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Prevalence, Anthropometric And Clinical Correlates Of Diastolic Dysfunction In Hypertensives Living With Type 2 Diabetes Mellitus Seen In University Of Portharcourt Teaching Hospital

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Abstract:
Background: Hypertension and type 2 diabetes mellitus co-morbidity significantly impact on the left ventricular function with diastolic dysfunction being the earliest and commonest complication. The prevalence and risk factors for diastolic dysfunction in this subset of patients are understudied.
Methodology: This is a cross-sectional descriptive study carried out in the Department of Internal Medicine of University of Port-Harcourt Teaching Hospital Rivers State, Nigeria. The study population consisted of 160 hypertensive patients living with type 2 DM greater than 18 years of age as cases and 80 hypertensive patients greater than 18 years of age as controls . Both the cases and controls were selected randomly among patients attending medical out-patient clinic of the hospital or admitted into the medical wards.
Data were collected from the cases who were considered hypertensive diabetic on the bases of blood pressure greater or equal to 140/90mmHg or existing diagnosis of hypertension and a fasting blood sugar greater or equal to 7.0mmol/L .Data were similarly collected from 80 hypertensive patients attending MOPC or admitted into the medical wards serving as controls.
Minimum sample size was calculated using the method of Kish .Relevant clinical and laboratory data were analyzed using SPSS 22 version
Results: A total of 160 patients living with type 2 DM and hypertension were recruited. The mean age of the cases was 57.51±9 years.A total of 80 hypertensives were similarly recruited The mean age of the control was 55.90±1 2 years.
Diastolic dysfunction was significantly higher in the cases compared to the control (40.6% verses 13.8% P=0.001) with grade 1 diastolic dysfunction being the commonest. Obesity and sedentary life style were statistically significant indices of diastolic dysfunction.
Conclusion: This study found that left ventricular diastolic dysfunction is high in hypertensive patients living with type 2 diabetes mellitus with grade 1 diastolic dysfunction being the commonest. Obesity and sedentary life-style were risk factors associated with diastolic dysfunction.

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I. Introduction:

Hypertension has significant impact on the incidence and progression of cardiovascular disease in type 2 diabetes mellitus and is clearly associated with increased prevalence of heart failure. The possible reason for this are the co-morbidity of hypertension, myocardial ischaemia and specific diabetic cardiomyopathy termed cardiotoxic triad. Diabetic cardiomyopathy is characterized by myocellular hypertrophy and myocardial fibrosis which lead to diastolic dysfunction. Diastolic dysfunction refers to impaired ventricular relaxation or filling regardless of symptoms or EF.[1] Diastolic dysfunction is present in 50-60% people living with type 2 diabetes mellitus and studies have shown that diastolic dysfunction is related to glycated hemoglobin and the most likely reason for this is accumulation of advanced glycosylation end-products in the myocardium and that lipotoxicity due to accumulation of free fatty acids and their oxidative products in the myocardium may also be a factor.[2] Hypertension can further damage contractile fibrils and generate a hypertrophic state that leads to mild diastolic dysfunction. The additional effect of myocardial ischemia converts moderately dysfunctional myocardium due to combined effect of diabetic cardiomyopathy and hypertension into severe dysfunctional myocardium. Anderson etal reported diastolic dysfunction of 60% among population living with diabetes mellitus and hypertension.[3]They concluded that diastolic dysfunction is common in hypertensive patient and diabetes

mellitus worsens it.[3] Some of the major risk factors for diastolic dysfunction are ischemic heart disease , left ventricular hypertrophy and and increasing age.[4,5]

Early recognition of diastolic dysfunction is important to prevent progression to heart failure with preserved EF. This study therefore aims at determining the prevalence and correlates of diastolic dysfunction in hypertensive patients living with type 2 DM attending University of Port-Harcourt Teaching Hospital Nigeria.

Study Design and Setting: This is a cross-sectional study carried out at the cardiology unit of Department of Internal Medicine of the University of Portharcourt Teaching Hospital. The hospital is a 500 bed facility and serves as a referral center for Rivers State and other neighboring states

Study Population: Consisted of 160 hypertensive subjects living with type 2 DM greater than 18 years or seen at the medical out-patient department or admitted into the medical ward of the hospital selected randomly. Data was collected from subjects who were considered hypertensive diabetic on the basis of blood pressure greater than or equal to 140/90mmHg or existing diagnosis and a fasting blood sugar greater than 7.0mmol/L. A control arm comprising 80 hypertensives matched for sex and age were randomly selected from members of staff and patient's relatives. All hypertensives 18 years and above living with type 2 DM who gave written consent were recruited .Patients with features of thyroid disease, significant alcohol history, retroviral disease or pregnant women , cancer or non consenting patients were excluded. All hypertensives not living with diabetes mellitus were recruited as controls. The minimum sample size needed for the study was calculated using the the method of Kish.[6]

Data collection : Baseline clinical and demographic characteristics of subjects and controls were obtained using structured questionnaire. Both subjects and controls underwent clinical examination to determine weight , height, Body Mass Index, waist circumference and waist-hip ratio.

Pulse was counted for one minute assessing rhythm , volume, rate, and synchrony. Blood pressure was measured using accusson sphygmomanometer to determine the brachial artery systolic and diastolic BP using the first and 5thkorotkoff sounds respectively.[7]Two BP measurements were taken three minutes apart and after five minutes rest with the arm at the heart level and the average recordedExercise, smoking and caffeine were avoided for atleast 30minutes pror to the BP measurement.

Hypertension was deemed present if BP≥140/90mmHg on at least 2 occasions or concurrent use of antihypertensive agent.[7]Hieght and weight were measured using standard beam balance and standiometer respectively. Body Mass Index was calculated using the formular weight in kg divided by height in $m^2$and classified as normal (18.5-24.9kg/m^2) overweight (25-29.9kg/m^2), class1 obesity(30-34.9/m^2), class 2(35-39.9kg/m^2), class3 (≥40kg/m^2).[8]

Venous samples were collected and analysed for fasting lipid profile, serum creatinine , urea and plasma glucose . Serum creatine was used to calculate estimated Glomerular Filtration Rate using cockroft-Gault formula.[9]Urinalysis was done to assay for protein .Fasting lipid profile including triglyceride, total cholesterol, high density lipoprotein, were measured using enzymatic method. HbA1c was assayed using BioRad laboratories

Echocardiographic assessment was done according to the recommendation of American Society of Echocardiography. [10]

LVM, LVMI and RWT were calculated. 'E'and 'A' wave velocities were measured and E/A ratios were documented. Deceleration time , IVRT, were calculated. Tissue Doppler parameters were obtained. E'-septal velocity and E/E' ratio were calculated. Ejection fraction and chamber sizes were measured.

Statistical analysis: Data was analysed using Statistical Package Social Science (SPSS) version 22

Results were presented as mean ± standard deviation for continous variables while categorical variables were expressed as proportions or percentages. Tables were used to illustrate results. The association of variables with left ventricular diastolic dysfunction was assessed with linear regression analysis . A P-value of less than 0.05 was considered statistically significant.

Ethical consideration : The study was approved by the medical ethical committee of the University of Portharcourt Teaching Hospital. A written informed consent was obtained from all study partiscipant before enrollment into the study.

II. Results

Demographic characteristics of study population.

A total of 240 subjects participated in this study of which 160 constituted participants with both hypertension and type2 diabetes mellitus (cases) and 80 participants with hypertension (controls) There were more females than males among the cases in the ratio of 1:5:1 as 96 (60%) were females and 64 (40%) were males.. Among hypertensive controls, there was a slight female preponderance as 49 (61.25%) were females and 31 (38.75%) were male giving ratio of 1:6:1.

There was no significant difference in sex distribution between the cases and the controls. Therefore, the cases and controls were matched for sex (P =0.453). The ages of the cases ranged between 39-87 years. The

ages of hypertensive controls ranged between 35-79 years with a mean of 57.51 ± 12.5. The cases and controls were matched for ages as there was no significant difference in their mean ages (P = 0.323).

This is shown in table 1 below.

Table 1 Age and sex distribution of the study population (N=240)

Variables	Cases N=160 (%)	Hypertensive control n =80%	Total n = 240%	P value
Age				
30-39 years	2(1.2)	8(10.0)	10(3.4)	
40-49years	22(13.8)	20(25.0)	42(18.1)	0.323
50-59years	7446.2)	20(25.0)	94(38.1)	
60-69years	48(30.0)	20(25.0)	68(30.0)	
70-79years	8(5.0)	12(15.0)	20(8.4)	
80-89years	6(3.8)	0(0.0)	6(1.9)	
SEX				
Male	64(40.0)	38(47.5)	102(41,6)	
Female	96(60.0)	42(52.5)	138(58.4)	

Key: cases: patients with hypertension. Control: patients with hypertension without diabetes.

Clinical characteristics of the study population

Body mass index.

The body mass index of cases ranged between 19-47kg/m^2 with a mean of 29.46 + 5.64kg/m^2, while the body mass index of the hypertensive control ranged between 22-39kg/m^2 with a mean of 26.66 ± 4.4kg/m^2.

There was statistically significant difference between the mean BMI of the cases and the hypertensive controls. (P= 0.022).

Other clinical characteristics are represented in the table 2 below.

Table 2: Clinical characteristics of the study population.

Variable	Cases n=160	Hypertensive controls n=80	P
	Mean ±SD	Mean ±SD	
BMI (kg/$m^{2)}$	29.46 ± 5.64	26.66 ± 4.40	0.022
WC (cm)	100.23 ± 10.54	97.78 ± 12.10	0.108
WHR	1.0 ± 0.09	0.95 ± 0.07	0.001*
SBP (mmHg)	137.54 ± 17.14	136.26 ± 20.21	0.599
DBP(mmHg)	83.41 ± 9.44	87.29 ± 11.00	0.0001*
PR (b/min)	83.78 ± 11.55	76.90 ± 9.l57	0.0001*
Pulse pressure (mmHg)	53.59 ± 13.85	49.00 ± 13.08	0.014*

Key:

Cases = patients with hypertension and diabetes.

Controls= patients with hypertension.without DM

P = P value for cases versus hypertensive controls.

Echocardiographic characteristics of the study population.

The mean E/A ratio was 1.2± 0.68 for the cases and 1.30 ± 0.59 for hypertensive control. This was statistically significant (P = 0.001*).

The mean IVRT of the cases was 101.27 ± 16.87ms , 98.88 ± 17.19ms for hypertensive controls. This did not show any statistically significant difference (P =0.138). The mean deceleration time was 208.63 ± 46.20ms for cases and 203.91 ± 40.03ms for hypertensive controls. There was no statistically significant difference in the mean DT when cases were compared with hypertensive control (P = 0.708).

Concentric hypertrophy was common among both cases and hypertensive control 66.9% and 55.0% respectively P= 0.073), other echocardiographic parameters are as shown in the table3 below.

Table 3

Echocardiographic features of the study population.

Variables	Cases n=160	Hypertensive control n = 80	P
	Mean ± SD	Mean ± SD	
LVEF	51.40 ± 15.38	57.76 ± 15.58	0.021*
LVFS	25.34 ± 9.74	31.59 ±10.50	0.036*
LVMI	124.39 ± 43.44	131.69 ± 44.10	0.388
RWT	0.74 ± 0.57	0.62 ± 0.28	0.125
LAD (cm)	3.48 ± 0.64	3.47 ± 0.67	0.967
IVSdd (cm)	1.43 ± 1.25	1.33 ± 0.29	0.180
LVIDd (cm)	4.28 ± 0.98	4.60 ± 0.90	0.020*

LVPWd (cm)	1.49 ± 1.61	1.31 ± 0.34	0.456
E/A	1.20 ± 0.68	1.30 ± 0.59	0.001*
IVRT (ms)	101.2 ±16.87	96.88 ± 17.19	0.138
DT (ms)	208.63 ± 46.20	203.9 ± 40.03	0.708
S/D	1.18 ± 0.52	1.17 ± 0.02	0.616
E/E^1	6.05 ± 2.05	7.38 ± 2.70	0.001*
GEOMETRY			
Normal	10(6.2%)	6(7.5%)	0.262
Concentric remodeling	27(16.2%)	18(22.5%)	0.293
Concentric hypertrophy	107(66.9%)	44(55%)	0.073
Eccentric hypertrophy	16(10.1%)	12(15.0%)	0.255

LVEF = Left ventricular ejection fraction, LVFS = left ventricular fractional shortening, LVMI = left ventricular mass index, RWT= Relative wall thickness, LAD = left atrial diameter, LVIDd = left ventricular internal diameter in diastole, LVPWD = left ventricular posterior wall thickness in diastole, E/A = mitral early inflow and late atrial inflow velocity ratio, S/D = pulmonary vein systolic / diastolic flow ratio, E/E'= mitral valve early velocity/ mitral annular tissue early velocity. P^1 = for cases versus hypertensive controls, cases= patients with hypertension and diabetes.

Association of clinical and anthropometric indices with diastolic dysfunction.

BMI and history of sedentary lifestyle showed statistically significant association with diastolic heart failure with P values of 0.35 and 0.31 respectively. Family history of DM, family history of hypertension, pulse pressure and pulse rate did not show statistically significant association with diastolic heart failure. This is shown in table below

Relationship between clinical /Anthropometric indices and diastolic dysfunction.

Table 4

Variables	Yes N = 65%	No N=95%	Total N = 160	P Value
Family History Of DM	36(44.4)	45(55.6)	81(100.0)	0.319
Family History Of HTN	44(44.1)	65(58.9)	107(100.0)	0.856
Family History Of IHDX	26(41.3)	37(58.7)	63(100)	0.894
History Of Sedentary Lif E Style	30(51.7)	28(48.3)	58 (100)	0.031*
Duration Of DM(Yrs)				
1-8	45(44.6)	56(55.4)	101(100.0)	0.391
9-16	15(38.5)	24(61.5)	39(100.0)	
17-24	3(21.4)	11(78.6)	14(100.0)	
25-31	0(0.0)	2(100)	2(100.0)	
>31	2(50.0)	2(50.0)	4(100.0)	
DURATION OF HTN				

Key: BMI: Body Mass Index, WHR: Waist Hip Ratio.

Prevalence and types of left ventricular dysfunction among cases and control.

Out of 160 cases, 126 (78.8%) had left ventricular dysfunction while among 80 hypertensive controls 45(56.2%) had left ventricular dysfunction. This was statistically significant with a P value of 0.001*. Among the cases 65(40.6%) had diastolic dysfunction. This was statistically significant with P value of 0.001*, This is represented in table 5 below

Table 5

prevalence and types of left ventricular dysfunction across the cases and controls

	Cases n =160(%)	Hypertensive control n =80(%)	Total n =240(%)	P
Left ventricular dysfunction	126(78.8)	45(56.2)	171(71.2)	0.001*
Systolic	61(38.1)	34(42.5)	95(39.6)	0.514
Diastolic	65(40.6)	11(13.8)	76(31.7)	0.001*

Key: cases: patients with hypertension and diabetes.
controls: patients with hypertension without DM
LVD: left ventricular dysfunction.

III. Discussion

This was a cross-sectional descriptive study of 160 hypertensives living with type 2 diabetes mellitus (cases) and 80 hypertensives as controls matched for age and sex. The study set out to determine the prevalence of diastolic dysfunction and clinical / anthropometric correlates of diastolic dysfunction in hypertensive patients living with type 2 diabetes mellitus presenting to UPTH.

The study documented prevalence of 40.6% of diastolic dysfunction in diabetic hypertensive population . Sustained hyperglycemia increases glycation of interstitial protein such as collagens resulting in myocardial stiffness hence diastolic dysfunction. [11]

Ganiyu etal in Jos northern Nigeria studied 50 hypertensive diabetic adults and 50 hypertensive controls and found significantly higher EF in the cases than the controls. They documented diastolic dysfunction in 34% of the hypertensive population population living with type2 diabetes. [12] The relatively lower prevalence in their study compared to ours may be due to younger age group enrolled into their study (mean age 49± 8 years).

Grade 1 diastolic dysfunction was found more in the cases than controls (50.6% versus 28.8%). This is expected considering the additive effect of type 2 DM and hypertension on the cardiac myocyte. The greater proportion of hypertensive control had grade 2 diastolic dysfunction than the cases 37.5%versus 23.1%. The explanation for this is not readily apparent from this study. Restrictive pattern was slightly higher in cases than controls but did not meet statistical significance. The finding in this study is in agreement with that documented in other studies[3, 13].

BMI was significantly higher in the cases than the controls with a mean of 29.46± 5.64kg/m^2, Anderson etal,[3] documented significantly higher BMI in hypertensive living with type 2 DM compared to hypertensive control similar to this study. Obesity is a common co-morbidity in hypertension and type 2 DM.

Sedentary lifestyle was significantly higher in hypertensive diabetic than hypertensive population (36.2% versus 23.8%). Another study documented similar trend.[14] History of angina was higher in the controls than hypertensives living with type 2 DM (50% versus 39.4%) this can be explained by the concept of silent ischemia common in patients living with type2 diabetes.[15] Other risk factors such as smoking , BP level did not show significant association with diastolic dysfunction.

IV. Conclusion:

The prevalence of diastolic dysfunction is high amoung hypertensives living with type 2 diabetes mellitus (40.6%) with grade 1 diastolic dysfunction being the commonest. Hypertension and type 2 DM co-morbidity heightens myocardial interstitial fibrosis predisposing to diastolic dysfunction. Obesity and sedentary life style showed significant association with diastolic dysfunction. There is need for early screening of hypertensives living with type 2 DM for early detection of diastolic dysfunction and its risk factors and hence early intervention.

Limitation of the study:

1-Different classes of antihypertensives and antidiabetic drugs administered to the subjects with different levels of control would have affected the outcome of this study.

2 Age and obesity related diastolic dysfunction is a cofounder in this study.