

## GENDER DIFFERENCES IN THE CLINICAL PROFILE AND SOCIODEMOGRAPHIC CHARACTERISTICS OF DILATED CARDIOMYOPATHY IN IBADAN, NIGERIA

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### ABSTRACT

**Background:** Cardiomyopathies contribute about 18.2-40.2% (average- 21.4%) to the global burden of heart failure of which dilated cardiomyopathy (DCM) is a major cause. DCM is the second commonest cause of heart failure in Ibadan. The gender differences in the clinical profile has not been described in our setting.

**Objective:** In this study, we set out to describe the gender differences in the pattern and presentation of DCM at the University College Hospital, Ibadan, Nigeria.

**Methods:** This was an analysis of a prospectively collected data over a period of 5 years (August 1, 2016 to July 31, 2021).

**Results:** A total of 117 subjects, 88 males (75.3%) and 29 females (24.8%) aged  $50.30 \pm 14.7$  years (range, 17 to 86 years). Males had significantly achieved a higher educational level than females ( $p = 0.004$ ). Males were more likely to be employed and had more monthly income compared to females. Males were significantly more likely to use alcohol and smoke cigarette ( $p = 0.0001$  and  $0.001$  respectively). Females were more likely to be in NYHA class III/IV. There was no statistically significant difference in the relationship between any medication and gender of participants ( $p > 0.05$ ).

**Conclusions:** DCM is a disease of young and middle-aged adults in our population. The commonest age group was 20-39 years and there was male preponderance. There were some gender differences in the clinical profile of the disease in our environment.

**Keywords:** Dilated cardiomyopathy, Heart failure, Left ventricular failure

### INTRODUCTION

Dilated Cardiomyopathy (DCM) is ranked second in the causes of heart failure in Nigeria behind hypertensive heart failure.<sup>1-3</sup> The clinical picture at the time of diagnosis can vary widely from patient to patient; some have no symptoms, whereas others have progressive refractory heart failure. Males have a 2.5-fold increase in risk, as compared with females, that is unexplained by socioeconomic factors, alcohol intake or other variables.<sup>4</sup>

Several gender differences have been reported in patients with DCM with respect to clinical presentation, risk factors, pathophysiology, and prognosis.<sup>5-9</sup> Women generally fare much better than men. Although these important gender differences have been previously investigated in patients with DCM in high income countries<sup>5-9</sup>, little is known about the gender differences

in DCM in Nigeria. The aim of this study is to determine the gender differences on the clinical and echocardiographic profile of patients with DCM in Ibadan, Nigeria.

### MATERIALS AND METHODS

This was an observational study conducted at the Cardiology Unit, Department of Medicine, University College Hospital, Ibadan, Nigeria. Ethical approval for the study was obtained from the University of Ibadan/University College Hospital, Ethics Review Committee as part of the Ibadan Heart Failure Project. Consecutive cases of DCM who presented to the hospital during the study period were recruited. They were recruited over a period of 5 years from August 1<sup>st</sup> 2016 to July 31<sup>st</sup> 2021. Data were collected using pretested structured questionnaire.

Information collected included biodata, clinical features and echocardiographic findings. After written informed consent, a detailed history was taken and physical examination was carried out. Key points of the history included the sociodemographic characteristics, presenting symptoms, type of underlying heart disease, drug history including cancer chemotherapy. All the participants had baseline anthropometric measurements of weight and height for the calculation of body mass index (BMI). Blood investigations in the form of complete blood count, fasting blood glucose, renal function tests were done. Echocardiography was done for all the patients.

DCM was diagnosed by the presence of ventricular dilatation and systolic dysfunction (LV ejection fraction <45%) on echocardiography in the absence of coronary artery disease, hypertension or valvular disease. (10) All the patients were treated for cardiac failure by using diuretics, ACE inhibitors, mineralocorticoid antagonist, cardio-selective beta blockers, and occasionally cardiac glycosides. In some of the patients, anticoagulants and anti-arrhythmic drugs were also used when indicated.

Subjects who were unwilling to participate, those with coronary artery disease, cancer, rheumatic heart disease, hypertrophic cardiomyopathy, hypertensive heart disease, and congenital heart disease, or evidence of restrictive cardiomyopathy or constrictive heart disease were excluded.

### Definitions

Significant alcohol consumption was defined as the intake of more than 4 drinks on any day or more than 14 drinks per week (for men) or, more than 3 drinks on any day or more than 7 drinks per week (for women).<sup>11,12</sup> Cigarette smoking was estimated in pack years. It was calculated by multiplying the number of packs of cigarettes smoked per day by the number of years the person has smoked.<sup>13,14</sup>

Dilated Cardiomyopathy (DCM) was defined as “a disease of the heart muscle characterized by enlargement and dilation of one or both of the ventricles along with impaired contractility defined as left ventricular ejection fraction (LVEF) less than 40%. By definition, patients have systolic dysfunction and may or may not have overt symptoms of heart failure.”<sup>2,15</sup>

Hypertensive heart failure was defined by previous history of hypertension or sustained BP of >140/90 mmHg in the presence of symptoms of HF, increased LV mass, LV systolic and/or diastolic dysfunction.<sup>2,15</sup>

Valvular heart disease was diagnosed in the presence of the following: i. Mitral stenosis:– presence of thickened and calcified mitral valve leaflets, loss of the classic M-shaped pattern of a normal mitral valve, diastolic doming and restriction of the mitral valve leaflet motions; ii. Mitral Regurgitation: Poor coaptation of the mitral valve leaflets in systole, thickened leaflets, dilated and hyperdynamic left ventricle; iii. Aortic stenosis: Presence of calcified aortic valve, reduction in aortic cusp separation, highly echo reflectant aortic valve leaflets; and v. Aortic regurgitation: Poor coaptation of the aortic cusps in diastole dilated left ventricles and fine fluttering of the anterior mitral valve in diastole.<sup>2,15</sup>

Ischaemic cardiomyopathy was diagnosed in the presence of history of previous myocardial infarction (MI). Diagnosis of MI was based on ECG changes, cardiac enzyme elevation and regional wall motion abnormality at echocardiography.<sup>2,15</sup>

### Electrocardiography

Standard 12-lead electrocardiography studies were done for the participants using a commercially available CONTEC® Workstation Model, CONTEC EC8000G, ECG machine (Made in China) at a speed of 25mm/sec and 1mV/10mm calibration while they were supine and at rest. The ECGs were analysed by a reviewer who was blinded to the clinical data of the patients. The Minnesota code classification system was used in the diagnosis of the various abnormalities.<sup>16</sup>

### Echocardiography

Echocardiography was performed with the available echocardiography machine-Toshiba Xario (Toshiba Medical Systems Corp) with a 3.5 MHz transducer. Two-dimensional guided M- mode measurements were made according to the recommendations of the American Society of Echocardiography (ASE).<sup>17</sup> LV internal dimensions, posterior wall thickness and interventricular septal thickness were measured at end-diastole and end-systole. The modified Simpson’s criteria were used for volume measurements according to the ASE criteria.

The left atrial dimension was measured between the leading edge of the posterior aortic wall and the leading edge of the posterior wall of the left atrium at end systole. The areas of the left atrium were determined by tracing the endocardial border of the left atrium at end systole (ventricular) before the opening of the mitral valve in the apical 4 chamber view (maximal LA area or Amax), excluding the LA appendage and pulmonary vein confluences.<sup>18,19</sup>

The Devereux and Reichek formula was used for the calculation of the left ventricular mass. This has been shown to yield LVM closely related to autopsy measurements ( $r=0.90$ )<sup>20,21</sup> and has good interobserver reproducibility ( $\kappa=0.93$ ) in one study.<sup>22</sup> We calculated the relative wall thickness (RWT) from the formula:

$$\frac{2 \times \text{Posterior Wall Thickness}}{\text{LV Internal diameter}}$$

Increased RWT was considered to be present when RWT exceeded 0.43. This represents the 97.5<sup>th</sup> percentile in normal subjects.<sup>23</sup> Left ventricular geometry was defined as follows: Normal geometry, when LVMI and RWT were normal; Concentric remodeling, when LVMI was normal and RWT increased; Eccentric hypertrophy, when LVMI was increased but normal RWT; and concentric hypertrophy, when both LVMI and RWT were increased.<sup>24</sup>

Transmitral flow velocities were obtained with the Doppler sample volume placed just beyond the tip of mitral valve leaflets. The parameters measured were early diastolic peak flow velocity (E), late diastolic peak flow velocity (A), the deceleration time of early mitral velocity and the ratio of E to A (E/A). Isovolumic

relaxation time (IVRT) was measured with pulse wave Doppler beam intersecting the LV outflow and inflow tracts.<sup>25</sup> Tissue Doppler imaging was only applied to identify true pseudonormalised filling pattern.<sup>25</sup>

Measurements were obtained in up to three cardiac cycles according to the ASE convention.<sup>26</sup> One cardiologist (OSO) performed all the echocardiography. In our laboratory, the intra-observer concordance correlation coefficient and measurement error have been reported.<sup>27</sup>

### Data management and Statistical analysis

The data management and statistical analysis was done using International Business Machines (IBM) Corporation Statistical Product and Service Solutions (SPSS) for Windows version 23.0 (Armonk, NY: IBM Corp). Comparison of continuous variables was performed with student *t* test while categorical variables used chi-square statistics. A two-tailed *P* value of <0.05 was considered to be statistically significant.

### RESULTS

A total of 117 subjects, 88 males (75.3%) and 29 females (24.8%) met the inclusion criteria. The overall

**Table 1:** Sociodemographic characteristics of the DCM patients

Variable	All (117)	Male (88)	Female (29)	Chi-Square	p-value
<b>Mean Age (years)</b>	50.3±14.7	57.8(14.7)	42.7±12.3		0.001
<b>Age range (years)</b>	17-86	17-86	23-70		
<b>Age category (n/%)</b>					
<40 years	31(26.5)	18(20.5)	13(44.8)	6.653	0.015
>40 years	86(73.5)	70(79.5)	16(55.2)		
<b>Marital status (n/%)</b>					
Ever Married	108(92.3)	80(90.9)	28(96.6)	0.978	0.448
Never Married	9(7.7)	8(9.1)	1(3.4)		
<b>Educational background (n=114)</b>					
Primary or less	25(21.4)	18(20.5)	7(24.1)	0.176	0.794
Secondary or more	92(78.6)	70(79.5)	22(75.9)		
<b>Occupation (n=88)</b>					
Employed	88(75.2)	62(70.5)	26(89.7)	4.313	0.029
Not employed	29(24.8)	26(29.5)	3(10.3)		
<b>Estimated monthly income (n=100)</b>					
<- 50000	69(59.5)	46(52.9)	23(79.3)	6.934	0.074
>- 50000	31(26.7)	26(29.9)	5(17.2)		
<b>Alcohol(n/%)</b>					
Never took	59(50.4)	32(36.4)	27(93.1)	28.09	<0.001
Ever took	58(49.6)	56(63.6)	2(6.9)		
<b>Smoking(n/%) (n=116)</b>					
Never smoked	87(75.0)	58(66.7)	29(100)	12.889	<0.001
Ever smoked	29(25.)	29(33.3)	0(0.0)		
<b>Previous admission for HF(n/%)</b>					
Yes	52(44.4)	38(43.2)	14(48.3)		
No	65(55.6)	50(56.8)	15(51.7)	0.229	0.671

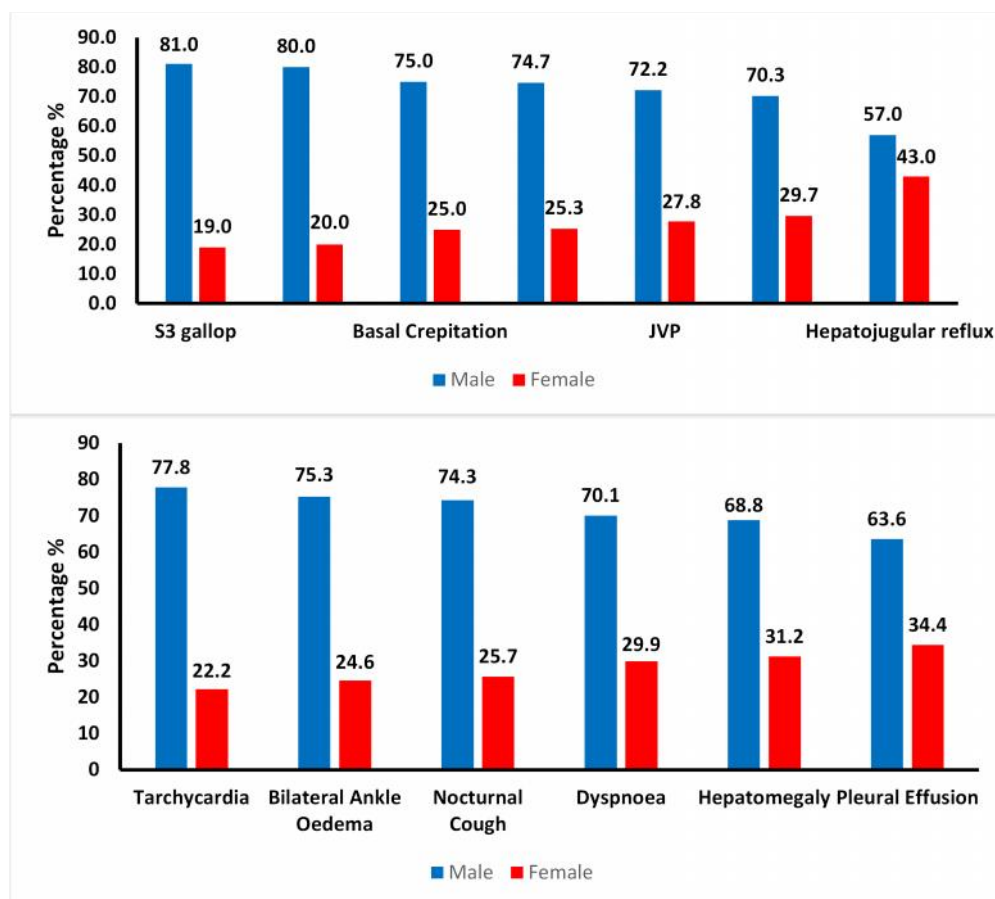
**Table 2:** Biophysical profile and laboratory findings in the DCM patients

Variable	All (116)	Male (89)	Female (27)	p-value
Weight (kg)	70.22 ± 12.83	61.02 ± 12.29	61.98 ± 11.64	0.002
Height(cm)	167.66 ± 8.57	159.36 ± 5.54	160.33 ± 5.47	0.002
BMI (kg/sqm)	27.44 ± 3.692	23.17 ± 7.33	24.21 ± 5.41	0.416
Pulse Rate(beats/min)	88.44 ± 15.56	74.60 ± 17.60	74.90 ± 14.90	0.713
Respiratory Rate(cycles/min)	27.74 ± 7.79	23.83 ± 4.47	24.28 ± 3.54	0.650
Systolic BP (mmHg)	108.79 ± 16.25	102.52 ± 18.43	102.5 ± 18.43	0.085
Diastolic BP (mmHg)	74.56 ± 13.149	71.28 ± 13.94	71.28 ± 13.93	0.256
Packed cell volume (%)	40.12 ± 5.298	39.38 ± 4.16	39.88 ± 4.16	0.494
White cell count (10 <sup>3</sup> / uL)	7.40 ± 3.414	8.32 ± 3.90	8.32 ± 3.91	0.227
Platelet count (10 <sup>3</sup> / uL)	191.29 ± 58.15	210.83 ± 79.23	210.83 ± 79.23	0.157
Sodium (mmol/L)	136.22 ± 4.96	135.83 ± 0.58	135.83 ± 5.83	0.720
Potassium (mmol/L)	3.89 ± 0.58	3.78 ± 0.52	3.78 ± 0.52	0.385
Urea (mg/dl)	51.15 ± 31.93	48.47 ± 32.91	48.47 ± 32.91	0.702
Creatinine (mg/dl)	1.77 ± 2.67	1.266 ± 3.467	1.27 ± 0.34	0.317
FBG (mg/dl)	98.55 ± 24.06	96.40 ± 19.70	96.41 ± 16.70	0.659

mean age of the population was 50.3 ± 14.7, with an age range of 17-86 years. About 7.7% of the population had never married. There was no statistically significant difference between the marital status of male and female participants (p=0.448).

Males were significantly more likely to be employed than females (p=0.029). Men had more monthly income compared to women. Men were significantly more likely to use alcohol and smoke cigarette (p < 0.001 and 0.001 respectively). (Table 1)

Figure 1 (upper panel & lower panel) shows the distribution of the symptoms and signs based on the Framingham major and minor criteria for heart failure between male and female participants. Men were more likely to have symptoms when compared to women. Figure 2 is a bar chart showing the distribution of the study participants in terms of New York Heart Association (NYHA) functional classification between men and women. Women were more likely to be in NYHA class III/IV (p = 0.04)



**Figure 1:** (Upper panel) Framingham major criteria for HF. (Lower panel) Framingham minor criteria for HF

Men were heavier and taller, however there was no statistical significance in the body mass index (BMI). There was also no statistical significance in other variables. (Table 2)

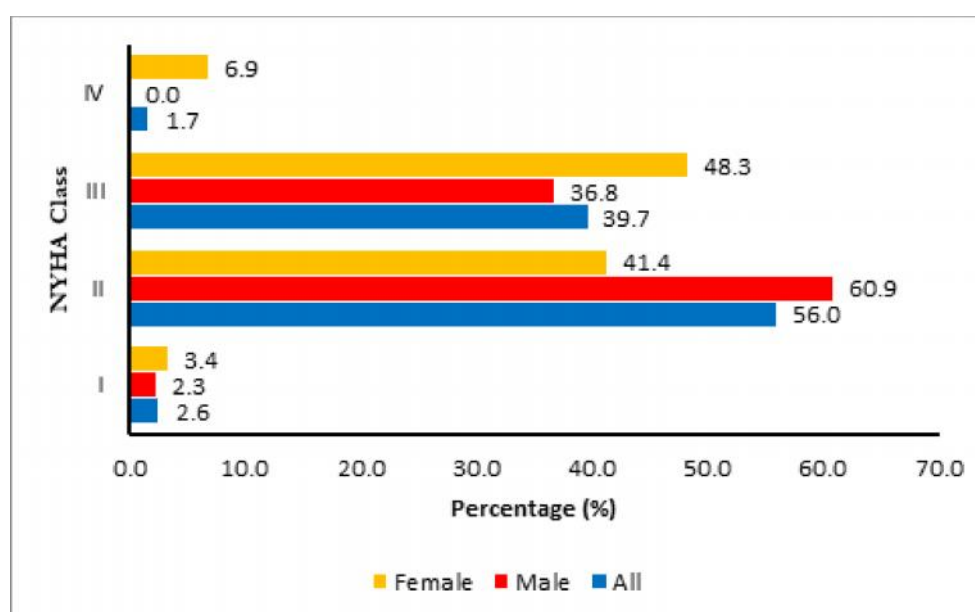
The 12 lead ECG variables were also not significantly different between men and women. (Table 3) However, on echocardiography, the aortic root diameter is significantly higher in men than women

( $p=0.001$ ) while other echocardiography findings showed no significant relationship with gender (Table 4).

MRA's and ACE inhibitors were the most common medications the participants were placed on (91.4% and 80.2%) (Figure 3). There was no statistically significant difference in the relationship between any medication and gender of participants ( $p > 0.05$ )

**Table 3:** 12- Lead electrocardiographic findings in the DCM patients

Variable	All	Male	Female	Chi square	p-value
Atrial abnormality/enlargement (n=102)				0.260	0.0655
Yes	60(58.8)	43(57.3)	17(63.0)		
No	42(41.2)	32(42.7)	10(37.0)		
Left ventricular hypertrophy				1.416	0.260
Yes	62(60.8)	43(57.3)	19(70.4)		
No	40(39.2)	32(42.7)	8(29.6)		
Right Ventricular hypertrophy				0.707	1.000
Yes	2(2.0)	2(2.7)	0(0.0)		
No	99(98.0)	73(97.3)	26(100)		
Any arrhythmia				1.781	0.261
Yes	49(48.0)	39(52.0)	10(37.0)		
No	53(52.0)	36(48.0)	17(63.0)		
Atrial fibrillation				0.941	0.332
Yes	13(12.7)	11(14.7)	2(7.4)		
No	89(87.3)	64(85.3)	25(92.6)		
Conduction abnormality				1.028	0.332
Yes	30(29.4)	20(26.7)	10(37.0)		
No	72(70.6)	55(73.3)	17(63.0)		
QT interval (ms)	402.03 ± 83.59	404.96 ± 87.115	394.56 ± 74.85	-	0.586
QTC interval (ms)	483.98 ± 81.30	479.97 ± 82.196	494.22 ± 79.56	-	0.433
Prolonged QTc (n=96) (n/%)	25(26.0)	18(26.1)	7(25.3)		0.602
QRS duration	123 (41.23)	125.92 ± 49.009	122.74 ± 36.93	-	0.761
Prolonged QRS duration (n=98) (n/%)	59 (60.2)	44(62.0)	15(55.6)		0.361

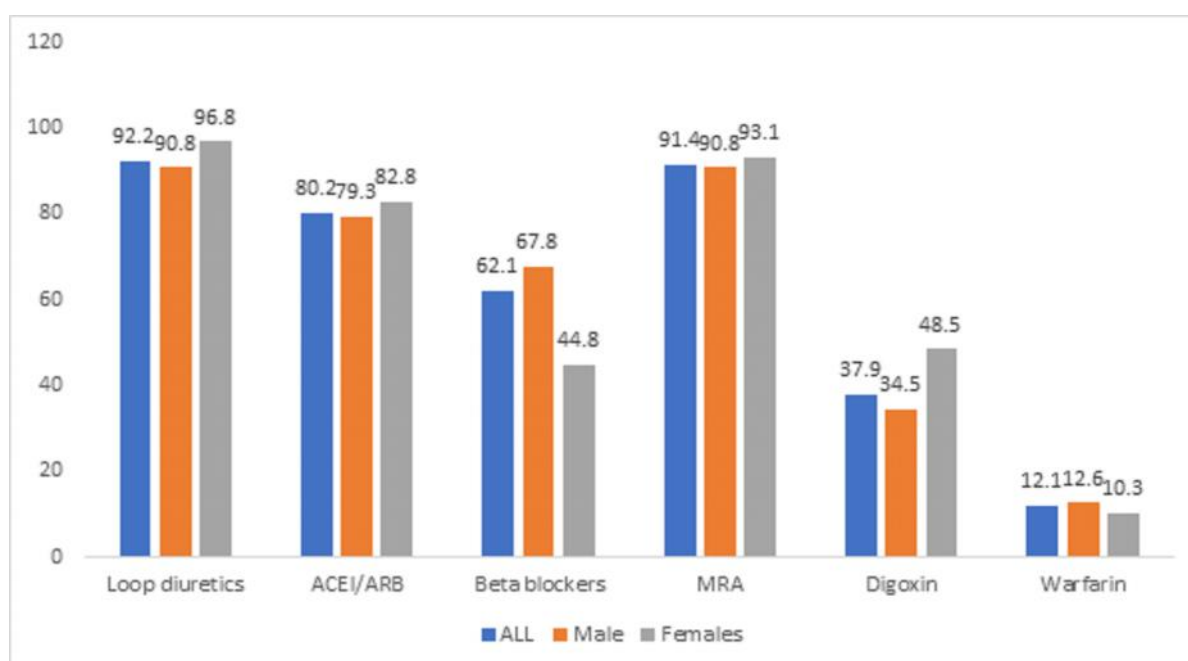


**Figure 2:** Distribution of the study participants in terms of NYHA functional classification

**Table 4:** Echocardiography findings in the DCM patients

Variable	All (116)	Male (89)	Female (27)	P -value
Aortic root diameter	2.97 ± 0.42	3.03 ± 0.57	2.63 ± 0.29	0.001
Left atrial diameter (cm)	4.36 ± 0.75	4.64 ± 0.89	4.60 ± 0.68	0.829
Interventricular wall thickness in diastole(cm)	1.04 ± 0.30	.938 ± 0.270	0.789 ± 0.23	0.019
Left ventricular posterior wall thickness in diastole(cm)	1.07 ± 0.30	1.04 ± 0.31	.89 ± .28	0.003
Left ventricular internal diameter in diastole (cm)	6.40 ± 1.11	6.39 ± 1.20	6.63 ± 0.62	0.351
Left ventricular internal diameter in systole (cm)	5.42 ± 1.29	5.34 ± 1.28	5.72 ± 0.58	0.175
Left ventricular ejection fraction (%)	32.76 ± 10.36	33.14 ± 10.99	32.18 ± 10.26	0.709
Left ventricular fractional shortening (%)	18.55 ± 10.60	17.81 ± 8.90	20.06 ± 19.86	0.551
TAPSE (cm)	1.79(0.47)	1.80 ± 0.49	1.82 ± 0.35	0.888
eMitral valve E velocity (m/sec)	0.89 (0.22)	86.74 ± 45.02	108.66 ± 67.35	0.382
Mitral valve A velocity (m/sec)	0.48(0.21)	0.90 ± 0.27	0.94 ± 0.25	0.541
E/A ratio	2.15(0.97)	2.35 ± 1.24	2.71 ± 1.31	0.235
Deceleration velocity of the mitral valve E velocity (msec)	156.27(52.72)	141.29 ± 52.23	119.39 ± 35.65	0.063
Isovolumic relaxation time (msec)	133.50(27.95)	123.49 ± 40.52	130.73 ± 50.93	0.571
Mitral regurgitation (n=91) (n/%)	66(72.5)	47(69.1)	19(82.6)	0.285
Tricuspid regurgitation (n=91) (n/%)	64(70.3)	45(66.2)	19 (82.6)	0.188
Pericardial effusion (n=90) (n/%)	23(25.5)	13(14.4)	10(11.1)	0.30
Spontaneous echoes (n=91) (n/%)	12(13.2)	9(13.2)	3 (13.0)	0.645
Intracardiac clot (n=91) (n/%)	2(2.2)	2(2.9)	0(0.0)	0.556

TAPSE= *Tricuspid annular plane systolic excursion*



**Figure 3:** Distribution of medications used by the study participants

## DISCUSSION

The present study has attempted to describe the contemporary sociodemographic characteristics and clinical profile of DCM in Ibadan, South-West, Nigeria. The mean age of the cohort was 50 years and men were significantly older than women. About 73.5% of the participants were above 40 years. The mean age is similar to the report by Thomas *et al.*<sup>28</sup> who reported a mean age of 49 years. However, it is older than the work by Jain *et al* who reported a mean age

of 42.6 years.<sup>29</sup> Majority of our participants were above 40 years similar to studies in Asia.<sup>30,31</sup>

We found that DCM is commoner in males in our cohort with a male to female ratio of 3:1. Ganesh *et al.*<sup>31</sup> and Singh *et al.*<sup>32</sup> in Asia reported a male to female ratio of 1.6:1 and 1.5:1 respectively. The plausible reason is that men may be more involved in risk factors for the development of dilated cardiomyopathy in

our environment than women; for example, consumption of alcohol and use of illicit drugs.

Furthermore, symptoms and signs of heart failure is commoner in males compared to females. This may be due to severity of the disease which may be worse in males. The common major criteria for the diagnosis of HF documented in the cohort were S3 gallop, acute pulmonary oedema and basal crepitation while the common minor criteria were tachycardia, bilateral ankle oedema and nocturnal cough. This is similar to findings in previous studies.<sup>34-37</sup>

The mean pulse rate, systolic blood pressure, diastolic blood pressure and body mass index in this study were 88 beats/minute, 109mmHg, 75mmHg and 27kg/m<sup>2</sup> respectively. These observations were similar to the findings of Kumar *et al.*<sup>37</sup>

We did not find any significant difference in the laboratory and 12-lead ECG findings in the males and females. Apart from the aortic root and LV wall thickness which is higher in males, the other echocardiographic parameters were not significantly different between the males and females.

The mean left ventricular internal dimensions in diastole and systole, the LV fractional shortening, and the LV ejection fraction were 6.40cm, 5.42cm 18.6% and 32.8% respectively. This is similar to the report of Goldberger *et al.*<sup>38</sup> and Hoque *et al.*<sup>39</sup>

### LIMITATION

Coronary angiography was not carried out in the cohort to exclude coronary artery disease. The procedure is currently not available in our centre. However, we made effort to exclude cases with ECG and ECHO evidences of possible coronary artery disease.

Hypertension was excluded based on history and physical examination. However, we recognize the possibility of burnt-out hypertension. We recognize that alcohol may also play a significant role in many of the cases presented here because of issues of denial and recall bias. We did not carry out genetic and biomarker studies in this cohort. Furthermore, this is a single centre study. A multicentre study in Nigeria may define a clearer picture of the disease in the country. Nevertheless, our data provide important information on this common disease in our environment.

### CONCLUSION

DCM is a disease of young and middle -aged adults in our population. The commonest age group is 20-39 years. There is male preponderance. Although we noticed some significant gender differences in the

sociodemographic characteristics, there is little difference in the laboratory, 12-lead ECG and echocardiographic findings.

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