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Case Report

Correlates and Severity of Left Ventricular Hypertrophy in Type 2 Diabetes Patients in an Afro-Arab-cross Ethnic Community

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Abstract

Background: The cardiovascular (CV) diseases, including left ventricular hypertrophy (LVH) are major causes of morbidity and mortality in T2DM. The LVH is associated with ventricular arrhythmias, ischemic heart disease (IHD), heart failure and sudden death. Although the LVH is frequent in T2DM, screening for this disorder is frequently done.

Material and Methods: In this study, 120 Sudanese T2DM patients were recruited, (70 with and 50 without LVH) from four cardiac centers in Khartoum, the latter is inhabited by most of the Sudanese Afro-Arab ethnic groups. Clinical data were obtained from almost all patients together with measurement of glycemic and renal parameters. Echocardiography was performed for each patient, the left ventricle geometry components including the relative wall thickness (RWT) were estimated and the left ventricle mass index (LVMI) was calculated.

Results: The commonest LVH type was eccentric (65.7%), and grade was severe (37.1%), and both were strongly associated, $p<0.001$, while the frequency of the mild LVH was 28.6%. Out of 10 tested variables only HhA1c ($p<0.001$), urea ($p=0.039$) and creatinine ($p=0.043$) were significantly associated with LVH, while the sex, age, T2DM duration, smoking, obesity, random and fasting blood glucose were not. Moreover, the LVMI was positively correlated with HbA1c (CC0.188, $p<0.039$), and negatively with RWT (CC-0.495, $p<0.000$). Finally, significantly higher number of patients with IHD ($p=0.038$) and cerebral complications ($p=0.014$) had LVH.

Conclusion: In this unique setting of interethnic cross, the results suggest that more genetic than environmental factors could be involved in diabetic LVH development.

Keywords: T2DM; left ventricular hypertrophy; left ventricular mass index; relative wall thickness; afro-arab ethnicity

Abbreviations

T2DM	Type 2vDiabetes mellitus
LVH	Left ventricular hypertrophy
LVMI	Left ventricle mass index
IHD	Ischemic heart disease
CNS	Cardiovascular
PVD	High density lipoprotein
FBG	Fasting plasma glucose
RBG	Random plasma glucose
MW	Mann-Whitney Rank Sum Test
KW	Kruskal-Wallis One Way Analysis of Variance on Ranks
χ^2	Chi-square
RWT	Relative wall thickness
IR	Insulin resistance
IDF	International Diabetes Federation
2H-OGTT	2-hours oral glucose tolerance test
IVS	Interventricular septal thickness
BMI	Body mass index
AV	One Way Analysis of Variance
OHA	Oral hypoglycemic agents

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia due to impaired insulin secretion, insulin resistance (IR), or both. The DM is proving to be a global public health burden, according to the latest 2019 data from the International Diabetes Federation (IDF), approximately 463 million adults had DM [1], this number is expected to increase by another 200 million by 2040 [2]. Type 2 diabetes mellitus (T2DM) makes up about 85-90% of all DM cases [1]. The prevalence and incidence rates of DM in Sudan, as in many other low-income countries, are increasing to epidemic levels, leading to emergence of a public health problem of major socio-economic impact [3,4]. In Sudan, DM is associated with poor glycemic control, high prevalence of complications, and low quality of life [5,6]. As well as, DM is the commonest cause of hospital admissions due to a non-communicable disease in Sudan, with an overall increased age-adjusted mortality and reduced life expectancy of about 5–10 years [7].

It is well established that various left ventricle (LV) abnormalities are strongly promote cardiac disease and death, in particular the left ventricular hypertrophy (LVH) and LV systolic dysfunction (LVSD) [8]. Impaired long axis contraction of the LV may also be associated with increased mortality. Furthermore, LV diastolic filling abnormalities has been shown to place an individual at an increased cardiovascular (CV) risk and is associated with impaired exercise tolerance [9]. The LVH is a condition in which there is an increase in LV mass, either due to an increase in wall thickness or due to left ventricular cavity enlargement, or both. Most commonly, the LV wall thickening occurs in response to pressure overload, and chamber dilatation occurs in response to volume overload [10]. Hypertension and aortic valve stenosis are the most common causes of LVH, in both conditions; the heart is contracting against an elevated after-load leading to concentric LVH as a result of an abnormal increase in LV myocardial mass [11]. Increased filling of the LV leads to diastolic overload, which is the underlying mechanism for eccentric LVH in patients with aortic or mitral regurgitation as well as in the case of dilated cardiomyopathy [10,11].

In LVH, the sustained increase in wall stress along with cytokine and neuro-activation stimulates the development of myocardial hypertrophy or increasing muscle thickness and deposition of the extracellular matrix [11], with concomitant development of myocardial fibrosis. Initially, fibrosis is clinically manifested by diastolic dysfunction, but systolic dysfunction also develops with progressive disease.

The DM is associated with LVH, LV diastolic dysfunction, LV systolic dysfunction and cardiac autonomic neuropathy [12,13]. A large proportion of patients with T2DM whom are not known to have a primary CV disease, have LVH [14], and the regression of LVH by pharmacological intervention is associated with an improvement in prognosis [15], which are objective clues for the link between DM and LVH. The IR, which frequently accompanies T2DM, is reported to be associated with LVH [16]. Moreover, the T2DM and IR are closely associated with obesity.

The complications of T2DM are common and largely account for the excess morbidity and mortality associated with this disease. As such routine screening of asymptomatic patients with T2DM for retinopathy, nephropathy and neuropathy is recommended. However, the DM is a major risk factor for ischemic heart disease (IHD), cardiomyopathy, and congestive heart failure, which are all the most important causes of morbidity and mortality in T2DM, accounting for approximately half of total mortality [17]. T2DM is associated with a high prevalence of hypertension, dyslipidemia, and microalbuminuria, which are all known as independent CV risk factors. Even in populations with low CV risk, DM is associated with an increased incidence of CV death [18].

Genetic and ethnic difference in susceptibility to the different DM complications is well known. The Sudanese are relatively heterogeneous population with marked cross–ethnic breed, due to the intermarriage between different tribes unlike the case in the Arab, African or American societies where there are clear ethnic segregation as in USA [19] and sub-Saharan Africans [20], and familial segregation (consanguinity) as in Arabic settings [21]. In Sudan the original Africans have frequent inter marriage with the Arabs and other ethnicities [22].

The LVH is a strong predictor of CV disease among T2DM patients. The objective of this study was to determine the type and severity of LVH in T2DM as well as the risk factors, including the association with other diabetic complication, but in a different setting of patients with different genetic complexion.

Materials and Methods:

Study design and area

This is a descriptive multicenter cross-sectional hospital-based study, conducted in Omdurman Teaching Hospital, Alshab Teaching Hospital, Ahmed Gasim Hospital and Alsalam Cardiac Center, in the period between April and August 2021.

Study population

The study subjects, men and women, are adult Sudanese patients, aged between 30-85 years and known to have T2DM. All diabetic patients referred from diabetic clinics or came for CV checkup to the above mentioned national cardiac centers, presented during the study period and accepted to participate in this study, were included. The exclusion criteria were; hypertension, aortic stenosis, hypertrophic obstructive cardiomyopathy, severely ill patients and professional athletics.

The T2DM diagnosis in Sudan is based on either the estimation of plasma glucose [fasting plasma glucose (FPG), 2-hours oral glucose tolerance test (OGTT) and random plasma glucose (RBG)] or HbA1c. For diagnosis of T2DM the following were nationally approved: a FPG of ≥ 126 mg/dL (7.0 mmol/L), 2-h OGTT ≥ 200 mg/dL (11.1 mmol/L), RBG ≥ 200 mg/dL (11.1 mmol/L) or HbA1c ≥ 6.5% (48 mmol/mol), along with symptoms of hyperglycemia/DM. The HbA1c has also been accepted for T2DM diagnosis [23]. However, all study subjects were known to be T2DM patients.

Diagnosis of LVH

Echocardiogram: According to the American Society of Echocardiography, the echocardiogram is the test of choice in diagnosis of LVH. Its sensitivity is significantly higher than ECG, and the test can also detect other abnormalities such as left ventricular dysfunction (systolic as well as diastolic) and valvular heart disease. Cardiac ultrasound utilizes transthoracic or transesophageal positioning of the transducer to measure the end-diastolic interventricular septal thickness (IVS), LV internal diameter, and posterior wall thickness. From these measurements and the patient's height and weight, the LV mass index was determined. The LVH was diagnosed when LV mass index (LVMI) was >115 g/m2 in men and >95 g/m2 in women. The LVMI (LVM [left ventricular mass] normalized for body surface area or height) is calculated using the following equation: LVMI=LVM/body surface area. The LVM $=0.8\ [1.04\ (LVEDD + IVSd + PWd)^3 - LVEDD^3)] + 0.6$ (Devereux et al'2000 [24]). The LVH were categorized according to the Relative Wall Thickness as follow: RWT= Posterior wall thickness x 2 / LV internal diameter at end-diastole. Based on RWT, and the LVMI, the LVH can be categorized into 2 types; concentric hypertrophy (increased LVMI and RWT more than 0.42) or eccentric hypertrophy (increased LVMI and RWT less than or equal to 0.42) [11].

Data collection tools

Data was collected through structured questionnaires consisting of the following parameters: demographic, social, clinical, therapeutic and laboratory investigations.

Data analysis

The LVH was the dependent variable, while the independent variables were; demographic data (age, gender, BMI), smoking, T2DM duration, diabetic complications and the laboratory variables (blood glucose, HbA1c, urea, creatinine). Data was analyzed by using a computer program Sigma Stat software, p value was considered as significant at level <0.05.

Ethical consideration

An ethical approval was obtained from Sudan medical specialization board (SMSB). Data used anonymously by using identity numbers to protect patient's identity. An oral informed consent was obtained from each patient.

Results

Characteristics of the study subjects

As seen in (Table 1), 120 T2DM patients were enrolled in this study, 50 patients without and 70 patients with LVH. Overall, 61.7% (74) were males and 38.3% (46) were females, their mean age was 59.8±11.3, (range 30.0-85.0), and 23.3% (28) of all the patients were smokers. The mean of their BMI was 28.8± 4.1, 20.0 - 39.0 kg/m, with 45% (54) were considered as obese (data not shown). The mean duration of their DM was 12.4± 7.1 (range 1.0 - 30.0) years. Most of the patients (61.7%, 74) were using oral hypoglycemic agents (OHA), 31.7% (38) insulin, 5% (6) both OHA and insulin and 1.7% (2) were on diet control (Table 2)

Study subjects	All	LVH		***P***
		Yes	No	
Number	120	70 (58.3%)	50 (41.7%)	
Age (Yrs) Mean Range	59.8±11.3 30.0 -85.0	61.4±12.2 30.0 -85.0	57.7±9.6 40.0 - 80.0	0.078 t-test
Gender (M/F) Males ratio	74/46 61.7%	46/24 (1.9:1) 65.7%	28/22 (1.3:1) 56.0%	0.374 χ^2
T2DM duration (yrs)	12.4 ± 7.1 (1.0 - 30.0)	12.8±7.2 (1.0-30.0)	11.9 ± 7.1 (1.0- 0.0)	0.495 t-test
Cigarette smoking	23.3% (28/120)	28.6% (20/70)	16.0% (8/50)	0.166 χ^2
Complications				
IHD	18	21.4% (15)	6% (3)	0.038
Renal	12	14.3% (10)	4.0% (2)	0.123
Cerebral	10	14.3% (10)	0.0% (0)	0.014
PVD	6	8.6% (6)	0% (0)	0.089
BMI Kg/m2 (range)	28.8±4.1 (20.0 - 39.0)	29.0, 27.0 - 32.0 (20.0 - 39.0)	28.0, 26.0 - 31.0 (22.0 - 33.0)	0.285 MW
Glycemic profile				
FBG (mg/dl)	123.7±32.2 (78.0-211.0)	120.0, 105.0-145.0	110.0, 99.5 - 133.0	0.063 MW
RBG (mg/dl)	227.4±67.0 (111.0-44.0)	240.0, 181.0-270.0	206.0, 180.0-226.0	0.111 MW
HbA1c (%)	8.8 ± 1.9, (6.0 - 12.7)	9.7, 8.8 - 11.0	7.0, 6.5 - 8.0	<0.001 MW
Renal function				
Urea (mg/dl)	49.2 ± 27.1, (14.0 -48.0)	43.0, 35.0 - 67.0	40.0, 26.0 - 55.0	0.039 MW
Creatinine (mmol/l)	1.04 ± 0.61, (0.40 - .50)	1.00, 0.70 - 1.30	0.80, 0.60 -1.00	0.043MW
Ecocardiography				
LV mass index (g/m^2)	116.8 ± 36.7	139.0, 121.0 - 158.0	86.0, 77.0 - 95.0	0.001
LVH types Eccentric Concentric	NA	 65.7% (46) 34.3% (24)	NA	
RWT	NA	0.399 ± 0.093	NA	

Table 1: Description of the study subjects, the type 2 diabetes mellitus (T2DM) with and without left ventricular hypertrophy (LVH) PVD= peripheral vascular disease, RWT= relative wall thickness, MW= Mann-Whitney Rank Sum Test, χ^2= Chi-square

Clinical and laboratory profiles: The frequencies of the diabetic complications were as follows; ischemic heart disease (IHD) 15% (18); renal disease 10% (12); central nervous system (CVS) disease 8.3% (10); and peripheral vascular disease (PVD) 5% (6) (Table 4).

The biochemical tests' results were as follows; mean FBG was 123.7 ± 32.2 (range 78.0 - 211.0) mg/dl, RBG was 227.4 ± 67.0 (range 111.0 - 444.0) mg/dl, and mean of HbA1c was 8.8 ± 1.9 (range 6.0 - 12.7). For the renal function tests, the mean plasma level of urea was 49.2 ± 27.1 (14.0 -148.0) mg/dl and creatinine was 1.04 ± 0.61 (range 0.40 - 4.50) mg/dl (Table 1).

The LVH types and severity in T2DM: Out of 120 patients with T2DM, 58.3% (70) had LVH (cases) and 41.7% (50) had no LVH (control). Based on RWT, the prevalence of the eccentric LVH was 65.7% (46) and that of the concentric LVH was 34.3% (24), while the mean RWT was 0.399 ± 0.093 (Table 1). The LVH was severe in 37.1% (26/70) of the cases, in 34.8% (24/70) was moderate and in 28.6% (20/70) it was mild (Table 3). The mean of the LVHI in all study subjects was 116.8 ± 36.7 g/m^2, and it was139.0, 121.0 - 158.0 in the cases and 86.0, 77.0 - 95.0, in the controls, p 0.001 (Table 1).

Study subjects	LVH grades of severity						p
	Mild		Moderate		Severe		
Number	28.6% (20)		34.3% (24)		37.1% (26)		
Type (ecc/con)	13% (6)	58.3% (14)	34.8% (16)	33.3% (8)	52.2% (24)	8.3% (2)	<0.001χ^2
Age (Yrs)	63.5, 53.0-70.0		64.0, 59.5-65.0		65.0, 55.0-68.0		0.880 KW
Gender (M/F)	10/10		18/6		18/8		
T2DM duration	14.3 ± 6.4		11.8 ± 6.8		12.6 ± 8.1		0.516 AV
BMI (kg/m^2)	28.0, 24.0-32.0		27.0, 25.5-31.5		31.0, 27.0-33.0		0.221 KW
Glycemic profile							
FBG (mg/dl)	130.5, 90.0-155.0		118.5, 109.0-140.5		122.0, 105.0-142.0		0.747 KW
RBG (mg/dl)	234.5, 181.0-250.0		210.0, 166.5-262.5		243.0, 219.0-270.0		0.184 KW
HbA1c (%)	8.6, 8.0-9.5		9.2, 9.0-11.5		11.0, 10.0-12.0		<0.001 KW
Renal function							
Urea	46.5, 38.0-71.0		33.5, 22.5-51.0		65.0, 39.0-72.0		0.004 KW
Creatinine	1.0, 0.60-0.600		0.85, 0.65-1.05		1.2, 0.8-1.40		0.043 KW

KW = Kruskal-Wallis One Way Analysis of Variance on Ranks
AV=One Way Analysis of Variance

Table 3: Description of types and grades of LVH in T2DM patients and associations of different parameters with the LVH severity grades

The LVH associations and correlates

The T2DM patients with and without LVH were of comparable sex distribution although males were more dominant in the former group, male to female ratio of 1.9:1 vs. 1.3:1, respectively, p 0.374 χ^2. The two groups had comparable mean age, 61.4±12.2 vs. 57.7±9.6 yrs., respectively, p 0.078. Moreover, both groups had comparable, T2DM disease duration (p 0.495), frequency of cigarette smoking (p 0.166), and BMI (p 0.285). The frequency of obesity (BMI ≥30kg/m) is comparable between the two study groups, 59.3% vs. 40.7%, p1.00 (Table 2). Also the usage of OHG (oral hypoglycemic drugs) and insulin was not significantly different between the patients with and without LVH, p 0.815 (Table 2). Of the T2DM complications, the prevalence of the renal (p 0.123) and PVD (p 0.089) diseases, were also comparable between the two groups. The biochemical profiles showed that the RBG (p 0.111) and FBG (p 0.063) were not significantly different between the T2DM patients with and without LVH, (Table 1). However, the prevalence of the IHD and renal complications were significantly higher in patients with LVH, p 0.038 and p 0.014, respectively. As well as, the HbA1c (p <0.001), blood urea (p 0.039), and creatinine (p 0.043), were significantly higher in the patient with LVH. The median (25% - 75%) LVMI in patients with LVH, was139.0, 121.0 - 158.0 gm/m2, while it was 86.0, 77.0 - 95.0 gm/m2 in patients with no LVH, p 0.001, (Table 1).

LVH - grades	Obese (BMI 30-39]	Non-obese (BMI 22-29)	p value	OHA	Insulin	p value χ^2
No	40.7% (22)	42.4% (28)		37.8% (28)	42.1% (16)	
Mild	14.8% (8)	18.2% (12)		10.8% (8)	26.3% (10)	
Moderate	18.5% (10)	21.2% (14)	= 0.765	24.3% (18)	15.8% (6)	0.107
Severe	25.9% (14)	18.2% (12)		27.0% (20)	15.8% (6)	
LVH					.	
No	40.7% (22)	42.4% (28)		37.8% (28)	42.1% (16)	
Yes	59.3% (32)	57.6% (38)	1.000	62.2% (46)	57.9% (22)	0.815

Note: 6 patients (5%) used both OHA and insulin, and 2 patients (1.7%) were on diet control, 2 from the former had mild LVH, while the rest (6) didn't had LVH. χ^2= Chi-square, LVH= left ventricular hypertrophy, BMI= body mass index, OHA= oral hypoglycemic agents

Table 2: The association between LVH and BMI and anti-diabetic treatment

For the variants which were significantly different between the study groups, the correlation analysis showed significant positive correlations between the LVMI and HbA1c, CC 0.641, p< 0.00, but no correlation with urea (p 0.113), and creatinine (p 0.142) or age as a major demographic variable, p 0.396, although the latter was significantly

correlated with the former variables which were all significantly positively inter-correlated (Figure. 1). The other variables, the disease duration (p 0.608), BMI (p 0.458), RBG (p 0.234) and FBG (p 0.845) were not correlated with the LVMI.

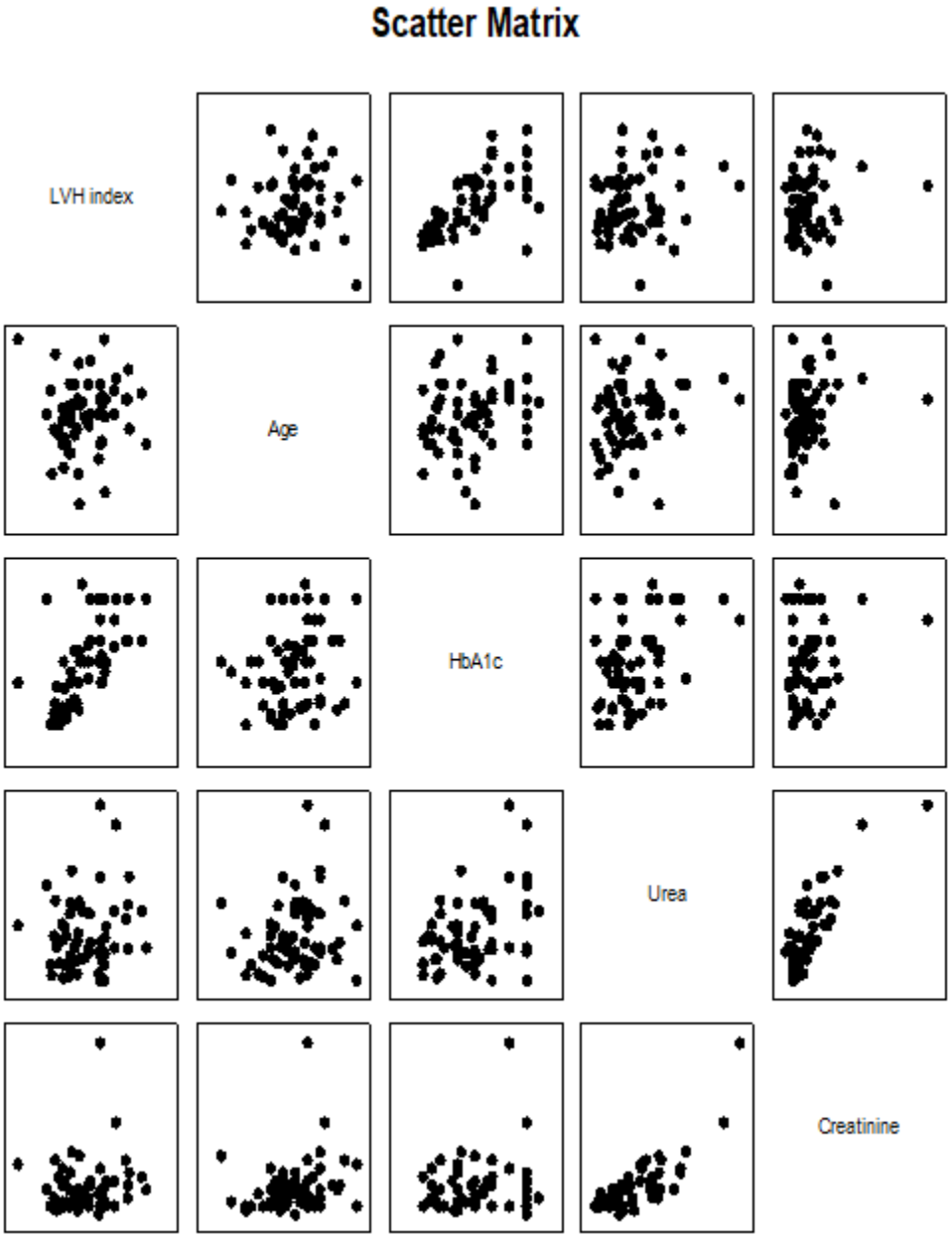

Figure 1: The correlation of the left ventricular mass index (LVMI) labeled as LVH, with age and the parameters which were significantly associated with the LVMI (shown in table 1), the HbA1c, blood urea, and plasma creatinine. Only HbA1c was significantly correlated with the LVH, CC 0.641, $p< 0.001$, Pearson Product Correlation Coefficient.

Finally, 52.2% (24) of the patients with eccentric LVH had severe, 34.8% (16) had moderate and only 13% (6) had mild LVH, while 8.3% (2) of patients with concentric LVH had severe, 33.3% (8) had moderate and 58.3% (14) had mild LVH, p <0.001, (Table 3). However, none of all the other tested variables was found to be associated with any of the types of the LVH (data not shown).

Comparisons between the different severity grades of the LVH

As seen in (Table 3, and Figure. 2), limiting the analysis to T2DM patients with LVH only, the prevalence of the three grades of LVH, mild, moderate and severe were 28.6% (20), 34.3% (24), and 37.1% (26), respectively. The three subgroups had similar median age distribution, 63.5, 53.0-70.0; 64.0, 59.5 - 65.0; 65.0, 55.0 - 68.0 years, respectively, p 0.880, mean T2DM disease duration, 14.3 ± 6.4; 11.8 ± 6.8; and 12.6 ± 8.1 years, respectively, p 0.516, and median BMI, 28.0, 24.0-32.0, 27.0, 25.5-31.5, and 31.0, 27.0 - 33.0 kg/m2, respectively, p 0.221. Among the glycemic parameters (RBG, FBG, and HbA1c), only higher HbA1c was significantly associated with LVH severity, 8.6, 8.0- 9.5; 9.2, 9.0 - 11.5;

and 11.0, 10.0 - 12.0, respectively, p <0.001, while both renal function parameters were significantly higher in severe LVH, the urea (median levels, 46.5, 38.0 - 71.0; 33.5, 22.5 - 51.0; and 65.0, 39.0 -72.0 mg/dl, respectively, p 0.004) and creatinine (median levels,1.0, 0.60 -.600; 0.85, 0.65- 1.05; 1.2, 0.8 - 1.40 mmol/L, respectively, p 0.043). Finally, the LVH index, was significantly higher with increasing severity, 107.0, 101.0 - 121.0; 139.5, 137.0 - 143.5; 161.0, 145.0 - 179.0, respectively, p <0.001. On the contrary, the RWT was significantly higher in the milder forms of LVH, 0.495, 0.360 - 0.520; 0.360, 0.320 - 0.480; 0.370, 0.340 - 0.380, respectively, p 0.013, (Figure. 2A&B). Furthermore, in patients with LVH, the LVH index was significantly negatively correlated with the RWT, cc-0.495, p<0.000, (Figure. 2 C).

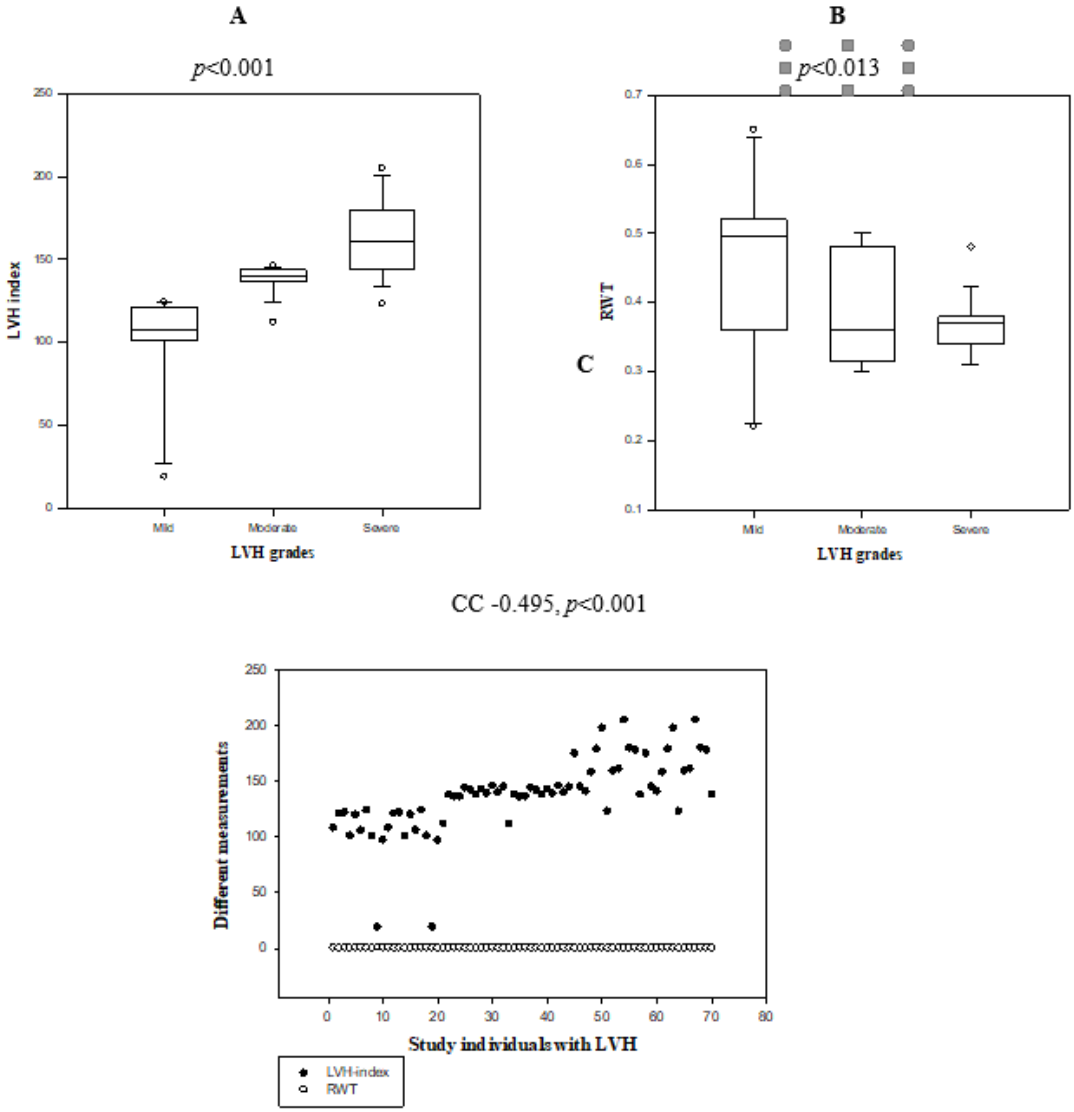

Figure 2. The relationship between the left ventricular hypertrophy (LVH) severity, left ventricular mass index (LVMI), and relative wall thickness (RWT), in diabetic patients:

A. Comparison of left ventricular mass index (LVMI) between the 3 grades of severity of LVH; mild, moderate and severe (median, 25% - 75%), 107.0, 101.0 - 121.0 vs. 139.5, 137.0 - 143.5 vs. 161.0, 145.0 - 179.0, respectively, p<0.001, Kruskal-Wallis One Way Analysis of Variance on Ranks (KW).
B. Comparison of the relative wall thickness (RWT) between the 3 grades of severity of LVH; mild, moderate and severe (median, 25% - 75%), 0.495, 0.360 - 0.520 vs. 0.360, 0.320 - 0.480 vs. 0.370, 0.340 - 0.380, respectively, p 0.013, KW.
C. The inverse (negative) correlation of the LVMI with RWT, CC -0.495, p <0.001, Pearson Product Correlation Coefficient.

Discussion

Heart diseases occur eventually in the majority of patients with DM and continue to be the outstanding factor in overall diabetic morbidity and mortality. An increased LVMI, the objective measure for LVH, may contribute to the increased CV risk because LVH is an ominous prognostic sign and an independent risk factor for sudden death, ventricular dysarrhythmia, IHDs and heart failure. In this study, the LVH and the associated risk factors among patients with DM were examined. The mean of LVMI was found to be 117±37 g/m2, indicating a significant hypertrophy among the affected patients, as reported elsewhere [18,25]. The mechanisms responsible for the LVH in DM remain unclear, but hyperglycemia/insulinemia and the IR state have been implicated in the pathogenesis of increased LVM [16]. In the present study the chronic hyperglycemia, as revealed by the strong association of the raised HbA1c with the prevalence of the LVH and its severity was the main and only evidence among the tested variables, in the implication of

T2DM in LVH. Undeniably, the role of hyper-insulinemia and IR in LVH cannot be ruled out since both abnormalities are cardinal features of T2DM.

The majority of patients with LVH in this study had eccentric left ventricular geometry (65.7%), in agreement with previous study [9]. Unlike in some other studies which showed association of concentric LVH with a higher risk of stroke, cardiac death and all-cause mortality than eccentric LVH [26, 27], in the present study the eccentric rather than the concentric LVH was associated with the severe grade of LVH, since more than 50% of the eccentric hypertrophy cases had severe LVH compared to only 8% of the concentric hypertrophy cases, $p < 0.001$ (Table 3). Extra DM complications were seen in patients with eccentric LVH but the differences were not significant (data not shown). Moreover, though severe LVH was significantly associated with increased HbA1c, blood urea and creatinine, neither the urea nor creatinine, or age, sex, obesity nor smoking were associated with the types of LVH, the eccentric and concentric, in this study (data not shown). For no doubt, poor glycemic control is risk factor for numerous diabetic complications including cardiac diseases [16]. In the present study LVH was strongly associated with raised HbA1c more evident in patients with HbA1c above 9% (data not shown). The association between glycemic control and LVM has been previously described in diabetic patients [28], and it is supposed to reflect a glucose-induced activation of epigenetic mechanism regulating cardiomyocyte hypertrophy, as well as accelerated collagen I and III synthesis by cardiac fibroblasts exposed to high glucose levels [29]. Increased plasma glucose levels also augment the generation of advanced glycation end-products (AGEs) [29], which stimulate the expression of extracellular matrix genes, and the tissue accumulation of AGEs has been shown to be associated with inappropriate LVM increment [30].

There have been reports suggesting that the relationship between T2DM and LVH is due to the associations of the former with age and obesity i.e., an epiphenomenon, rather than the effect of T2DM per se [31]. In pre-diabetic and diabetic elderly subjects, the fat mass was shown to be a major determinant of LVM in women [32]. In the present study, the diabetic patients with LVH although were relatively older than the patients without LVH, the difference was not significant (Table 1), and there was no correlation between LVMI and age (Figure 1). Other studies reported a significant influence of increasing age on the LVM [33, 34]. In addition, unexpectedly, no influence for T2DM duration on the LVMI in the current study (Table 1& 2), in contradistinction to what was mentioned before [18,33]. Also the LVH prevalence and LVMI were comparable between the obese and non-obese diabetics (Table 1 & 2), and there was no correlation between LVMI and BMI. In addition obesity was not associated with types or severity of LVH in this study (Table 2). There have been several studies showing that high BMI is strongly associated with increased LVM [31,18]. Because obesity and insulin resistance are closely associated with each other, obesity itself may have an impact on increased LVM in diabetics [31]. Furthermore, no association between smoking and LVH was noticed in this study, as reported in other studies [35,36], however, the number of smokers was generally small in this study.

Not unexpected was that the diabetic patient with LVH, had significantly higher frequency of IHD and CNS complications and a trend (below the significant level) of high prevalence of PVD and renal diseases (Table 1) independent of the patient age or disease duration. The coronary artery disease has been demonstrated to play a role in the pathogenesis of LVH, as compensation for tissue that has become ischemic or infracted with concomitant development of myocardial fibrosis [37]. In contrast, the LVH is known to predispose to IHD [8], and to be important risk factor for ischemic stroke [38].

Finally and importantly, in this study the demographic and biochemical determinants of LVH in T2DM were unexpectedly limited as seen from significant correlates and associations, which cannot explain the generally high prevalence of LVH seen in diabetic patients, thus genetic predisposition would be expected to play a major role as seen in hypertension [13]. Unlike in most of the Arabs and Africans countries, this setting is unique in the sense that the genetic makeup of the Sudanese, including the study subjects, is mostly a cross between several Africans and Arabs and other ethnic minorities, although some ethnic groups are conserved [22], unlike the multi-ethnicity in USA [31], which is coupled with ethnic segregation in marriage. It is difficult to classify most people in Sudan to a single tribe biologically, although socially is doable. In such setting, defining common genetic traits associated with LVH adds to existing data/knowledge and fills the gaps. Of the limitations of this study; the relatively small number of patients, no long term follow up to track for future LVH conversion, and importantly lack of data about genetic markers.

In conclusion, the frequency of severe and eccentric LVH was relatively high among diabetic patients in this setting. The risk factors associated with development of LVH were mainly, the poor glycemic control, high urea and creatinine levels and co-existence of IHD. The association of cerebral and vascular diseases with T2DM can equally be consequences or causes of the LVH. Finally, the study suggest a greater role for genetic factors in development of LVH in diabetic patients.

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