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CARDIO-PULMONARY SYMPTOMS ASSOCIATED WITH METABOLIC SYNDROME AMONG SUB-SAHARA BLACK AFRICAN ADOLESCENTS – NIGERIANS: A FOLLOW-UP STUDY.

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Abstract: Background: Cardiopulmonary symptoms (CPS) may possibly reinforce the effect of metabolic syndrome (MetS) or vice versa. However, there is scanty data on the possible association between MetS and symptoms such as easy fatigability, chest pain, shortness of breath and heart disease among Black adolescents in sub-Sahara Africa
Objective: Metabolic syndrome is recognized as a cluster of three of five risk factors including obesity, hypertension, abnormally high levels of triglyceride (TG), dyslipidemia (abnormally high concentrations of total cholesterol (TC), low-density lipoprotein (LDL) and an abnormally low level of high-density lipoprotein (HDL) and hyperglycemia. Its association with cardio-pulmonary symptoms is not well documented. There is dearth of scientific data focusing on MetS and its association with cardio-pulmonary symptoms among adolescents in sub-Saharan populations. This study, therefore, aimed at determining the prevalence and possible association of MetS and CPS among Black adolescents living in Lagos, Nigeria
Research design and methods: Six hundred and thirteen Secondary school students (age range: 10–19 years, both sexes) were recruited into this cross-sectional study, epidemiological. In addition to questionnaires which included cardio-pulmonary symptoms that were administered, anthropometric measurements (weight in kilograms, height, and waist circumferences in centimeters) were measured for each student. Fasting venous blood was aseptically collected and preserved for lipid profile and blood glucose assessments. Systolic and diastolic blood pressures were taken. MetS was assessed using appropriate diagnostic criteria for adolescents. NCSS 22 software was used for data analysis.
Results: A total of 613 Secondary School students aged between 10 and 19 years (mean (±sd) age:14.7 (2.1) yrs. were included. The BMI (Kg/m2) of girls was significantly higher (t-test=-2.22, P-value=0.03) than that of boys. Though overweigh/obese students were significantly younger (t-test=4.02, P-value=0.0002), their systolic blood pressure was significantly higher (t-test=-3.32, P-value=0.002) than that of lean subjects. Girl's waist circumference status (χ^2=7.13, P-value=0.008) and high systolic blood pressure (χ^2=8.00, P-value=0.005) were significantly higher among girls than among boys. Height (cm) (t-test = -2.03, P-value =0.047), weight (kg) t-test = -3.78, P-value = 0.0004), BMI (kg/m2) (t-test = -3.51, P-value = 0.0008), BMI-for-age percentile (t-test=-4.37, P-value = 0.00005) and waist circumference (t-test = -3.45, P-value = 0.001) were significantly higher in those with, than those without MetS. Pearson's correlation coefficient only shows strong association with MetS among study subjects with shortness of breath (r = 0.12, t = 3.01, P-value = 0.003, 95% CI: -0.04, 0.20). Girls who were easily fatigued were 1.27 times more likely to have MetS, whereas girls with chest pain (OR= 0.83, 95% CI=0.31, 2.19), shortness of breath (OR= 0.33, 95% CI=0.09, 1.15). The mean SBP of study participants with MetS who were easy fatigued was significantly higher (t-test=-2.51, P-value=0.02) than that of participants without MetS.
Conclusion: The study agrees that preventing the escalating burden of blood lipid and glucose abnormalities among Nigerian secondary school students is essential. Shortness of breath, which may be a precursor of hypertension, diabetes, and coronary heart disease, was significantly associated with MetS. Therefore, governments at Federal and State levels

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should consider appropriate interventions to curtail these early onset morbidities among adolescents. Clinicians should also be aware of them.

Keywords: Cardio-pulmonary symptoms, Metabolic syndrome, Diabetes, Adolescents, Sub-Sahara Africa

Introduction

Coronary heart disease has, as significant risk factors, abnormally high blood concentrations of LDL and non-high-density lipoprotein cholesterol [1]. Hyperlipidemia, a state of health in which LDL, TC, TG levels, or lipoprotein levels greater than the 90th percentile or HDL below the 10th percentile in comparison to the general population, is common in the Western world [2] and is now being observed as of public health significance in sub-Saharan Africa [3-8]. On the other hand, dyslipidemia refers to abnormalities in the plasma lipids which, quantitatively, reflects elevated levels of plasma TC, LDL-cholesterol, TG, and reduced HDL-cholesterol levels, occurring singly or in combinations or qualitatively, may suggest alterations in structure of LDL-C which includes small dense LDL-C, increased TG content or increased electronegativity of LDL-C [2]. While hypercholesterolemia may be due to primary, genetic or familial cause, or it may be of secondary or acquired causes [1], studies have shown that age is a vital risk factor for it irrespective of gender [9–11] and may go undetected among young people aged 18–25 years [12] and most probably among adolescents. The terminology "Metabolic syndrome" (MetS) is gradually gaining grounds in Africa mainly due to the observation of transition in dietary pattern from traditional African foods to western diet and also by sedentary lifestyle, among others. For example, Okafor [13] refers to MetS as "a constellation of interrelated risk factors of metabolic origin (metabolic risk factors) that appear to directly promote the development of atherosclerotic cardiovascular disease. Studies have also shown that in adults, MetS, a cluster of symptoms, may increase the risk of developing cardiovascular diseases (CVDs) and type 2 diabetes mellitus [14] and may consists of obesity, high blood pressure, hyperglycemia, or insulin resistance [15], low levels of HDL-C and elevated TG levels [16]. Because MetS is linked with insulin resistance, chronic low-grade inflammation [15], as well as with oxidative stress [17] its evaluation by clinicians among patients is a useful tool the determination of disease progression, and prognosis. It is contended that, among children and adolescents, the concept of MetS is problematic to define due to on-going physiological changes throughout their growth and development, racial differences, and due to apparent the lack of cardiovascular events [18,19]. The number of clinical trials existing on this cohort, especially in Africa, is very scarce, and therefore, a universal definition for children and adolescents does not exist thus far [18,19–21]. Symptoms are personal clinical findings generally reported by the patient during an interview a while taking a history from such patient.

The main symptoms accompanying cardiopulmonary disorders are cough, sputum production, hemoptysis, shortness of breath (dyspnea), and chest pain. Other less specific complaints include dizziness and fainting; ankle swelling (peripheral edema); fever, chills, and night sweats; snoring; personality changes; daytime somnolence (sleepiness); and gastric reflux. A study has hypothesized that MetS in individuals with lung function impairment is associated with increased cardiopulmonary morbidity and mortality [22]. Further, it has been reported that, low-grade systemic inflammation probably plays a role in the development of several chronic diseases, though, the importance of this low-grade inflammation for the progress, and prognosis of cardiopulmonary decompensation remains contentious [23, 24]. From this perspective, it is pertinent to explore the part played by MetS in association with not only low-grade systemic inflammation, obesity, and lung function but also with cardiopulmonary symptoms which may be precursors to cardiovascular disease which are outstanding causes of morbidity and mortality globally. There is a gaping void in the general knowledge of lipid anomalies among adolescents in Nigeria, which may be due to low access to information, lack of experts in the field, availability of equipment for lipid determination and cost. As a result, the current study is necessary. At the present time, studies on MetS and its link to other morbidities are conducted in a few geo-political zones and smaller sub-groups of

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Nigeria's population, mainly deriving data from the healthcare sources. Therefore, the current study calls for a national study of this disease among adolescents to prevent its occurrent in future adults. As MetS is now acknowledged to be a global public health burden and given the increasing prevalence of METs in the Nigerian population, there is a clear need for more studies so as to establish sex-specific, BMI-for-age specific and stage-of adolescence-specific reference point and cut-off values for estimating not only anthropometric indices for Africans but also the lipids, blood glucose, and other indices associated with MetS. Accordingly, the objective of this study was to explore the association of MetS and cardiopulmonary symptoms among a cohort of Nigerian Secondary School students.

Materials and Methods

This was a descriptive, epidemiological study involving 613 secondary school students in Lagos State, Nigeria, aged 10-19 years, from whom primary data was collected. Participants were recruited into the study which was conducted between October 2019 and March 2020. Ethical approval was given by the Nigerian Institute of Medical Research (IRB/18/062) after which documented informed consents were obtained from parents before the participants gave verbal agreement. The study was carried out according to the Helsinki Declaration (2000).

Study site: The study was carried out in Lagos State, Southwest Nigeria which lies on the Atlantic Ocean coastline, with a population of 20, million heterogenous people. Lagos city is the economic hub of Nigeria with seas port, international and domestic airports, modern infrastructures and five military barracks.

Sample size, sampling technique and procedure: The sample size was designed for a single population with 95% confidence interval [25], 54 % proportion, a margin of error 5%, and allowing for 12% non-response. To ensure that results of the study are representative of all Nigerian ethnic groups resident in Lagos State, the sample size would then be 650 students to cater for attrition and missing data. There are three Senatorial Districts – Lagos East, Lagos West and Lagos Central – with 5, 10 and 5 Local Government Areas respectively. Participants were recruited using simple random sampling, probability proportional to size and systematic sampling technique.

Inclusion and exclusion criteria. To be involved in the study, a student's age must be between 10 and 19 years, must be a registered and regular student in the school of study, must be Nigerian resident in the community of study for a minimum of 2 years. Those on therapeutic diet or drugs, and those on admissions to a health facility in previous 6 month were excluded from the study. Pregnancy, suspected pregnancy, breastfeeding, or use of oral contraceptive were also exclusion criteria.

Questionnaire: A part of the study involved administration of questionnaire of which responses to cardio-respiratory symptoms such as (i) gets tired easily (ii) chest pain (iii) finds it difficult to breath and (iv) has or a close relative has heart disease are relevant to this paper.

Measurements: Anthropometric measurements taken by trained field workers included body weight (to the nearest 0.1 kg, with minimal clothing and no shoes), height, and waist circumferences. Weight was measured using an electronic scale (FBS machine Model HBF-514C and DP scale HN-283); height was measured (no shoes) to the nearest millimeter using a portable stature meter (SURGILAC) and waist circumferences was measured to the nearest millimeter midway between the lowest rib and the iliac crest. World Health Organization (WHO) AnthroPlus V1.0.4 (Geneva, Switzerland) was used to calculate BMI-for-age and height-for-age percentiles for boys and girls separately [26]. Sex-specific categorization was used for BMI. Cut-offs available for Nigerian or African for waist circumference was 0.94 m for boys and 0.80 m for girls, no Nigeria- or Africa- specific limits being available for this age group. Blood pressure (upper arm) and pulse rate were measured after 30 min sitting using automatic blood pressure monitor for {Medical Instrument WUXI, Ltd, EN-BL-8030 [China]}. The average of three measurements was used. After overnight fasting, 5 ml of venous blood was taken and separated into fluoride oxalate tubes for fasting blood glucose (FBG) analysis, and into Lithium heparin tubes for lipids analyses. Both sets of tubes were stored at -20ºC before centrifuging for the production of plasma. Randox Glucose-PAP (Randox Laboratories, UK) reagent was used for analyzing FPG and lipid profile – total cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) –

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using a photo spectrometric analyzer (BioSystems EN ISO 13485 and EN ISO 9001 standards (Barcelona, Spain).

Statistical analysis: This has also been earlier reported. Briefly participants were segregated by sex (boys and girls), by BMI-for-age percentile (Lean or BMI <85th percentile and overweight/obese or BMI ≥85th percentile) and by stage of adolescence (early or 10-14.9 years of age; late or 15-19.9 years of age). The data was subjected to descriptive statistics, Analysis of variance, Chi-square with odds ratios and Spearman's correlation using NCSS version 22 (Kaysville, Utah, USA). Values were initially reported as mean (±) standard deviation (SD) and 95% CI for the continuous variables. Kolmogorov-Smirnov Normality test for normality of data distribution for continuous measures was conducted and when the test failed, Mann-Whitney U-test and Kruskal-Wallis one-way ANOVA were used to determine differences between 2 and 3 medians respectively. Independent Student's t-tests were used to identify differences in anthropometric measurements. MetS severity calculator [27], which considers the adolescent's height (cm), weight (kg), sex, serum triglyceride, HDL-C, fasting glucose, systolic blood pressure, and ethnicity (non-Hispanic, Black), was used to calculate continuous metabolic syndrome (cMetS) risk score for early occurrence of MetS. An unadjusted p-value <0.05 was considered statistically significant.

Definitions:

Dyslipidemia was defined as a combination of total cholesterol ≥200 mg/dL, low-density lipoprotein-cholesterol (LDL-C) ≥ 130 mg/dL, triglycerides (TG) ≥130 mg/dL, or high-density lipoprotein cholesterol (HDL-C) < 40 mg/dL [39, 40]. The NHLBI criteria specific for children and adolescents were used to identify MetS among participants aged 10 to 19 years [28]. This requires three or more of (i) BMI-for-age of ≥95th percentile; fasting plasma levels of (ii) TG ≥130 mg/dL; (iii) HDL-cholesterol <40 mg/dL; (iv) LDL-cholesterol ≥130 mg/dL; (v) total cholesterol ≥200 mg/dL; (vi) glucose ≥100mg/dL; (vi) pre-hypertension as Systolic/Diastolic BP (SBP/SDP) 120-129/ <80 mmHg, stage 1 hypertension, BP 130-139/80-89, and stage 2 ≥140/90 mmHg [29]. However, for the purpose of this study, BMI-for-age percentile, fasting plasma levels of glucose, triglycerides, and total cholesterol were the variables taken for the assessment of MetS. Subjects with BMI for age <85th and ≥85th percentile were classified as lean, overweight/obese respectively using the BMI age chart [30]. Fasting blood glucose (FPG) of <70mg/dL, 70-<100 mg/dL, 100-125.9 mg/dL and ≥126mg/dL were taken as low, normal, impaired, pre-diabetic and diabetic [31].

Results

Mean values of waist circumference, systolic and diastolic blood pressures and median value of fasting blood glucose and lipid profiles – Table 1.

Table 1. Mean values of waist circumference, systolic and diastolic blood pressures and median value of fasting blood glucose and lipid profiles relative to sex, BMI—for-age percentile, and stages of adolescence of secondary school students in Lagos, Nigeria, 2019–20

Variable	All (n=613)	Sex		t-test or MW U (P-value)	BMI-for-age percentile		t-test or MW U (P-value)	Stages of adolescence		t-test or MW U (P-value)
		Boys (n=236)	Girls (n=377)		Lean (n=563)	O/O (n=50)		Early (n=297)	Late (n=316)	
Mean (±sd)										
Age (years)	14.7 (2.1)	14.8 (2.2)	14.6 (2.1)	1.11 (0.27)	14.8 (2.1)	13.5 (2.2)	4.02 (0.0002)	12.9 (1.3)	16.4 (1.2)	-34.57 (<0.00001)
Weight (Kg)	47.4 (11.6)	46.5 (12.4)	47.9 (11.1)	-1.42 (0.16)	45.8 (10.1)	65.6 (12.2)	-11.1 (<0.00001)	45.3 (11.6)	49.3 (11.4)	-4.30 (0.00002)

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Height (cm)		156.7 (12.3)	157.7 (12.9)	156.0 (11.9)	1.64 (0.10)	156.8 (10.7)	154.6 (24.3)	0.63 (0.53)	154.3 (13.4)	158.9 (10.8)	-4.66 (<0.0000 1)
BMI (Kg/m^2)		19.2 (4.3)	18.7 (4.5)	19.5 (4.1)	-2.22 (0.03)	18.5 (3.3)	27.0 (6.0)	-9.89 (<0.0000 1)	18.8 (3.6)	19.6 (4.8)	-2.34 (0.02)
Waist circumference		65.4 (6.7)	64.9 (6.7)	65.7 (6.7)	-1.44 (0.15)	64.5 (5.5)	76.1 (9.6)	-8.42 (<0.0001)	64.7 (7.2)	66.0 (6.2)	-2.39 (0.02)
Blood Pressure (mm Hg)	Systolic	108.2 (12.4)	108.5 (13.9)	108.1 (11.4)	0.37 (0.71)	107.8 (12.4)	113.6 (11.8)	-3.32 (0.002)	106.7 (12.4)	109.6 (12.3)	-2.91 (0.004)
	Diastolic	66.2 (9.6)	65.0 (10.4)	66.9 (9.1)	-2.31 (0.02)	65.8 (9.5)	70.8 (9.7)	-3.50 (0.0009)	65.5 (9.4)	66.8 (9.8)	-1.68 (0.09)
Median											
Fasting	FBG	87.3	89.3	86.1	0.63 (0.53)	87.3	87.4	0.31 (0.76)	87.6	86.9	0.54 (0.59)
	TC	199.3	204.1	197.9	0.74 (0.46)	198.7	221.2	1.14 (0.25)	207.1	196.2	1.94 (0.05)
	TG	181.4	185.4	181.4	0.81 (0.41)	181.4	189.3	0.34 (0.73)	171.7	193.6	-2.49 (0.01)
	HDL	55.7	54.0	56.4	-0.64 (0.52)	55.5	57.4	0.14 (0.89)	56.5	55.1	1.18 (0.24)
	LDL	291.1	267.7	295.7	-3.03 (0.002)	290.0	303.8	0.43 (0.66)	295.7	278.4	1.80 (0.07)

Table 1 illustrates the general anthropometric characteristics of the study subjects based on sex (boys: 236, 38.5%, girls; 377, 61.5%), BMI-for-age percentile (Lean: 563, 91.8%; Overweight/Obese: 50, 8.2%) and stage of adolescence (Early: 297, 48.4%; Late: 316, 51.6%). The overall means (±sd) of age (years), weight (kg), height (cm), BMI (kg/m2) and waist circumference (cm) are as shown in the Table. Overweight/Obese subjects were significantly younger (t-test = 4.02, P-value = 0.0002) than lean subjects. The mean BMI (kg/m^2) of girls was significantly heavier (t-test = -2.22, P-value = 0.03) than that of boys. As expected, the means of all anthropometric indices of overweight/obese subjects and of those in late adolescence were significantly higher than those of the lean subjects and those in early adolescence respectively. Further, mean systolic blood pressure of overweight/obese was significantly higher (t-test = -3.32, P-value = 0.002) than that of lean subjects and that of students in late adolescence was also significantly higher (t-test = -2.91, P-value = 0.004) than those in early adolescence. While there was no significant change in the median value of FBG relative to sex, BMI-for-age percentile and stage of adolescence, the difference in the median value of TC of those in early adolescence (207.1 mg/dL) was marginally significant ((Mann-Whitney U = 1.94, P-value = 0.05) compared to that of students in late adolescence (196.2 mg/dL). On the other hand, the median TG level of late adolescents (193.6 mg/dL) was significantly higher (Mann-Whitney U-2.49, P-value = 0.01) than that of those in early adolescents. Median value of LDL among girls (295.7 mg/dL) was also significantly higher (Mann-Whitney U = -3.03, P-value = 0.002) than the values for boys (267.7 mg/dL).

Distribution of metabolic syndrome components by sex. Table 2.

Table 2. Distribution of metabolic syndrome components by sex

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Variables		Sub-variables	Sex		χ^2	P-values
			Boys (n=236)	Girls (n=377)		
Waist circumference		Normal	235 (99.6)	360 (95.5%)	7.13*	0.008!
		High	1 (0.4)	17 (4.5%)		
BMI-for-age percentile		Normal	213 (90.6)	336 (89.1)	0.20	0.66
		High	23 (9.4)	41 (10.9)		
Systolic Blood Pressure		Normal	181 (76.7)	323 (80.9)	8.00	0.005!
		High	55 (23.3)	54 (19.1)		
Fasting Blood Glucose		Normal	165 (69.9)	259 (68.7)	0.10	0.75
		High	71 (30.1)	118 (31.3)		
Dyslipidemia status	Total cholesterol	Normal	97 (41.1)	147 (39.0)	0.27	0.60
		High	139 (58.9)	230 (61.0)		
	Triglyceride	Normal	84 (35.6)	121 (32.1)	0.80	0.37
		High	152 (64.4)	256 (67.9)		
	High-density lipoprotein	Normal	134 (56.8)	212 (56.2)	0.02	0.89
		Low	102 (43.2)	165 (43.8)		
	Low-density lipoprotein	Normal	22 (9.3)	25 (6.6)	1.48	0.22
		High	214 (90.7)	352 (93.4		

**Fisher's Exact Test; !=statistically significant*

Table 2 compares the various components of MetS syndrome among boys and girls. High waist circumference status (χ^2=7.13, P-value=0.008) and high systolic blood pressure (χ^2=8.00, P-value=0.005) were significantly higher among girls than among boys. The prevalence of dyslipidemia in both boys and girls was identical.

Anthropometric characteristics of study subjects with and without metabolic syndrome - Table 3.

Table 3. Anthropometric characteristics of study subjects with and without metabolic syndrome

Variables	MetS <90th percentile			Mets ≥90th percentile			Comparing <90th and ≥90th percentile					
	Sex											
	All	**Boys**	**Girls**	**All**	**Boys**	**Girls**	**All**		**Boys**		**Girls**	
n (%)	561 (91.5)	202 (36.0)	359 (64.0)	52 (8.5)	34 (65.4)	18 (34.6)						
	Mean (±sd)						t-test	P-value	t-test	P-value	t-test	P-value
Age (yrs.)	14.7 (2.1)	14.8 (2.2)	14.7 (2.1)	14.4 (2.2)	14.4 (2.2)	14.5 (2.4)	0.94	0.35	0.98	0.33	0.35	0.73
Height (cm)	156.4 (12.5)	157.2 (13.3)	155.9 (12.1)	159.3 (9.6)	160.3 (10.7)	157.4 (7.1)	-2.03	0.047	-1.51	0.14	-0.84	0.41
Weight (Kg)	46.8 (11.4)	45.9 (12.6)	47.3 (10.7)	53.5 (12.3)	50.1 (11.1)	60.0 (12.2)	-3.78	0.0004	-2.00	0.05	-4.33	0.0004

BMI (Kg/m^2)	19.0 (4.3)	18.5 (4.7)	19.3 (4.0)	21.0 (3.9)	19.5 (2.9)	23.8 (4.1)	-3.51	0.0008	-1.67	0.10	-4.55	0.0002
BMI-for-age percentile.	36.3 (29.6)	31.5 (28.4)	39.1 (30.0)	57.3 (33.5)	48.3 (33.9)	74.1 (26.0)	-4.37	0.00005	-2.73	0.009	-5.53	0.00002
WC (cm)	65.0 (6.3)	64.5 (6.3)	65.3 (6.4)	69.4 (9.0)	67.5 (8.2)	73.2 (9.5)	-3.45	0.001	-2.03	0.048	-3.49	0.003
	Anthropometric status											
	All	**Lean**	**O/O**	**All**	**Lean**	**O/O**	**All**		**Lean**		**O/O**	
n (%)	561 (91.5)	524 (93.4)	37 (6.6)	52 (8.5)	39 (75.0)	13 (25.0)						
	Mean (±sd)						t-test	P-value	t-test	P-value	t-test	P-value
Age (yrs.)	14.7 (2.1)	14.8 (2.1)	13.8 (2.2)	14.4 (2.2)	15.0 (2.0)	12.7 (2.1)	0.94	0.35	-0.60	0.55	1.60	0.12
Height (cm)	156.4 (12.5)	156.6 (10.7)	153.1 (27.7)	159.3 (9.6)	159.4 (10.0)	158.8 (8.5)	-2.03	0.047	-1.62	0.11	-1.11	0.27
Weight (Kg)	46.8 (11.4)	45.4 (10.1)	66.2 (12.0)	53.5 (12.3)	50.0 (10.0)	63.9 (13.1)	-3.78	0.0004	-2.77	0.008	0.56	0.58
BMI (Kg/m^2)	19.0 (4.3)	18.4 (3.3)	27.5 (6.7)	21.0 (3.9)	19.5 (2.7)	25.6 (3.5)	-3.51	0.0008	-2.41	0.02	1.29	0.20
BMI-for-age percentile.	36.3 (29.6)	32.8 (26.4)	86.8 (26.7)	57.3 (33.5)	44.2 (28.3)	96.5 (3.2)	-4.37	0.00005	-2.44	0.02	-2.17	0.04
WC (cm)	65.0 (6.3)	64.3 (5.4)	75.2 (9.2)	69.4 (9.0)	66.3 (5.9)	78.8 (10.5)	-3.45	0.001	-2.05	0.046	-1.10	0.29
	Stage of adolescence											
	All	**Early**	**Late**	**All**	**Early**	**Late**	**All**		**Early**		**Late**	
n (%)	561 (91.5)	273 (48.7)	288 (51.3)	52 (8.5)	24 (46.2)	28 (53.8)						
	Mean (±sd)						t-test	P-value	t-test	P-value	t-test	P-value
Age	14.7 (2.1)	13.0 (1.3)	16.4 (1.2)	14.4 (2.2)	12.4 (1.3)	16.2 (1.0)	0.94	0.35	2.17	0.04	0.99	0.33
Height	156.4 (12.5)	154.0 (13.6)	158.7 (11.0)	159.3 (9.6)	157.9 (10.3)	160.5 (9.0)	-2.03	0.047	-1.73	0.09	-0.99	0.33
Weight	46.8 (11.4)	44.6 (11.1)	48.9 (11.4)	53.5 (12.3)	52.5 (14.6)	54.3 (10.3)	-3.78	0.0004	-2.59	0.02	-2.62	0.01
BMI	19.0 (4.3)	18.6 (3.4)	19.5 (4.9)	21.0 (3.9)	21.0 (4.4)	21.0 (3.6)	-3.51	0.0008	-2.60	0.02	-2.03	0.049

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BMI-for-age percentile.	36.3 (29.6)	42.3 (31.0)	30.7 (27.1)	57.3 (33.5)	67.1 (34.7)	48.9 (30.6)	-4.37	0.00005	-3.38	0.002	-3.03	0.005
WC (cm)	65.0 (6.3)	64.4 (6.6)	65.7 (6.0)	69.4 (9.0)	69.1 (10.8)	69.7 (7.4)	-3.45	0.001	-2.10	0.046	-2.77	0.009

O/O=overweight/obese

Table 3 shows the anthropometric characteristics of the study subjects according to the presence (MetS ≥90th percentile) or absence (MetS <90th percentile) of MetS and relative to sex (boys and girls), anthropometric status (lean and overweight/obese) and stage of adolescence (early and late) in Lagos, Nigeria. Study subjects with MetS had significantly higher means of height (cm) (159.3±9.6 vs 156.4±12.5 cm; t-test = -2.03, P-value =0.047), weight (Kg) (53.5±12.3 vs 46.8±11.4; t-test = -3.78, P-value = 0.0004), BMI (Kg/m^2) (21.0±3.9 vs 19.0±4.3; t-test = -3.51, P-value = 0.0008), BMI-for-age percentile (57.3±33.5 vs 36.3±29.6; t-test=-4.37, P-value = 0.00005) and waist circumference (69.4±9.0 vs 65.0±6.3; t-test = -3.45, P-value = 0.001) than those without MetS. These differences are also generally reflected in the domains of sex, anthropometric status and in the different stages of adolescence. There was no notable variation in the waist circumference of overweight and obese subjects with and those without MetS.

Analysis of possible association between common cardio-pulmonary symptoms and metabolic syndrome among adolescents – Table 4.

Table 4. Analysis of possible association between common cardio-pulmonary symptoms and metabolic syndrome among adolescents.

Metabolic syndrome status		Easy fatigability		Has chest pain		Shortness of breath		Has or a close relative has heart disease	
		Yes	No	Yes	No	Yes	No	Yes	No
Metabolic syndrome percentile	All	296 (48.3)	317 (51.7)	266 (43.4)	347 (56.6)	227 (37.0)	386 (63.0)	82 (13.4)	531 (86.6)
	<90th	272 (91.9)	289 (91.2)	244 (91.7)	317 (91.4)	217 (95.6)	344 (89.1)	79 (96.3)	482 (90.8)
	≥90th	24 (8.1)	28 (8.8)	22 (8.3)	30 (8.6)	10 (4.4)	42 (10.9)	3 (3.7)	49 (9.2)
χ^2 (P-value)		0.10 (0.75)		0.03 (0.87)		7.71 (0.005)		2.17 (0.14)*	
OR (95% CI)		0.91 (0.52, 1.61)		0.95 (0.54, 1.69)		0.38 (0.19, 0.77)		0.37 (0.11, 1.23)	
RR (95% CI)		0.92 (0.2, 1.55)		0.96 (0.67, 1.62)		0.40 (0.21, 0.79)		0.40 (0.3, 1.24)	
Pearson's correlation (r)		0.01		0.003		0.12		0.08	
t (P-value)		0.29 (0.77)		0.06 (0.95)		3.01 (0.003)		1.90 (0.05)	
95% CI		0.07, 0.09		- 0.08, 0.08		-0.04, 0.20		-0.003, 0.16	

*Fisher's Exact Test

Table 4 presents possible association between common cardio-pulmonary symptoms and MetS among the study subjects. Of the 613 respondents, 296 (48.3%), 266 (43.4%), 227 (37.0%) and 82 (13.4) respectively reported easy fatigability, chest pain, shortness of breath and has or a close relative has heart disease. Of those that reported easy fatigability, 24 (8.1%) were categorized as having MetS, while 8.3%, 4.4% and 3.7% of those with chest pain, shortness of breath and those who had or had a close relative has heart disease were categorized as having MetS. However, Pearson's correlation coefficient only shows strong association with MetS among study subjects with shortness of breath (r = 0.12, t = 3.01, P-value = 0.003, 95% CI: -0.04, 0.20).

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Cardio-pulmonary symptoms by severity of Metabolic Syndrome, relative to gender, anthropometry, and stage of adolescence. Table 5.

Table 5. Cardio-pulmonary symptoms by severity of Metabolic Syndrome, relative to gender, anthropometry, and stage of adolescence.

	Easy fatigability		Has chest pain. (Chest pain)		Shortness of breath (Dyspnea)		Has or a close relative has heart disease.	
	MetS <90th percentile (n=561, 91.5%)							
	Yes (n=272)	No (n=289)	Yes (n=244)	No (n=317)	Yes (n=217)	No (n=344)	Yes (n=79)	No (n=482)
Girls	178 (65.4)	181 (62.6)	156 (63.9)	203 (64.0)	136 (62.7)	223 (64.8)	41 (51.9)	318 (66.0)
Boys	94 (34.6)	108 (37.4)	88 (36.1)	114 (36.0)	81 (37.3)	121 (35.2)	38 (48.1)	164 (34.0)
χ^2 (P-value)	0.48 (0.49)		0.0006 (0.98)		0.27 (0.61)		5.83 (0.02)	
OR (95% CI)	1.13 (0.80, 1.60)		1.00 (0.70, 1.41)		0.91 (0.64, 1.30)		0.56 (0.34,0.90)	
Lean	256 (94.1)	268 (92.7)	231 (96.7)	293 (92.4)	202 (93.1)	322 (93.6)	76 (96.2)	448 (92.9)
Overweight/Obese	16 (5.9)	21 (7.3)	13 (3.3)	24 (7.6)	15 (6.9)	22 (6.4)	3 (3.8)	34 (7.1)
χ^2 (P-value)	0.43 (0.51)		1.12 (0.29)		0.06 (0.81)		0.70 (0.40)*	
OR (95% CI)	1.25 (0.64, 2.46)		1.46 (0.73, 2.92)		0.92 (0.47, 1.82)		1.92 (0.58, 6.42)	
Early adolescence	139 (51.1)	134 (46.4)	121 (49.6)	152 (47.9)	114 (52.5)	159 (46.2)	32 (40.5)	241 (50.0)
Late adolescence	133 (48.9)	155 (53.6)	123 (50.4)	165 (52.1)	103 (47.5)	185 (53.8)	47 (59.5)	241 (50.0)
χ^2 (P-value)	1.26 (0.26)		0.15 (0.70)		2.12 (0.14)		2.44 (0.12)	
OR (95% CI)	1.21 (0.87, 1.68)		1.07 (0.76, 1.49)		1.29 (0.92, 1.81)		0.68 (0.42, 1.10)	
	MetS ≥90th percentile (n=52, 8.5%)							
	Yes (n=24)	No (n=28)	Yes (n=22)	No (n=30)	Yes (n=10)	No (n=42)	Yes (n=3)	No (n=49)
Girls	10 (41.7)	8 (28.6)	7 (31.8)	11 (36.7)	3 (30.0)	15 (35.7)	1 (33.3)	17 (34.7)
Boys	14 (58.3)	20 (71.4)	15 (68.2)	19 (63.3)	7 (70.0)	27 (64.3)	2 (66.7)	32 (65.3)
χ^2 (P-value)	0.96 (0.33)		0.13 (0.72)		0.00 (1.00)		0.00 (1.00) *	
OR (95% CI)	1.79 (0.56, 5.66)		0.81 (0.25, 2.58)		0.77 (0.17, 3.43)		0.94 (0.08, 11.14)	
Lean	19 (79.2)	20 (71.4)	18 (81.8)	21 (70.0)	7 (70.0)	32 (76.2)	2 (66.7)	37 (75.5)
Overweight/Obese	5 (20.8)	8 (28.6)	4 (19.2)	9 (30.0)	3 (30.0)	10 (23.8)	1 (33.3)	12 (24.5)
χ^2 (P-value)	0.10 90.750		0.42 (0.52)		0.00 (1.00)		0.00 (1.00) *	
OR (95% CI)	1.52 (0.42, 5.47)		1.93 (0.51, 7.33)		0.73 (0.16, 3.36)		0.65 (0.05, 7.80)	
Early adolescence	7 (29.2)	17 (60.7)	8 (36.4)	16 (53.3)	6 (60.0)	18 (42.9)	1 (33.3)	23 (46.9)
Late adolescence	17 (70.8)	11 (39.3)	14 (63.6)	14 (46.7)	4 (40.0)	24 (57.1)	2 (66.7)	26 (53.1)
χ^2 (P-value)	5.08 (0.02)		1.44 (0.23)		0.39 (0.53)		0.00 (1.00) *	
OR (95% CI)	0.27 (0.08, 0.85)		0.50 (0.16, 1.54)		2.00 (0.49, 8.15)		0.57 (0.05, 6.65)	
Comparing MetS <90th and MetS ≥90th percentile								

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Girls	χ^2 (P-value)	0.24 (0.62)	0.15 (0.70)	2.47 (0.12)*	0.15 (0.70)*
	OR (95% CI)	1.27 (0.49, 3.29)	0.83 (0.31 2.19)	0.33 (0.09, 1.15)	0.46 (0.06, 3.52)
Boys	χ^2 (P-value)	0.34 (0.56)	0.004 (0.95)	4.72, 0.03)	2.60 (0.11)*
	OR (95% CI)	0.80 (0.38, 1.68)	1.02 (0.49, 2.13)	0.39 (0.16, 0.93)	0.27 (0.06, 1.17)
Lean	χ^2 (P-value)	0.003 (0.99)	0.06 (0.80)	6.59 (0.01)	1.95 (0.16)*
	OR (95% CI)	1.00 (0.52, 1.91)	1.09 (0.57, 2.09)	0.35 (0.15, 0.80)	0.31 (0.08, 1.35)
O/O	χ^2 (P-value)	0.00 (1.00)	0.00 (1.00)*	0.63 (0.43)*	0.00 (1.0)
	OR (95% CI)	0.82 (0.23, 2.99)	0.82 (0.21, 3.19)	0.44 (0.10, 1.87)	0.94 (0.09, 9.97)
Early	χ^2 (P-value)	4.16 (0.04)	1.08 (0.30)	2.56 (0.11)	0.62 (0.43)*
	OR (95% CI)	0.40 (0.16, 0.99)	0.63 (0.26, 1.52)	0.46 (0.18, 1.21)	0.33 (0.04, 2.51)
Late	χ^2 (P-value)	2.15 (0.14)	0.55 (0.46)	4.34 (0.04)*	1.01 (0.31)*
	OR (95% CI)	1.80 (0.81, 3.98)	1.34 (0.62, 2.92)	0.30 (0.10, 0.89)	0.39 (0.09, 1.72)

Comparing those with and those without MetS, girls who were easily fatigued were 1.27 times more likely to have MetS, whereas girls with chest pain (OR= 0.83, 95% CI=0.31, 2.19), shortness of breath (OR= 0.33, 95% CI=0.09, 1.15) or those who had or a close relative had heart disease (OR= 0.46, 95% CI=0.06, 3.52) were 0.83, 0.33 and 0.46 less likely to belong to the group with MetS. Boys with chest pain were 1.02 times more likely to be having MetS (OR 1.02, 95% CI=0.49,2.13) while boys with easy fatigability, shortness of breath and those with heart disease or with a close relative that has heart disease were not likely to belong to the cohort with MetS. Lean subjects with chest pain were 1.09 times more likely to have MetS (OR1.09, 95% CI=0.57, 2.09) while those with dyspnea or heart disease (with a close relative that has heart disease) were not likely to be categorized as having MetS. Incidentally, no obese subject or anyone in early adolescence fell into metabolic syndrome category regardless of any cardio-pulmonary symptom.

Clinical and biochemical characteristics of study subjects according to degree of Metabolic Syndrome and relative to cardio-pulmonary symptoms – Table 6, Figures 1a- 1e.

Table 6. Clinical and biochemical characteristics of study subjects according to degree of Metabolic Syndrome and relative to cardio-pulmonary symptoms.

Cardio-pulmonary symptom	Metabolic syndrome	Freq. (%)	Blood pressure (mm Hg)		Fasting levels (mg/dL)				
			Systolic	Diastolic	Blood Glucose	Total cholesterol	Triglyceride	Low-density Lipoprotein	High-density lipoprotein

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	percentile		Mean (±sd)		Median				
Gets tired easily. (n=296, 48.3%)	<90th	272 (91.9)	107.6 (12.8)	65.5 (9.1)	85.0	204.6	186.8	279.2	58.6
	≥90th	24 (8.1)	113.8 (11.5)	67.2 (11.0)	119.9	170.3	250.5	321.1	33.9
	t-test (P-value)		-2.51 (0.02)	-0.74 (0.47)	-	-	-	-	-
	Mann-Whitney (P-value)		-	-	5.7 (<0.0001)	-2.11 (0.04)	2.76 (0.006)	0.26 (0.79)	-4.51 (0.00001)
Has chest pain. (n=266, 43.4%)	<90th	244 (91.7)	108.7 (12.1)	66.5 (9.3)	83.2	200.5	183.8	279.8	58.4
	≥90th	22 (8.3)	110.9 (10.7)	66.0 (10.9)	119.9	159.4	274.9	313.6	31.6
	t-test (P-value)		-0.91 (0.37)	0.21 (0.84)	-	-	-	-	-
	Mann-Whitney (P-value)		-	-	5.10 (<0.0001)	2.38 (0.02)	2.91 (0.004)	0.29 (0.76)	-4.77 (<0.00001)
Shortness of breath. (n=227, 37.0%)	<90th	217, (95.6)	109.1 (12.4)	66.7 (9.0)	83.3	206.2	179.5	290.1	59.9
	≥90th	10 (4.4)	111.4 (13.0)	67.7 (13.6)	141.6	196.3	181.2	325.9	35.3
	t-test (P-value)		-0.55 (0.60)	-0.23 (0.82)	-	-	-	-	-
	Mann-Whitney (P-value)		-	-	3.77 (0.0002)	-0.53 (0.60)	0.44 (0.66)	-0.11 (0.92)	-2.89 (0.004)
Has or a close relative that has heart disease. (n=63, 10.3%)	<90th	60 (95.2)	109.3 (13.8)	66.2 (9.1)	86.1	212.8	191.9	281.8	59.4
	≥90th	3 (4.8)	112.7 (8.4)	68.3 (0.6)	93.9	276.1	500.0	127.9	21.1
	t-test (P-value)		-0.66 (0.56)	-1.71 (0.09)	-	-	-	-	-
	Mann-Whitney (P-value)		-	-	0.43 (0.67)	0.51 (0.61)	2.58 (0.01)	-1.15 (0.25)	-2.11 (0.03)

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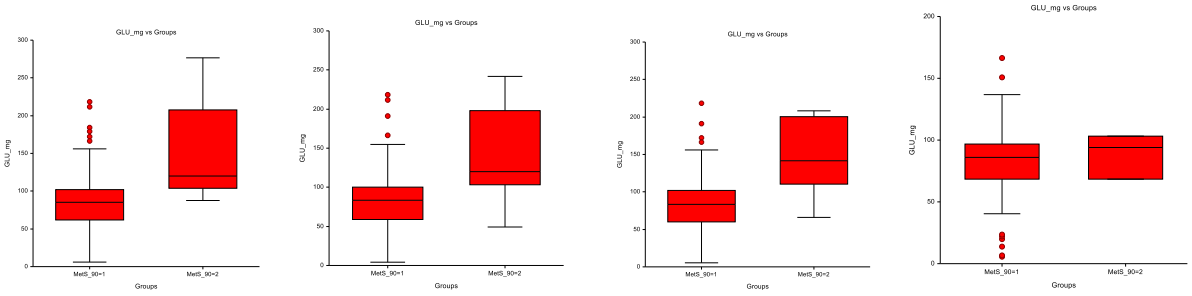
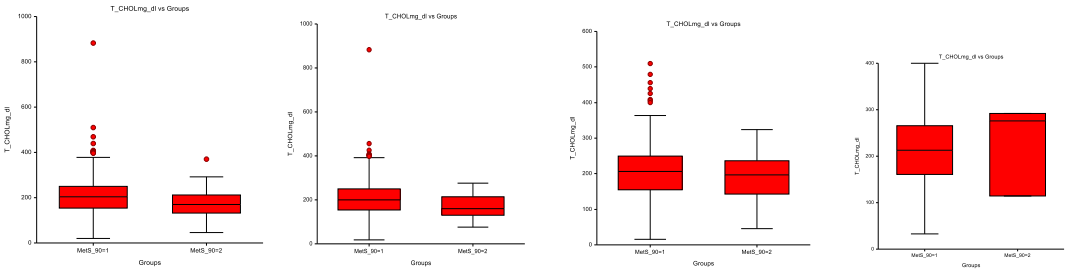


Z=5.71, P<0.000001 Z=5.10, P<0.000001 Z=3.77, P-0.0002 Z=0.43, P=0.67

(i) Gets tired easily (ii) Has chest pain (iii) Finds it difficult to breath (iv) Has or a relative has heart disease

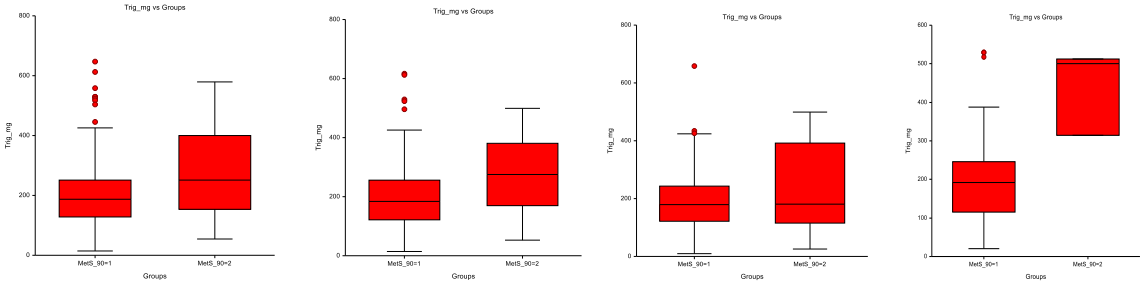
Figure 1a (i-iv). Fasting Blood Glucose analysis



Z = -2.11, P=0.04 Z = -2.38, P=0.02 Z= -0.53, P=0.60 Z=0.51, P=0.61

(i) Gets tired easily (ii) Has chest pain (iii) Finds it difficult to breath (iv) Has or a relative has heart disease

Figure 1b (i-iv). Fasting Total Cholesterol analysis



Z=2.76, P=0.006 Z=2.91, P=0.004 Z=0.44, P=0.66 Z=2.58, P=0.01

(i) Gets tired easily (ii) Has chest pain (iii) Finds it difficult to breath (iv) Has or a relative has heart disease

Figure 1c (i-iv). Fasting Triglyceride analysis

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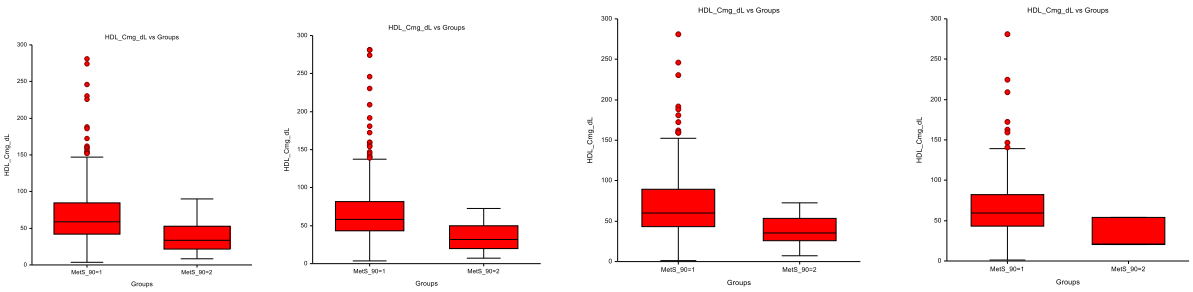
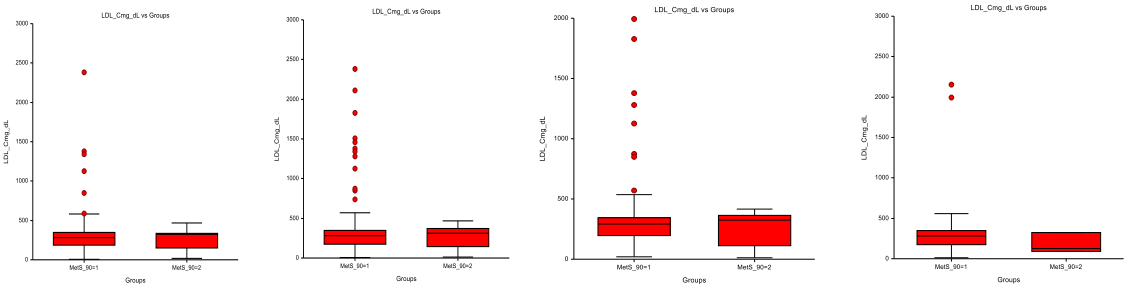


Z=-4.51, P-0.00001 Z = -4.77, P<0.00001 Z= -2.89, P=0.004 Z= -2.11, P=0.03

(i) Gets tired easily (ii) Has chest pain (iii) Finds it difficult to breath (iv) Has or a relative has heart disease

Figure 1d (i-iv). Fasting High-density lipoprotein analysis



Z=0.26, P=0.79 Z=0.29, P=0.76 Z= -0.11, P=0.92 Z= *1.15, P=0.25

(i) Gets tired easily (ii) Has chest pain (iii) Finds it difficult to breath (iv) Has or a relative has heart disease

Figure 1e (i-iv). Fasting Low-density lipoprotein analysis

The mean SBP of study participants who were easily fatigued and who had MetS was significantly higher (t-test=-2.51, P-value=0.02) than that of participants without MetS. The median FBG (119.9 vs 85.0 mg/dL), TC (170.3 vs 204.6 mg/dL), TG (250.5 vs 186.8 mg/dL), LDL (321.1 vs 279.2 mg/dL), and HDL (33.9 vs 58.6 mg/dl) levels of study subjects with easy fatigability were significantly higher among those with MetS compared with those without MetS. However, among those with chest pain and those with shortness of breath, the median LDL levels in subjects with and without MetS were unimportant. These data are corroborated with the illustrations expressed in Figures 1a-1e.

Discussion

A vast array of clinical trials and studies in adults, but very few among adolescents, has consistently demonstrated that elevated levels of LDL cholesterol increase a person's risk for the development of atherosclerotic plaques and subsequent vascular disease. On the other hand, HDL-cholesterol supports the regulation of cholesterol levels to avoid imbalances that would otherwise elevate the risk of atherosclerotic vascular disease. Although, participants in this study recorded high level of LDL, there was no significant difference in its level among those with MetS who presented with various cardiopulmonary symptoms. The scenario is different from adults among whom hypercholesterolemia is more common with increased risk of cardiovascular diseases. In the present study with 631 Secondary School students from Lagos State, we found that the metabolic syndrome was significantly associated

with shortness of breath or dyspnea. The most possible explanation for why MetS is linked with dyspnoea may be related to the various components of MetS which include high levels of FBG, TC, TG, LDL, and low level of HDL – all of which are risk factors for atherosclerotic cardiovascular disease [32]. It has been argued that since triglycerides can be degraded by most cells, but cholesterol cannot be degraded by any, the cholesterol content of triglyceride-rich lipoproteins – referred to remnant cholesterol – is more likely to be the cause of atherosclerosis and cardiovascular disease rather than raised triglycerides per se [32]. Incidentally, the mean TG levels of participants with shortness of breath among those with and those without MetS was not statistically significant but the mean FBG and mean HDL were statistically. Probably it is cholesterol, not triglycerides, that gathers in intimal foam cells and in atherosclerotic plaques, and remnant lipoproteins just like LDL can enter the arterial intima, especially in the pulmonary tissue, causing shortness of breath. However, the role of high blood glucose in this pathway is not clear. It was initially thought that dyslipidemia was rare in Black Africa, including Nigeria as earlier reports advocated lower prevalence among Blacks in general probably as a result of genetic, nutritional, and environmental factors [33]. An older study reported that protective HDL-cholesterol was significantly higher in Tropical Africa [34] similar to reports showing that populations with increased intake of fish and marine mammals have high levels of HDL-C [2]. The present study hints at the downward trend of health among Nigerian adolescents, consistent with other studies [35–39]. Hence, suitable intervention is urgently required to prevent the burden of unwanted and adverse health state on the individual as well as the health system in Nigeria.

Study limitations:

There are certain limitations in this study that need clarification. There may have been a bias in the sample size because the exact prevalence used in calculating the sample size was assumed. Therefore, the sample size would have been smaller or bigger than necessary. The study was conducted in Southwest Nigeria on the Atlantic Ocean coastline and did not take into consideration other ecological zones in the country. Thus, the study was skewed towards this ethnic group in urban setting.

Conclusion and recommendations

In conclusion, in the student population of a low-income country, the presence of the metabolic syndrome was associated with shortness of breath, a novel finding, in individuals with metabolic syndrome.

Conflict of interest

The authors declare no competing interest

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