BASELINE CLINICAL CHARACTERISTICS OF CONTEMPORARY ADULT CHRONIC RHEUMATIC HEART DISEASE IN IBADAN, NIGERIA

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ABSTRACT

Introduction: **Rheumatic heart disease (RHD) is a major public health issue, especially in developing countries. Globally, the largest increase in RHD incidence over 30 years was seen in sub-Saharan Africa, further contributing to the burden of cardiovascular disease in a region with high rates of hypertensive heart disease and cardiomyopathies. There are few reports describing the contemporary clinical profile of RHD in Nigeria.**

Objective: **The objective of the study is to describe the profile of RHD at the University College Hospital Ibadan.**

Methodology: **This is an analysis of data collected on adult patients aged 18 years and above attending the cardiology service of the University College Hospital, Ibadan, Nigeria between September 1, 2016, and August 31, 2021. We collected information on the bio-data, clinical features, and echocardiographic diagnoses.**

Results: **During this period, 92 cases of RHD were diagnosed and 24 (26.1%) were male. The mean age of the study population was 49.67 ± 17.54 years, with ages ranging from 16 to 86 years. Most participants (45.7%) were within the age group of 30-49 years. Most (70.8%) of the participants presented in NYHA Class II heart failure. The most common presentation mode was dyspnea on exertion and nocturnal cough (64.1%). Mitral regurgitation was the commonest lesion (65.4%)**

Conclusion: **Rheumatic heart disease is still a common cause of adult heart disease in Ibadan. There is a need for concerted efforts to tackle the burden of this disease by increasing screening among high-risk groups, improving access to healthcare, and increasing the uptake of secondary prophylaxis in those with a previous history of rheumatic fever.**

Keywords: Rheumatic fever, Rheumatic heart disease, Valvular heart disease, Clinical epidemiology.

INTRODUCTION

Rheumatic heart disease (RHD) is a chronic disease where severe damage occurs to heart valves due to a systemic immune process that follows pharyngeal infection by beta-hemolytic streptococcus.[1] Some of the commonly linked sequelae of rheumatic heart disease include heart failure, chronic atrial fibrillation, infective endocarditis and stroke.[1]

In 2019, about 2.79 million new cases of RHD were diagnosed globally and more than 40 million individuals were affected.[2] The largest increase in RHD incidence over 30 years was seen in sub-Saharan Africa, further contributing to the burden of cardiovascular disease in a region with high rates of hypertensive heart disease and cardiomyopathies.[3]

Poor hygiene, overcrowding, and low socioeconomic status are widely recognized as factors responsible for the persisting burden of RHD. Health system challenges such as inadequate facilities for diagnosis, inadequate treatment of pharyngitis, and reduced access to health care are also notable drivers of RHD.[4] Although the social determinants of RHD have been characterized and the opportunities for prevention at both primary and secondary levels have been broadly discussed, RHD is still a significant cause of cardiovascular-related morbidity and mortality in developing countries.[4]

The Global Rheumatic Heart Disease Registry (REMEDY) study which recruited more than 3000 patients with RHD reported that severe valvular disease was a strong predictor of mortality.[5] Death rates were

highest in developing countries where there is a scarcity of infrastructure and personnel to provide operative management for RHD.[4] In Nigeria, large-scale epidemiological studies to describe the burden and outcomes of rheumatic heart disease are sparse.[6-9] Multiple reports that have employed handheld echocardiography for screening in a healthy population have placed the prevalence of RHD between 3.1% and 9.8%.[9-11]

This current study aims to describe the clinical characteristics, echocardiography findings, and outcomes of RHD seen at the University College Hospital, Ibadan, Nigeria.

MATERIALS AND METHODS

Study design

This is a prospective cross-sectional study of adult patients aged 18 years and above were recruited into the study which is part of the wider Ibadan acute and chronic heart failure project which commenced in September 2016. (ClinicalTrials.gov Identifier: NCT05936957) Informed consent was obtained from all the participants and the project was approved by the institution's ethics review committee. The study conformed with the international regulations on research on human subjects as enshrined in the Declaration of Helsinki.[12] In this paper, we report cases of RHD seen over 5 years (September 1, 2016, to August 31, 2021)

Place of the study

The study was conducted at the Cardiology Unit of the Department of Medicine, University College Hospital (UCH), Ibadan, Oyo state, Nigeria.

Data Collection

All consenting adult patients aged 18 years and above with heart disease attending the cardiology clinic of the Medical Out-patient clinic or admitted into the Cardiology ward of the University College Hospital were entered into the prospective registry. There were no exclusion criteria except for lack of consent from the patient. All patients had full echocardiography to confirm the diagnosis.

Pretested questionnaires were used to collect the participants' information on sociodemographic characteristics, presenting symptoms, types of underlying diseases, past medical history, and drug history. All participants had baseline vital signs and anthropometric measurements of weight and height for the calculation of body mass index (BMI). Echocardiography and 12-lead Electrocardiography were also performed. Laboratory results of blood tests such as serum electrolytes, fasting lipid profile, and complete blood count were also abstracted from participants' clinical records.

Echocardiography

Transthoracic echocardiography was carried out on each subject using the available machine GE S70N (General Electric Company, 5 Necco Street, Boston, MA 02210), The echocardiographic machine was set for the optimal image and colour Doppler acquisition. The Nyquist limits for colour Doppler were set to maximum to avoid overestimation of jet length. The images for the assessment of the valves and thickness of the chordae were acquired with the tissue harmonics turned off. The probe frequency was set at ≥2.0MHZ. The gain settings were adjusted to achieve optimal image quality. The machine depth, sector size, and focus were optimized to achieve a maximum frame rate of 30-60 frames per second.[13]

Echocardiographic measurements were according to the leading-edge-to-leading-edge convention as recommended by the American Society of Echocardiography.[14] Two dimensionally guided M-mode measurements were acquired according to standard guidelines.[15] The dimensions of the left atrium and left ventricle were measured following standard guidelines and the measurements were averaged over 3 cardiac cycles.[16] The LV fractional shortening using the standard formula while Simpson's method of disc was used for the estimation of the left ventricular ejection fraction.[17]

Doppler echocardiography was used in the assessment of the presence or absence of valvular regurgitation. Left ventricular diastolic function was assessed by studying the filling dynamics of the left ventricle by evaluating the transmitral 'E' wave velocity (peak early mitral inflow velocity) and the 'A' wave velocity (peak atrial inflow velocity), the E/A ratio, and the deceleration time (DT): time interval of peak E wave velocity to its extrapolation to the baseline. The E/A ratio was not evaluated in individuals with atrial fibrillation or marked tachycardia.[18]

The diagnosis of rheumatic valve disease was based on clinical features and fulfillment of the World Heart Federation (WHF) criteria for echocardiographic diagnosis of RHD[13] and recently updated[1] The criteria for the diagnosis of pathological mitral regurgitation (MR) were the presence in at least two views of i. pan-systolic jet in at least one envelope, ii. pan-systolic Jet ≥2cm in at least one echocardiography view, iii. MR jet velocity ≥3m/s in one complete envelope.[13]

The criteria for the diagnosis of pathological aortic regurgitation (AR) were the presence in at least two

views of, i. pan-diastolic jet ≥1cm, ii. AR jet velocity ≥3m/s in early diastole and iii. AR pan-diastolic jet in at least one envelope[13]

The diagnoses of valvular lesions as well as the quantification of cardiac chambers were based on the recommendations of the World Heart Federation and the American Society of Echocardiography.[13,19] The complications of RHD were categorized as follows: 1. Congestive heart failure 2. Infective endocarditis 3. Atrial fibrillation 4. Thrombo-embolic episodes (stroke, pulmonary thrombo-embolism, limb ischemia, etc) LV systolic dysfunction was defined as an ejection fraction less than 50%. Pulmonary hypertension was based on the presence of elevated pulmonary systolic pressure identified by Right Ventricular systolic pressure (RVSP) of 35 mmHg or more.[15]

DATA ANALYSIS

Analysis was performed with SPSS statistical package version 21. Descriptive statistics were used for the continuous and categorical variables. Continuous variables were compared with the student's *t-test* while categorical variables used chi-square statistics. A p-value of <0.05 was considered to be statistically significant.

RESULTS

Sociodemographic Characteristics

During the study period, 92 cases of RHD were diagnosed based on clinical symptoms and signs and echocardiographic findings. Among these, 24 (26.1%) were male and 68 (73.9%) were female. The mean age of the study population was 49.67 ± 17.54 years, with ages ranging from 16 to 86 years. The majority (45.7%) of the participants were within the age group 30-49 years. Most of the patients (83.7%) had been married at one point or the other. Although about 94% lived in an urban setting, the majority (84.6%) of the patients had a monthly income of less than N50,000. (Table 1). History of alcohol consumption and cigarette smoking were statistically significant when male participants with RHD were compared to female participants (p-values 0.006, 0.001 respectively).

Table 1: Sociodemographic characteristics of the study participants

Variable	All (92)	Male (24)	Female (68)	Chi-square	p-value
Mean Age (years)	47.96 ± 17.54	47.83 ± 19.50	48.00 ± 16.95	-	0.97
Age Range (years)	16 - 86	17 - 52	16 – 86	-	-
Age Category (n/%)					
<40 years	31 (33.7)	7 (29.2)	24 (35.3)	0.298	0.63
≥40 years	61 (66.3)	17 (70.8)	44 (64.1)		
Marital Status (n/%)					
Ever Married	77 (83.7)	18 (75.0)	59 (86.8)	1.799	0.63
Never Married	15 (16.3)	6 (25.0)	9 (13.2)		
Educational Background (n/%)					
Primary or less	34 (37.0)	6 (25.0)	28 (41.2)	1.992	0.21
Secondary or more	58 (63.0)	18 (75.0)	40 (58.8)		
Occupation (n/%)					
Employed	24 (26.1)	8 (33.3)	16 (23.5)	0.889	0.64
Unemployed	42 (45.7)	10 (41.7)	32 (42.1)		
Retired	26 (28.3)	6 (25.0)	20 (29.4)		
Place Lived Most Life (n/%)					
Rural	6 (6.5)	0 (0.0)	6 (8.8)	2.265	0.64
Urban	86 (93.5)	24 (100)	62 (91.2)		
Estimated Monthly Income (n/%)					
<50,000	72 (84.6)	15 (62.5)	57 (83.8)	4.741	0.043
≥50,000	20 (21.7)	9 (37.5)	11 (16.2)		
Alcohol (n/%)					
Never took	77 (84.6)	15 (65.2)	62 (91.2)	8.897	0.006
Ever took	14 (15.4)	8 (34.8)	6 (8.8)		
Smoking (n/%)					
Never smoked	85 (92.4)	18 (75.0)	67 (98.5)	13.971	0.001
Ever smoked	7 (7.6)	6 (25.0)	1 (1.5)		
Previous Admission for HF (n/%)					
Yes	47 (51.1)	14 (58.3)	33 (48.5)	0.682	0.48
No	45 (48.9)	10 (41.7)	35 (51.5)		

HF = Heart Failure

Table 2: Biophysical profile and laboratory findings in the study participants

Variable	All (92)	Male (24)	Female (68)	p-value
Weight (kg)	61.02 ± 12.34	64.77 ± 14.72	59.69 ± 11.20	0.082
Height (cm)	161.92 ± 6.79	167.21 ± 7.38	160.05 ± 5.51	<0.001
BMI (kg/sqm)	23.20 ± 3.99	22.98 ± 4.09	23.27 ± 3.98	0.76
Pulse Rate (beats/min)	88.80 ± 16.56	87.71 ± 17.07	89.19 ± 16.49	0.71
RR (cycles/min)	24.16 ± 2.45	24.75 ± 4.71	23.96 ± 2.89	0.34
Systolic BP (mmHg)	112.60 ± 18.77	113.58 ± 20.01	112.25 ± 18.46	0.77
Diastolic BP (mmHg)	72.76 ± 13.25	69.13 ± 12.17	74.04 ± 13.47	0.12
Packed Cell Volume (%)	38.62 ± 5.18	38.27 ± 6.89	38.75 ± 4.48	0.69
White Cell Count ($10^3/\mu L$)	6.72 ± 2.92	7.42 ± 2.03	6.46 ± 3.14	0.17
Platelet Count ($10^3/\mu L$)	228.88 ± 92.05	249.13 ± 133.49	227.74 ± 72.06	0.21
Sodium (mmol/L)	137.61 ± 5.68	134.79 ± 7.38	138.63 ± 4.61	0.004
Potassium (mmol/L)	3.87 ± 0.51	3.94 ± 0.57	3.85 ± 0.49	0.46
Urea (mg/dl)	35.45 ± 21.57	46.17 ± 31.69	41.66 ± 15.22	0.004
Creatinine (mg/dl)	1.04 ± 0.46	1.25 ± 0.73	0.97 ± 0.37	0.011
FBG (mg/dl)	91.22 ± 13.34	90.54 ± 19.26	91.46 ± 10.68	0.78
Total Cholesterol (mg/dl)	141.01 ± 25.09	135.96 ± 33.30	142.79 ± 21.50	0.25
LDL Cholesterol (mg/dl)	88.08 ± 21.13	81.33 ± 28.34	90.46 ± 17.57	0.069
HDL Cholesterol (mg/dl)	39.00 ± 11.26	41.08 ± 16.05	38.26 ± 9.04	0.29
Triglycerides (mg/dl)	82.16 ± 10.73	79.63 ± 12.80	83.06 ± 9.84	0.18

BMI = Body Mass Index; BP = Blood Pressure; FBG = Fasting Blood Glucose; HDL = High Density Lipoprotein; LDL = Low Density Lipoprotein; RR = Respiratory Rate

Clinical Profile

Most (70.8%) of the participants were in the New York Heart Association (NYHA) Class II heart failure. The most common mode of presentation was dyspnea on exertion and nocturnal cough (64.1%). Other common symptoms were peripheral edema and paroxysmal nocturnal dyspnea. Figure Ia shows the medications used by the study participants and Figure Ib shows the distribution of study participants according to comorbidities. Out of the 92 participants, 8 (8.6%) had coexisting hypertension and 4 (4.3%) each had diabetes, arthritis, and kidney disease.

Table 2 shows the biophysical profile and laboratory findings stratified by gender. Vital signs taken at the presentation were similar in both genders and there was no difference in the complete blood count or fasting lipid profile parameters of male and female patients with chronic rheumatic disease. However, serum sodium was significantly lower in men while

Table 3: Echocardiographic parameters in the study participants

Variable	All (81)	Male (20)	Female (61)	p-value
Aortic Root Diameter (cm)	2.74 ± 0.60	3.04 ± 0.39	2.64 ± 0.63	0.010
Left Atrial Diameter (cm)	4.96 ± 1.08	5.43 ± 1.06	4.80 ± 1.05	0.024
IV septal thickness in diastole (cm)	1.08 ± 0.40	1.09 ± 0.31	1.08 ± 0.42	0.41
IV septal thickness in systole (cm)	1.29 ± 0.48	1.40 ± 0.43	1.25 ± 0.50	0.21
LV posterior wall thickness in diastole (cm)	1.07 ± 0.32	1.13 ± 0.26	1.05 ± 0.34	0.36
LV posterior wall thickness in systole (cm)	1.47 ± 0.38	1.61 ± 0.39	1.42 ± 0.36	0.057
LV internal diameter in diastole (cm)	5.90 ± 1.13	6.19 ± 1.07	5.81 ± 1.15	0.19
LV internal diameter in systole (cm)	4.59 ± 1.20	4.89 ± 1.15	4.49 ± 1.21	0.19
LV ejection fraction (%)	47.43 ± 16.18	47.88 ± 15.98	47.28 ± 16.38	0.89
LV fractional shortening (%)	24.77 ± 5.79	25.34 ± 6.69	24.58 ± 5.51	0.61
TAPSE (cm)	2.26 ± 0.63	2.42 ± 0.45	2.21 ± 0.67	0.19
Mitral valve E velocity (m/sec)	1.26 ± 0.44	1.29 ± 0.41	1.25 ± 0.46	0.74
Mitral valve A velocity (m/sec)	0.71 ± 0.57	0.95 ± 1.09	0.66 ± 0.32	0.089
Deceleration time of Mitral valve E velocity (msec)	162.25 ± 49.73	160.05 ± 40.49	162.97 ± 52.70	0.82
Isovolumic relaxation time (msec)	130.23 ± 34.57	127.25 ± 23.86	131.21 ± 37.54	0.66

IV = Interventricular; LV = Left Ventricular; TAPSE = Tricuspid Annular Plane Systolic Excursion

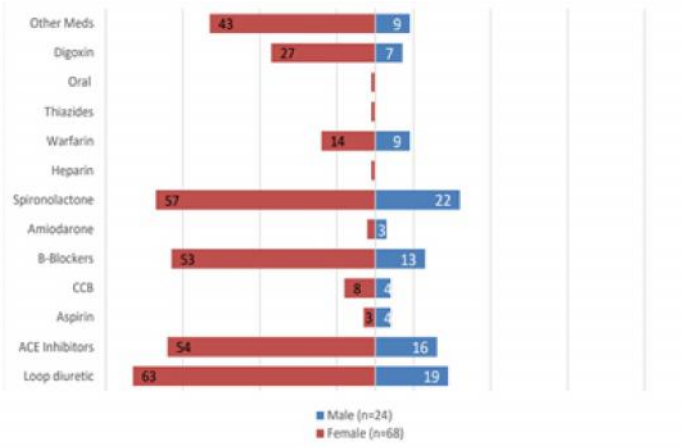

Figure 1a. Distribution of medications used by study participants (n = 92)

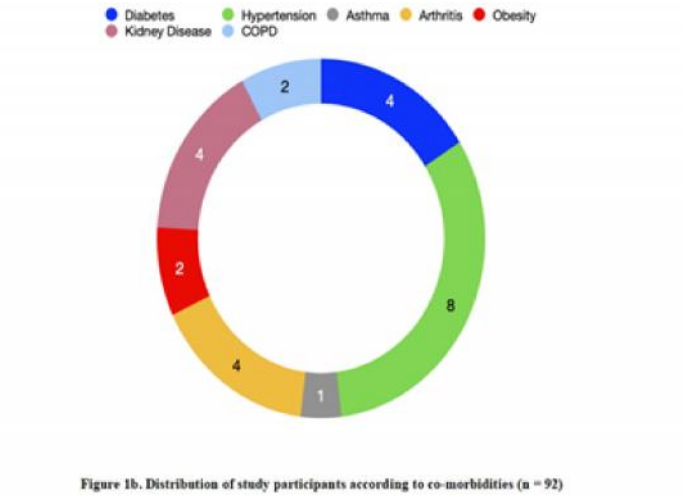

Figure 1b. Distribution of study participants according to co-morbidities (n = 92)

Table 4: Other echocardiographic findings in the study participants

Variable	All (81)	Male (20)	Female (61)	Chi-square	p-value
Aortic Incompetence (n/%)					
Yes	22(27.2)	6 (30.0)	16 (26.2)	0.108	0.77
No	59 (72.8)	14 (70.0)	45 (73.8)		
Aortic Stenosis (n/%)					
Yes	6 (7.4)	3 (15.0)	3 (4.9)	2.232	0.16
No	75 (92.6)	17 (85.0)	58 (95.1)		
Mitral Incompetence (n/%)					
Yes	53 (65.4)	13 (65.0)	40 (65.6)	0.002	1.00
No	28 (34.6)	7 (35.0)	21 (34.4)		
Mitral Stenosis (n/%)					
Yes	4 (4.9)	2 (10.0)	2 (3.3)	1.449	0.25
No	77 (95.1)	18 (90.0)	59 (96.7)		
Tricuspid Incompetence (n/%)					
Yes	48 (59.3)	12 (60.0)	36 (59.0)	0.006	1.00
No	33 (40.7)	8 (40.0)	25 (41.0)		
Pulmonary Incompetence (n/%)					
Yes	14 (17.3)	2 (10.0)	12 (19.7)	0.986	0.49
No	67 (82.7)	18 (90.0)	49 (80.3)		
Pericardial Effusion (n/%)					
Nil	58 (71.6)	15 (75.0)	43 (70.5)	3.678	0.30
Negligible	6 (7.4)	0 (0.0)	6 (9.8)		
<1 cm	10 (12.3)	4 (20.0)	6 (9.8)		
1-2 cm	7 (8.6)	1 (5.0)	6 (9.8)		
Spontaneous Echoes (n/%)					
Yes	8 (9.9)	1 (5.0)	7 (11.5)	0.710	0.67
No	73 (90.1)	19 (95.0)	4 (88.5)		

Figure 2: (a) Framingham Major Criteria for HF (b) Framingham Minor Criteria for HF (c) Distribution of study participants in terms of NYHA functional classification

serum urea and creatinine were significantly higher in men (p-value= 0.004, 0.004, 0.0011 respectively).

12-Lead ECG findings

The average heart rate was 96±21.45 beats per minute. Most (79.7%) of the participants had normal axis, and there was a significant association between gender and axis. Male participants were noted to have a longer QRS duration than female participants (p-value =0.002). Twenty-eight (32.6%) of participants had atrial fibrillation, and a little more than half (52.3%) had left ventricular hypertrophy. Three participants had right ventricular hypertrophy.

Echocardiography findings

Complete echocardiography results were available in the clinical records for only 81 (88%) out of the 92 patients seen during the study period. Tables 3 and 4 show the echocardiography findings among the participants. Left atrial diameter and aortic root diameter were significantly larger in male patients. All other parameters were similar in both genders.

Valvular Defects

Mitral incompetence (65.4%) and tricuspid incompetence (59.3%) were the most frequently identified valvular lesions. More than one-quarter of the participants had aortic incompetence (27.2%) and pulmonary incompetence was noted in 17.3%. Stenotic valvular lesions were rare with only 4 and 6 participants having mitral stenosis and aortic stenosis respectively.

DISCUSSION

This study explores the sociodemographic and clinical characteristics of patients with chronic rheumatic heart disease (RHD) in Ibadan, Nigeria. We made diagnosis

of RHD in 92 patients. The number of females with RHD in our study was almost thrice that of males (male-to-female ratio of 1:2.8). In contrast, many other studies in Nigeria[11,20-23] and Africa[24-28] have found that RHD is more common in males than in females. This gender predilection in the prevalence of RHD was not evident in our study until the age of 20 years when the difference began to be noticed. This finding may suggest that the disease is more lethal in males and thus, many of them do not live as long as their female counterparts. This was demonstrated in a global RHD registry where the female gender was shown to be protective of RHD-related mortality.[5] The difference may also be due to selection bias.

Although RHD is known to be a problem in children and young adults, findings from our study suggest that it is present among all age groups, being most common among ages 30-49 years. The mean age of the subjects was 49.67 ± 17.54 years. This is a little bit higher than what was found in the Heart of Soweto Study[26] and another study in Abeokuta[11], where the mean age of presentation was 43 years. Also, studies in the Northern part of the country have described younger mean ages of presentation, ranging from 19.5 to 24 years.[9,22] The older mean age of presentation in our study may be due to late presentation, probably because the disease progressively becomes more severe with increasing age. It may also mean that subclinical forms of the disease are more common in the younger population in this environment. Also, poor diagnostic techniques and inadequate expertise may result in underdiagnosis in the younger age group. Hence, more sensitive diagnostic measures should be put in place to ensure early diagnosis.

In our cohort, cardiomegaly and paroxysmal nocturnal dyspnea were the commonest findings from the Framingham major criteria and this was consistent in both genders. Also, more than half of our patients had dyspnea on exertion, nocturnal cough, or bilateral ankle swelling.

Most (91.6%) of our study participants presented with heart failure in NYHA classes II and III. This is different from studies in Abeokuta and Uganda[11,29] which reported that most of the patients presented in NYHA classes III and IV. It is similar to the heart of Soweto study[26] where only 18% were in NYHA classes III and IV. This may suggest that the disease runs a milder course in our environment.

The findings in this study provide valuable insight into the prevalence of atrial fibrillation (AF) and left ventricular hypertrophy (LVH) in patients with RHD. In our study, 32.6% of the patients which RHD had coexisting AF which is consistent with a met-analysis of studies across 42 countries which concluded that about one in three patients with RHD would have AF.[30] In contrast, a Ugandan study reported that 63.7% of the 449 participants developed AF.[29] According to the REMEDY study, a fifth of children with symptomatic RHD are found to have AF.[4] Such discrepancies may be attributed to regional differences in access to healthcare or variations in the methodology of the study.

Regarding LVH, 52.3% of participants in this study were found to have this condition. Another study in the eastern part of Nigeria found that 63.6% of RHD patients aged 12 years and above had LVH.[23] These differences in LVH highlight the potential impact of environmental factors on the development of LVH in RHD patients.

In our study, mitral incompetence was the most commonly observed valvular defect. This was in line with studies done in Nigeria[11,23,31] other parts of Africa[26,27,29,32], other parts of the world[33-36] as well as in multinational studies.[5] This was closely followed by tricuspid incompetence, which is similar to what was reported in a 2020 study done in Indonesia.[37]

STRENGTH AND LIMITATION

The strength of the paper is that it is a dedicated registry of RHD in a large tertiary hospital. The cases were well defined. The fact that is hospital based is a limitation as it may not be true reflection of the hospital burden. The outcomes of these patients were also not documented and this will be the focus of future studies as well as community based estimate of the condition especially amongst young and adolescent school population.

CONCLUSION

Rheumatic heart disease is still a common cause of heart failure among adult Nigerians.

There is a notable female preponderance and slight gender differences existing in the sociodemographic, clinical profile, ECG and echocardiographic findings of our cohort. There is a need for concerted effort to tackle the burden of this disease by increasing screening among high-risk groups, improving access to healthcare and increasing uptake of secondary prophylaxis in those with previous history of rheumatic fever.

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