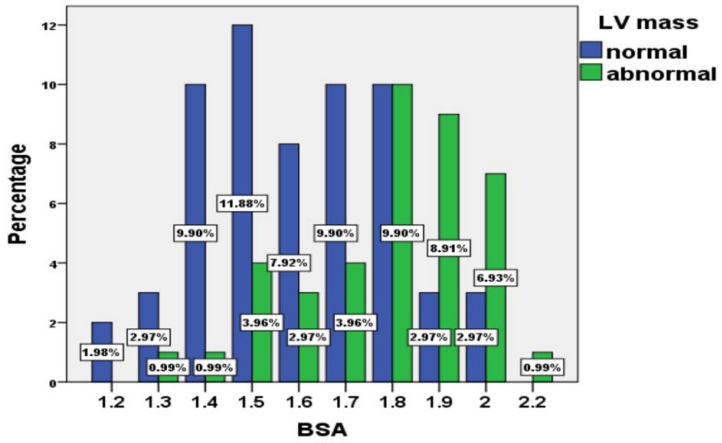

Figure 4.

Relationship between LVM and BSA.

Similar results were found regarding the correlation of LVMI with diabetic characteristics. Diastolic function assessment revealed that 38-patients (37.6%) had DD. While, the remaining had normal diastolic function, as shown in figure 5.

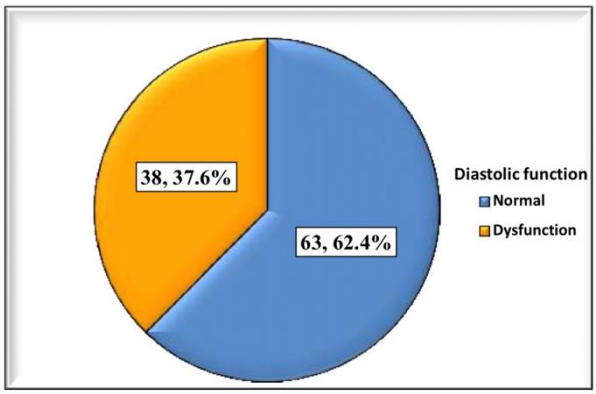

Figure 5.
Distribution of patients according to the diastolic function.

Diastolic dysfunction was significantly correlated with increased age, P-value was< 0.001. Also, it was significantly correlated with type 2 DM, P-value was 0.002.

Discussion

In this study there was no significant relationship between type of DM and LVH (represented by LVM & LVMI). While Eguchi *et al*., in Northern Manhattan /Colombia university found that there was a significant relationship between type 2 DM and increased LVM, independent of obesity, race/ethnic it, physical activity [11]. This is may be due to number of patients included in this study not so enough compared with previous studies which included large number of patients (400 -500 patients) and the patients recruited from only one center (single hospital). Regarding the duration of DM and HbA1c level, in this study there was no significant correlation between them and LVH. Same result was found by Rothargpui *et al*., Geeta et al in their study in Manipure in India [12]. Similarly, to that, Evrim et al., in Baltimore university in USA, found that Long-term glycemic control, measured by mean HbA1C levels, failed to show an independent association with LVM (i.e., cardiac hypertrophy) in patients with type 1 DM [13].While Sukamal *et al*., in Kolkata hospital in India ,found that LVM in DM patients increases with the increased the duration of DM and patients with a longer duration of DM have more chances of having LVH [14].

This may be due that most of the of patients (64 patient) in this study had duration less than 10 years. Regarding to the type of treatment, it had no significant correlation with

LVH. This may be due the fact that most patients were not committed with treatment and didn't use their treatment on regular basis. In addition to that 14.9% of patients were without treatment. Previous studies had shown different effects of medications used by diabetic patient on LVM, some medications had adverse effect on LVM other had beneficial effect. In this study, there was significant correlation between age and LVM, LVMI. Similar result was found by James and Edward in their study in National Institute of Health, Baltimore. There are many structural changes in the heart that occur with normal aging process that lead to change in LVM. So LVH may be related to normal physiological changes due to aging process per se and DM may accelerate this process [15]. In this study, there was significant association between LVM, LVMI with BSA and near significant for BMI. BMI considered to be the strongest predictor of LVM. This consistent with previous studies which find obesity to be a risk factors for LVH and increase cardiac mass and BSA is part from equation that used to measure LVMI, so it significantly associated with heart mass. Similar to the result found by Maria et al in Indianapolis university in Indiana, who found that 1 unit decrease in BMI will decrease LVMI by 1 unit ($g/m^{1.7}$) [16]. Regarding to lipid abnormalities, there was no significant relationship between LVH and lipid profile. This may be due to using only single reading for each patient and not all readings were in fasting state and some of patients were already on antilipo medications, these factors may effects on the results of the study. Compared to that, Rothangpui *et al*., Geeta et al, found that TC and HDL not significantly associated with LVH, while increased LDL, TG were significantly associated [12]. Regarding ECG finding in LVH, in this study, only 4 patients (4%) had LVH criteria. This is due to the fact that ECG is not sensitive for diagnosis of LVH and it affect by age, sex and body weight. Luteal, Torlakson et al., were demonstrates that ECG-LVH was present in 15.7% of type 1 and 15.5% of type 2 DM Tanzanian patients [17]. In this study, diastolic function assessment revealed that 38 patients (37.6%) had DD, while 63 (62.4%) not. While Cioffi *et al*., conducted a study on 960 diabetic patients without overt cardiac disease from 2006 to 2008 in Villa Bianco hospital/Italy and found a symptomatic diastolic dysfunction in 66.5% of diabetics [18]. DD was significantly associated with older age and higher proportion was reported in those aged > 60 years, ($P<0.001$). Suresh et al, Reheat *et al*., in Tertiary care hospital in south India, in their study found no significant correlation between the age and DD. While, Masugata *et al*., in their case control study found that, the

cardiac DD without LV systolic dysfunction in patients with well-controlled type 2 DM is related neither to HT nor LVH but rather to aging and the duration of type 2 DM (19,20).DD also was significantly associated with type 2 DM (50%), compared to those with type 1 (16.7%) and those with GDM (0%). Shraavana *et al*., in Tagro medical college in India demonstrated the prevalence of DD in type 2 DM was 66 (55.0%). This finding is in accordance with the study conducted by Patil *et al*., in which the prevalence rate of DD was 54.33% [21]. DD more in type 2 DM than type 1, because in type 2, the patients are older and had more insulin resistant than type 1, longer duration of disease and associated comorbidities. These factors effect on myocytes contractile function, manifesting as DD. In this study, there is only one case of GDM and its not associated with increasing in LVM, LVMI or changes in diastolic function. Zakovicova *et al*., previously reported LV diastolic dysfunction among 31 women with GDM compared with 34 healthy control subjects. Duke Appiah, Pamela in their study in University of Minneapolis, found that GDM was positively associated with changes in LVM and LVMI in 20 years of follow up [22].

Inconclusions; there was no significant correlation between LVH and DM characteristics, but it was significantly correlated with increased age and higher BMI and BSA.

Limitations

This study had no control group and the LVH may be due to normal aging process and obesity. Exclusion of ischemic heart disease was depending only the clinical history and normal ECG results. Clearly this not enough to exclude subclinical coronary artery disease.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

The contributions of individual authors to this paper were as follows; Haider Sobhy Al Hadad, Basma Edankadhum Kkarem Al Naffi participated in this study. All shared in the conception and design, acquisition, analysis and interpretation of data, development of the hypothesis and research plan, establishment of methodology, drafting of the

manuscript and critical revision of the manuscript for intellectual content and Final approval of the version to be published. All authors read and approved the final manuscript.

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