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Knowledge and Prevalence of Heart Disease Risk Factors Among Staff of a Tertiary Institution in Nigeria

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Abstract

Background: Cardiovascular disease is the most common cause of mortality worldwide. Hence, awareness of cardiovascular risk factors is an essential step towards effective reduction of the disease burden. This study determined the knowledge and prevalence of cardiovascular risk factors among Staff of Ekiti State University. Ado-Ekiti, Nigeria.

Methods: A cross-sectional study which comprised of 223 members of staff.

Results: There were 103 males (46.2%). Low knowledge of heart disease risk factors was found in 68.6% of the respondents. The prevalence of hypertension, diabetes mellitus, overweight, obesity, physical inactivity was 35.4%, 12.1%, 31.8%, 23.3%, and 83% respectively. Family history of hypertension was a predictor of a high level of knowledge.

Conclusion: A low level of knowledge and increasing prevalence of cardiovascular risk factors existed among staff of Ekiti State University, Nigeria. Hence, there should be a step-up of awareness campaigns and promotion of healthy lifestyle among this category of people.

Keywords

heart disease, knowledge, prevalence, cardiovascular, risk factors, University, Nigeria

Introduction

Current projections suggest that the burden of cardiovascular (CV) diseases and related risk factors in sub-Saharan Africa countries are rapidly growing.[1] Globally, cardiovascular disease (CVD) is the leading cause of death. Its burden is fueled by the rising prevalence of cardiovascular risk factors in Nigeria and almost all parts of Africa.[2–4] Gaps in knowledge of CVD conditions and their risk factors are barriers to effective prevention and treatment. Therefore, adequate awareness of CVD and their risk factors may contribute to prevention and control strategies. The relationship between risk factors and CVD has been previously documented.[5] Notably, few data exist on the knowledge of CVD and risk factors in sub-Saharan Africa with contrary reports about the effect of educational status on the level of awareness of cardiovascular risk factors.

Yet, evidence on the awareness and knowledge level of CVD and associated risk factors among populations of SSA is scarce. Levels of knowledge and awareness for CVD and risk factors were generally low.[6,7] Akintunde et al. in a university study in south-west Nigeria reported a good knowledge of heart disease risk factors in one-fifth of their study population. Similarly, Ansa et al. in south-south, Nigeria also reported a poor level of knowledge of cardiovascular risk factors and poor practice of lifestyle modification strategies regardless of educational status among university staff.[7] In the same vein, a systematic review done among the sub-Saharan African countries reported a low level of awareness and knowledge of cardiovascular risk factors while also revealing that high educational attainment

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and place of residence were associated with good level of knowledge for CVDs among SSA populations.[8] In the review, the proportion of participants who were unable to identify a single risk factor and clinical symptom for CVDs ranged from 1.8% in a study among hospital staff in Nigeria to a high of 73% in a population-based survey in Uganda and 7% among University staff in Nigeria to 75.1% in a general population in Uganda respectively.[8]

Questionnaires such as Heart Disease Fact Questionnaire (HDFQ),[9,10] Behaviour Risk Factor Surveillance System (BRFSS), International Physical Activity Questionnaire (IPAQ), National Health and Nutrition Examination Surveys (NHANES) have been used in prior researches. Behaviour Risk Factor Surveillance System is a self-report telephone survey which can also provide data concerning behavioural risk factors and is usually used in adults aged 50 years or older.[11] Also, IPAQ was reported to overestimate physical activity, even though it was used in the young and middle-aged adults (15-64 years).[12] Whereas, NHANES is used to assess nutritional status and its association with health promotion and disease prevention.[13] Noteworthily, HDFQ has been used in prior studies to measure knowledge of heart disease risk factors and has shown reliable test-retest reliability, internal consistency and satisfactory discriminant validity.[14]

The knowledge of heart disease risk factors is essential to make an informed decision that may reduce the individual's overall cardiovascular risk. In the Health Belief Model (HBM), there must be perceived susceptibility to a disease before people are motivated to effect a behavioural change.[15] Hence, adequate knowledge and perception of risk are essential in stimulating behavioural change towards better health. This study determined the level of knowledge and prevalence of risk factors for heart disease among staff of Ekiti State University, Ado-Ekiti, Ekiti State, Nigeria.

Methodology

Materials and Methods

This was a cross-sectional study involving 223 adult Nigerians aged between 20-64 years. The inclusion criteria were adults who are 18 years and above. The exclusion criteria were those with a history of memory or neurological impairments or both, that would limit reading, talking, or writing.

Measurements

The demographic data obtained include age, gender, marital status, level of education, weight, height and blood pressure. Two hundred and twenty-three participants which included staff of Ekiti State University, Ado-Ekiti, Nigeria were recruited.

Table 1. Clinical and Demographic Parameters of the Study Population.

Variables	Total (223) Mean ± SD
Age	40.7± 9.4
Sex: Male	103 (46.2%)
Female	120 (53.8%)
Mean knowledge score (%)	51.3 ± 26.1
Body mass index (kg/m^2)	26.8 ± 5.4
Male	25.3 ± 3.9
Female	28.2 ± 6.2
Body fat percentages (%)	
Male	23.7 ± 5.6
Female	37.6 ± 8.3
Systolic blood pressure (mmHg)	121.7 ± 19.6
Diastolic blood pressure (mmHg)	77.9 ± 13.2
FPG (mmol/L)	5.5 ± 1.5

Abbreviation: FPG, fasting plasma glucose.

This study used a self-administered questionnaire; Heart Disease Fact Questionnaire (HDFQ) as shown in Table 1.[9,10] was used to measure knowledge of heart disease risk factors. This instrument, has been used in prior studies with reliable test-retest reliability, internal consistency and satisfactory discriminant validity.[14] It is brief, understandable to respondents, easy to administer and score. It is a 25-item measure of heart disease knowledge (as shown in Table 1) that evaluates the knowledge of risk factors for heart disease, the link between diabetes and heart disease and how to reduce the risk for heart disease. This measure of heart disease risk knowledge Participants was asked to pick one of the options including 'True', 'False' or 'I don't know'. HDFQ scores differentiated respondents by knowledge of their cardiovascular health. Scores were calculated in percentages by summing the total number of correct answers with a higher score indicates a higher knowledge. Participants with a score of $<70\%$ were classified as low level of knowledge while those with HDFQ score $\geq 70\%$ as a high level of knowledge.

Anthropometry: The weight of participants was taken with light clothing on with the aid of a weighing scale with the weights measured to the nearest 0.1kg. Height was measured using a SECCA stadiometer. Body mass index (BMI) was then calculated from weight (in kilograms) divided by the square of the height (in metres).

Classification of Body mass index: Based on the World Health Organization of body mass index (BMI), BMI is defined thus: underweight $<18.5\,kg/m^2$, normal 18.5–24.9 kg/m^2, overweight 25–29.9 kg/m^2 and obese $\geq 30\,kg/m^2$.[16]

The body fat percentage (BF%) was analyzed using the formula:[17]

$$BF\% = 1.20 \times BMI + 0.23 \times age - 10.8 \times sex - 5.4.$$

Age and sex (males =1, females = 0) were taken into consideration. The prediction error with this formula is comparable to that obtained with other methods of estimating BF %, such as skinfold thickness measurements or bioelectrical impedance.[17]

Body Fat Percentages was classified based on: For men, normal < 20.1%, overweight= 20.1 – 24.9% obesity ≥ 25% while for women, normal < 30.1%, overweight=30.1-34.9% and obesity≥35%.[18]

Blood pressure (BP): BP measurement was done following the WHO protocol as thus: Each participant was asked to sit quietly and rest for 15 minutes with legs uncrossed and then the BP was measured in the left arm in the sitting position with the aid of Omron M6. Appropriate cuffs were used for each participant, with the level of the cuff placed at the heart level during measurement. Three BP measurements were taken three minutes apart; the mean of the second and third readings was taken as the final BP. The mean BP was used to classify the subjects into BP category: normal BP, prehypertension and hypertension according to JNC 7 criteria.[19]

Hypertension: Defined as a positive history of hypertension, use of antihypertensive medications or persistently elevated BP (≥140/90 mmHg).[19]

Diabetes mellitus (DM) was defined as a positive history of DM, use of hypoglycaemic agents or fasting plasma glucose ≥126 mg/dl (≥7.0 mmol/L).[20]

Inadequate intake of fruits and vegetables: The general recommendation for fruit and vegetable intake is at least 400 grams per day, or five servings of 80 grams. One 80-gram serving is equivalent to a small piece about the size of a tennis ball. Inadequate fruits/vegetables is less than five servings of 80 grams each per day.[21]

Statistical analysis was performed with the aid of the Statistical Package for Social Sciences SPSS 23.0 (Chicago Ill). Data were summarized using means and standard deviation for quantitative variables and frequencies and percentages for qualitative variables. Logistic regression analysis was used to assess the predictors of good knowledge of heart disease risk factors. P-value < 0.05 was taken as statistically significant.

Results

The mean age of the study participants was 40.7 ± 9.4years (range = 20–64 years). There were 103 males (46.2%) and female participants 120(53.8%). The mean body mass index was 26.8 ± 5.4 kg/m^2 as shown in Table 1. The mean HDFQ score was 51.3 ± 26.1% while the mean systolic and diastolic blood pressures were 121.7 ± 19.6 mmHg and 77.9 ± 13.2 mmHg respectively as shown in Table 1. The majority (68.6%) of the study population had low knowledge while about one-third (31.4%) had high knowledge of heart disease risk factors.

Table 2. Socio-demographic Factors Associated With Respondents' Knowledge of Heart Disease Risk Factors.

	Knowledge			
Variable	High n (%)	Low n (%)	Total N(%)	p-value
Age group (in years)				
20–29	5 (22.7)	17 (77.3)	22 (9.9)	0.358
30–39	25 (28.4)	63 (71.6)	88 (39.5)	
40–49	21 (31.3)	46 (68.7)	67 (30.0)	
50 and above	19 (41.3)	27 (58.7)	46 (20.6)	
Gender				
Male	32 (31.1)	71 (68.9)	103 (46.2)	0.923
Female	38 (31.7)	82 (68.3)	120 (53.8)	
Marital status				
Married	65 (34.2)	125 (65.8)	190 (85.2)	0.147
Single	5 (17.9)	23 (82.1)	28 (12.6)	
Divorced	0 (0.0)	3 (100.0)	3 (1.3)	
Widowed	0 (0.0)	2 (100.0)	2 (0.9)	
Level of education				
None	2 (66.7)	1 (33.3)	3 (1.3)	0.154
Primary	1 (12.5)	7 (87.5)	8 (3.6)	
Secondary	11 (21.2)	41 (78.8)	52 (23.3)	
Tertiary	34 (34.0)	66 (66.0)	100 (44.8)	
Post graduate	22 (36.7)	38 (63.3)	60 (26.9)	

Table 2 shows the age category, with the highest being from 40 to 49 years. The majority of the respondents had tertiary (44.8%) and postgraduate degrees (26.9%). Table 3 shows the response of the participants to the questions in the Heart disease fact Questionnaire in this study. The majority of the respondents had high knowledge about the significance of smoking cessation, hypertension and blood pressure control in relation to heart disease. However, the level of knowledge about diabetes and cholesterol is low. Table 4 shows the clinical and demographic parameters of the study population stratified based on their level of knowledge.

The relationship between selected risk factors and respondents' knowledge of heart disease risk factors were shown in Table 5. The prevalence of hypertension was 35.4%. It showed that 67.1% of those with the diagnosis of hypertension also had low knowledge of heart disease risk factors. Prevalence of diabetes mellitus was 12.1%, about 60% of those who had diabetes also had poor knowledge. Using both BMI and body percentages scale, the prevalence of overweight was 31.8% and 29.6% respectively while obesity prevalence were 23.3 and 46.2% respectively. Family history of hypertension is statistically significant between the two categories of level of knowledge as more people with a negative family history of hypertension had low knowledge of cardiovascular risk factors. More people with low knowledge of cardiovascular risk factors also had inadequate daily consumption of fruits/vegetables.

Table 6 shows the association between risk factors and a high level of knowledge. Logistic regression was performed

Table 3. Measures of Heart Disease Knowledge.

Variables	Truen (%)	Falsen (%)	Don't known (%)
A person always knows when they have heart disease.	73 (32.7)	24 (10.8)	126 (56.5)
If you have a family history of heart disease, you are at risk of developing heart disease.	78 (35.0)	36 (16.1)	109 (48.9)
The older a person, the greater their risk of having heart disease.	90 (40.4)	16 (16.1)	97 (43.5)
Smoking is a risk factor for heart disease	180 (40.4)	36 (16.1)	97 (43.5)
A person who stops smoking will lower their risk of heart disease.	162 (72.6)	13 (5.8)	48 (21.5)
High blood pressure is a risk factor for heart disease	151 (67.7)	13 (5.8)	59 (26.5)
Keeping blood pressure under control will reduce a person's risk for developing heart disease	161 (72.2)	13 (5.8)	49 (22.0)
High cholesterol is a risk factor for developing heart disease	150 (67.3)	14 (6.3)	59 (26.5)
Eating fatty foods does not affect blood cholesterol levels	56 (25.1)	106 (47.5)	61 (27.4)
If your good cholesterol (HDL) is high you are at risk for heart disease	93 (41.7)	39 (17.5)	91 (40.8)
If your bad cholesterol (LDL) is high you are at risk for heart disease	114 (51.1)	18 (8.1)	91 (40.8)
Being overweight increases a person's risk for heart disease	138 (61.9)	14 (6.3)	71 (31.8)
Regular physical activity will lower a person's chance of getting heart disease	152 (68.2)	19 (8.5)	52 (23.3)
Only exercising at a gym or in an exercise class will lower a person's chance of developing heart disease	80 (35.9)	77 (34.5)	66 (29.6)
Walking and gardening are considered an exercise that will help lower a person's chance of developing heart disease	145 (65.0)	17 (7.6)	61 (27.4)
Diabetes is a risk factor for developing heart disease	128 (57.4)	12 (5.4)	83 (37.2)
High blood sugar puts a strain on the heart	119 (53.4)	10 (4.5)	94 (42.2)
If your blood sugar is high over several months it can cause your cholesterol level to go up and increase your risk of heart disease	121 (54.3)	11 (4.9)	91 (40.8)
A person who has diabetes can reduce their risk of developing heart disease if they keep their blood sugar levels under control	140 (62.8)	10 (4.5)	73 (32.7)
People with diabetes rarely have high cholesterol	67 (30.0)	57 (25.6)	99 (44.4)
If a person has diabetes, keeping their cholesterol under control will help lower their chance of having heart disease	127 (57.0)	11 (4.9)	85 (38.1)
People with diabetes tend to have low HDL (good) cholesterol	56 (25.1)	36 (16.1)	131 (58.7)
A person who has diabetes can reduce their risk of developing heart disease if they keep their blood pressure under control	135 (60.5)	11 (4.9)	77 (34.5)
A person who has diabetes can reduce their risk of developing heart disease if they keep their weight under control	137 (61.4)	9 (4.0)	77 (34.5)
Men with diabetes have a higher risk of heart disease than women with diabetes	67 (30.0)	14 (6.3)	142 (63.7)

Table 4. Clinical and Demographic Parameters of the Study Population Stratified According to the Level of Knowledge.

	Knowledge of heart disease risk factors		
Variable	High (n = 70) Mean ± SD	Low (n = 153) Mean ± SD	p-value
Age	42.3 ± 9.6	40.0 ± 9.3	0.082
Mean Knowledge score (%)	79.2 ± 6.5	38.5 ± 21.3	**<0.001***
Body mass index (kg/m^2)	26.9 ± 5.2	26.8 ± 5.5	0.971
Body fat percentages (%)	31.6 ± 9.5	30.9 ± 10.2	0.650
Systolic blood pressure (mmHg)	120.8 ± 18.0	122.2 ± 20.4	0.634
Diastolic blood pressure (mmHg)	78.2 ± 12.7	77.7 ± 13.5	0.774
FPG (mmol/L)	5.7 ± 1.7	5.5 ± 1.4	0.271

Abbreviation: FPG, fasting plasma glucose
*, statistically significant.

to ascertain the effects of family history of hypertension and fruit/vegetable consumption on the likelihood that respondents have a high level of knowledge of heart disease risk factors. Respondents with a family history were twice more likely to exhibit a high level of knowledge.

Discussion

This study revealed that the majority (68.6%) of the study participants had a low level of knowledge of cardiovascular risk factors, as good level of knowledge was found in less than one-third (31.4%) among staff of Ekiti State University, southwest, Nigeria. It also showed increasing prevalence of cardiovascular risk factors: hypertension (35.4%), overweight (31.8%), obesity (23.3%), diabetes (12.1%), physical inactivity (83%) and inadequate consumption of fruits and vegetables (67.7%) among the study population. The finding of low knowledge of cardiovascular risk

Table 5. Relationships Between Some Risk Factors and Respondents' Knowledge of Heart Disease Risk Factors.

	Knowledge			
Variables	High (n = 70)n (%)	Low (n = 153)n (%)	Total (N = 223)N (%)	p-value
Blood pressure category				
Normal	32 (33.7)	63 (66.3)	95 (42.6)	0.295
Pre-hypertension	15 (23.1)	50 (76.9)	65 (29.1)	
Stage 1 hypertension	16 (40.0)	24 (60.0)	40 (17.9)	
Stage 2 hypertension	7 (30.4)	16 (69.6)	23 (10.3)	
Hypertension	26 (32.9)	53 (67.1)	79 (35.4)	0.414
Receiving medication (n = 79)	8 (34.8)	15 (65.2)	23 (29.1)	0.821
Diabetes mellitus, FPG >7.0 mmol/L	11 (40.7)	16 (59.3)	27 (12.1)	0.264
BMI (kg/m^2)				
Underweight	0 (0.0)	1 (100.0)	1 (0.4)	0.827
Normal	29 (29.3)	70 (70.7)	99 (44.4)	
Overweight	24 (33.8)	47 (66.2)	71 (31.8)	
Obesity	17 (32.7)	35 (67.3)	52 (23.3)	
Body fat percentage				
Normal	17 (31.5)	37 (68.5)	54 (24.2)	0.280
Overweight	16 (24.2)	50 (75.8)	66 (29.6)	
Obesity	37 (35.9)	66 (64.1)	103 (46.2)	
Family history of hypertension				
Yes	24 (46.2)	28 (53.8)	52 (23.3)	**0.009***
No	46 (26.9)	125 (73.1)	171 (76.7)	
Family history of myocardial infarction	3 (50.0)	3 (50.0)	6 (2.7)	0.598
Family history of diabetes mellitus	11 (40.7)	16 (59.3)	27 (12.1)	0.264
Physical inactivity	59 (31.9)	126 (68.1)	185 (83.0)	0.722
Inadequate fruit/vegetable intake	41 (27.2)	110 (72.8)	151 (67.7)	**0.048***
Tobacco use	2 (40.0)	3 (60.0)	5 (2.2)	0.675

Abbreviation: FPG, fasting plasma glucose
*, statistically significant.

Table 6. Predictors of Good Knowledge of Heart Disease Risk Factors.

Variables	Adjusted odd ratio	95% confidence interval	p-value
Age	1.03	0.998–1.069	0.064
Sex	0.86	0.476–1.548	0.611
Cadre	1.40	0.671–2.902	0.372
Academic qualification	0.47	0.205–1.061	0.069
Family history of hypertension	2.01	1.025–3.922	**0.042***

*, statistically significant.

factors in this study is in tandem with previous Nigerian studies: Akintunde *et. al.* reported a low level of knowledge of risk factors in majority of their study population as only one-fifth (19.9%) had good knowledge of heart disease risk factors. In other words, this present study revealed that 31.4% of our study population had good knowledge of heart disease risk factors unlike 19.9% that was reported by Akintunde et. al. in Ogbomoso, Oyo state. Accounting for a relative increase in level of knowledge of cardiovascular risk factors in our study compared with the latter study could be due to a higher literacy rate in Ekiti state; higher academic qualifications has been associated with good knowledge of heart disease risk factors.[7] However, unlike the Nigerian studies, a study among African-Americans reported a good knowledge of CVD risks.[22] The reason for the improved knowledge in the latter study could be the place of residence, as they reside in a high-income country with better access to health-related information. Place of residence has been associated with the level of knowledge of CVDs, risk factors and clinical symptoms.[8]

Notably, this study revealed that the participants' level of knowledge as it concerns its association with diabetes and cholesterol fractions was generally poor. Additionally, there was poor practice of lifestyle modification strategies in this present study. For instance, a high number of participants (>70%) agreed that being overweight is a risk factor for heart disease. However, this did not translate to good practice as more than three-quarter of the study population had inadequate physical activity. In addition, about one-third of our study population were overweight. One possible reason for the poor practice of healthy lifestyle could be related to the previous report about education and wealth having strong influences on the epidemiologic transition and serving

as a double-edged sword of benefit and risk.[23] While improved education and enhanced resources are necessary to reduce infectious, parasitic, and perinatal diseases, these factors are also associated with unhealthy lifestyles such as consumption of unhealthy diets (high fat/high salt foods, inadequate fruits/vegetable consumption) and adoption of unhealthy behaviour (sedentary lifestyle without physical exercise).[23] It has been reported that in many countries worldwide, the vast majority of the population consumes less than the recommended amount of five servings of fruit and vegetables per day.[24] Inadequate intake of fruits and vegetables has been estimated to cause 4.7% of the global disease burden.[25] It has been reported that a higher consumption of fruit and vegetables is associated with a lower risk of all-cause mortality, particularly cardiovascular mortality.[21] Ansa et al. also corroborated a predominance of unhealthy lifestyle modification choices in their study population irrespective of their educational status.[7]

Furthermore, the prevalence of hypertension in this study (35.4%) is higher than studies carried out a few years earlier in Nigeria with the prevalence of hypertension of 21.5% in an urban university community in Nigeria[26] while a survey on non-communicable diseases and cardiovascular risk factors done in South-East Nigeria reported a rate of 31%..[27] This is an indication that the prevalence of hypertension may be on the increase in the country. However, the prevalence of hypertension in this study is slightly lower than 38.1% that was recently reported.[28] It is also lower than 40.8% that was reported in a similar university study.[3] The difference in hypertension prevalence between this and the latter study may be due to the relatively younger participants in our study; reports have it that hypertension is associated with increasing age.[29] The prevalence of overweight in this study was 31.8% which is similar to 31.0% that was reported by a study in the sub-Saharan African countries.[30] However, the prevalence of generalized obesity (23.3%) in our study was lower than 34% that was reported in the latter study. Furthermore, the prevalence of diabetes mellitus in our study population is 12.1%. Diabetes is a risk factor for cardiovascular diseases and there are reports of the increasing prevalence of prediabetes and diabetes in Nigeria.[31]In 2015, a meta-analysis on 42 Nigerian studies carried out between 1990 and 2015, reported that the prevalence of type II DM has increased from 2.0% in 1990 to 5.7% in 2015.[32] Type II diabetes mellitus has been associated with poor dietary choices, obesity and lack of exercise,[32] which are notable in this study.

Even though most of the cardiovascular risk factors were higher in those with a low level of knowledge, this difference was not statistically significant. Significant percentage of those with high level of knowledge had adequate consumption of fruits/vegetables. However, respondents with a family history were twice more likely to exhibit a high level of knowledge. The presence of hypertension in a family member would possibly create increased awareness about the risk factors of heart disease. It has been previously documented that cues to action, a component of health model belief prompts actions that are consistent with increase in level of knowledge among family members. This explains why those with a positive family history of hypertension have high knowledge of cardiovascular risk factors. Africans have been shown to have higher rates of cardiovascular disease.[4,22,33] Therefore, increasing the level of knowledge of heart disease risk factors and prevention of cardiovascular disease remains a major way to reduce the burden of cardiovascular diseases among Africans.

Conclusion

A low level of knowledge of heart disease risk factors and an increasing prevalence of cardiovascular risk factors existed among members of staff of Ekiti State University, Ado-Ekiti, Nigeria. Lifestyle modification strategies are still not widely accepted irrespective of educational status. Hence,a step-up of awareness campaigns and promotion of healthy lifestyle to improve the present level of knowledge and establish behavioural changes are needed.

Limitation of the Study

Since the data are cross-sectional, causal inference is weak, but hypotheses generated from it can be tested in other populations to obtain more definitive answers.

Authors' Contributions

DBF made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. RTH made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. JOF made substantial contributions to conception and design, acquisition, of data and was involved in revising the manuscript critically for important intellectual content. AEA made substantial contributions to conception and design, acquisition, of data and was involved in revising the manuscript critically for important intellectual content. OOD made substantial contributions to conception and design, acquisition, of data and was involved in revising the manuscript critically for important intellectual content. ADD made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. DSA made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. AOA made substantial contributions to conception and design, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important intellectual content. OJA made substantial contributions to conception and design, acquisition, analysis and interpretation of data and was involved in drafting the manuscript and revising it critically for important

intellectual content. All authors read and approved the final manuscript.

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