Relationship Between Microalbuminuria and Risk Factors for Cardiovascular Diseases Among Secondary School Student in Ilorin, Nigeria

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ABSTRACT

Introduction: Globally, cardiovascular diseases (CVDs) are the leading causes of deaths with more than half due to coronary heart disease linked with the development of atherosclerosis. Hypertension (HTN) and obesity are leading risk factors for atherosclerotic CVDs, presence of which is predicted by microalbuminuria (MA). We wanted to evaluate the relationship between microalbuminuria and risk factors for CVDs (obesity, overweight, pre-hypertension and hypertension) among secondary school students in Ilorin, North central Nigeria.

Methods: We conducted a descriptive, cross-sectional study from December 2017 to March 2018 among secondary school students. We recruited 584 students, aged 10 to 18 years from 14 schools across the three Local Government Areas (LGAs) in Ilorin. We measured their blood pressure and anthropometrics following standard protocols and determined microalbuminuria in their early morning urine using Microalbumin 2-1 Combo strip and spot urinary albumin - creatinine ratio.

Results: The prevalence of MA was 30.1%. MA was more common in obese and hypertensive adolescents ($p < 0.001$ and $p < 0.01$ respectively). Occurrence of MA correlated strongly with subject's weight ($r = 0.790$, $p = 0.004$, $p < 0.01$); systolic blood pressure ($r = 0.884$, $p = 0.001$, $p < 0.01$) and body mass index ($r = 0.710$, $p = 0.001$, $p < 0.01$). Independent predictors of MA were obesity, adjusted odds ratio (aOR) 4.9, (95% CI 1.124, 20.913), overweight (aOR 3.6, 95% CI 1.184, 10.174), older age (aOR 1.1, 95% CI 1.007, 1.219) and presence of systolic hypertension (aOR 3.1, 95% CI 1.903, 5.042).

Conclusions: This study shows a high prevalence of MA among the adolescents. CVDs risk factors predictive of MA are overweight, obesity, systolic hypertension and older age.

Keywords: Adolescents; hypertension; microalbuminuria; obesity; overweight; prehypertension

INTRODUCTION

Microalbuminuria (MA) is defined as elevated urinary protein level higher than normal range but lower than the level that can be detected with the use of albustix[1]. The MA corresponds to urine protein level between 20 μg/min and 200 μg/min in a timed urine or 24-hour urine protein between 30 mg and 300 mg.[2,3] Microalbuminuria results from systemic endothelial damage.[4] Microalbuminuria is an early, independent and reliable predictor of atherosclerosis in patients with cardiovascular diseases (CVDs).[5] According to Steno hypothesis, MA can signal the risk of development of CVDs even in the apparently healthy subjects.[6] The sensitivity and specificity of MA in detecting atherosclerosis is 90.0% and 95.0% respectively.[7]

Many risk factors have been linked to the emergence of atherosclerosis and ultimately cardiovascular diseases in both children and adult populations. The factors include physical inactivity, alcohol consumption, cigarette smoking, elevated blood pressure, overweight and obesity.[8,9] Of these factors, hypertension has been identified as a leading risk factor for atherosclerotic cardiovascular diseases.[10] Regarding obesity, another risk factor for CVDs, there has been an increase in the prevalence of childhood obesity[11] and this portends a significant risk for morbidity and mortality in adulthood.[12] Childhood obesity is associated with increased risk of coronary heart diseases, diabetes mellitus and metabolic syndrome in later life.[13] Studies have shown tracking of obesity in young children to adolescence and adulthood.[13,14]

Most of the studies that involved children focused on determining the prevalence of MA with little or no appraisal of its relationship with the occurrence of specific cardiovascular risk factors. There is therefore the need to assess the prevalence of MA and determine its relationship with the occurrence of identified cardiovascular diseases' risk factors in children. We intended to evaluate the relationship between MA and risk factors for CVDs (obesity, overweight, pre-hypertension and hypertension) among secondary school students in Ilorin, Nigeria.

METHODS

This was a descriptive cross-sectional study conducted among private and public secondary schools in Ilorin, North Central Nigeria. This study was carried out from December 2017 to March 2018. We estimated the minimum sample size for the study using a prevalence of microalbuminuria reported in an earlier Nigeria study[15]. A multi-stage stratified sampling technique was used for selection of students from each of the three local governments that make up Ilorin. Secondary school students aged 10 to 18 years whose parents gave consent and who assented to participate were included. This study excluded subjects with fever at the time of the study, subjects with clinical symptoms of urinary tract infection or whose urinalysis showed presence of leucocyte esterase / nitrites or haematuria and proteinuria suggestive of acute glomerulonephritis, subjects on drugs causing glomerular injury such as cyclosporine, allopurinol and sulfasalazine for > two weeks, subjects engaging in vigorous exercise prior to recruitment, subjects with clinical features of cardiac disease and menstruating female subjects or those within seven days of completion of menstruation. Ethical clearance was obtained from the Ethical Review Committee of the University of Ilorin Teaching Hospital (UITH), Ilorin. A written permission for the study was obtained from Kwara State Ministry of Education.

The students had their anthropometrics and blood pressure measured. Weight was measured in kg using a digital bathroom weighing scale. Subject wore light clothing (school uniform only) without heavy jackets, cardigans, caps or hats; each subject removed their shoes / sandals, before being weighed to nearest 100g. Height was measured to the nearest 0.1 cm using a stadiometer with a fixed vertical backboard and an adjustable headpiece. Body mass index (BMI) was derived from the ratio of weight (kg) per height squared (m^2) for each subject. Subjects were categorized into underweight, normal weight, overweight and obese using CDC growth charts.[16] Underweight was defined as BMI < 5^{th} centile, normal weight when BMI was between 5^{th} and 84^{th} centile, overweight when BMI was between 85^{th} and 95^{th} centile and obese when BMI centile was > 95^{th} percentile. Waist circumference was taken with the upper clothes folded up exposing the lower abdomen and

Table 1. Comparison of socio-demographic characteristics among subjects with and without MA

Variable	MA positive (n = 176) Number (%)	MA negative (n = 408) Number (%)	Chi square	p value
Gender	72 (27.4)	191 (72.6)	0.826	0.364
Male n = 263	104 (32.4)	217 (67.6)		
Female n = 321				
Age group (years)	43 (18.6)	188 (81.4)	3.678	0.005
10-12 n = 231	61 (29.9)	143 (70.1)		
13-15 n = 204	72 (48.3)	77 (51.7)		
16-18 n = 149				
School type	64 (29.6)	152 (70.4)	0.113	0.737
Private n = 216	112 (30.4)	256 (69.6)		
Public n = 368				

MA: microalbuminuria

waist; arms were folded across both shoulders with the hands resting on opposite shoulders[17]. Hip circumference was measured with inelastic tape over the major trochanters to the nearest 0.1cm[18]. Waist to hip ratio was subsequently calculated from the measurement of waist circumference and hip circumference taken from each subject[18]. Blood pressure was measured on the right arm with the child sitting quietly for at least five minutes; subject's back was supported with the feet flat on the ground; right arm was flexed and the flexed elbow positioned at the level of the heart on the measuring table positioned beside subject. The mercury sphygmomanometer was then positioned at the observer's eye level. The blood pressure was recorded on three consecutive days to nearest 2 mm Hg and the mean of the readings was used for analysis.

Determination of microalbuminuria: The first morning urine of subjects was tested for MA using the Microalbumin 2-1 Combo strip manufactured in San Diego with Lot number 92121. Results obtained were compared with the colour shades printed on the bottle. There were five colour shades on the test strip vial (0, 10, 30, 80, 100 mg / L) reflecting the categories of albumin concentrations. A reading of 30 mg / L and above signified microalbuminuria. Spot urinary albumin-to-creatinine ratio (ACR) was carried out on those that had positive microalbuminuria through the combo strip for further confirmation.

Data were entered into a Statistical Package for Social Sciences version 21 spreadsheet. Continuous data were checked for normal distribution (blood pressure and anthropometric parameters) and were summarized as mean with standard deviation. Discrete data were summarized as frequency and charts. Means from continuous variables were compared using t-test. Logistic regression analysis was used to determine the effect of the cardiovascular risk factors predictive of microalbuminuria. The magnitude of correlation between the presence of MA and cardiovascular disease risk factors was determined using Spearman rho correlation. In all cases, the

Table 2. Comparison of anthropometric characteristics of subjects with and without microalbuminuria (MA)

Variable	MA positive (n = 176) Mean ± SD	MA negative (n = 408) Mean ± SD	T	p value
Weight (kg)	52.1 ± 11.9	45.5 ± 9.4	7.449	0.004
Height (cm)	157.5 ± 10.1	153.9 ± 10.2	4.042	0.814
Body mass index (kg / m2)	20.8 ± 3.6	19.0 ± 2.7	6.804	< 0.001
Hip circumference (cm)	83.7 ± 9.1	79.5 ± 7.3	6.019	0.004
Waist circumference (cm)	70.3 ± 7.6	66.7 ± 7.3	5.625	0.005
Waist to hip ratio	0.9 ± 0.1	0.8 ± 0.1	0.053	0.192

Table 3. Relationship between weight categories and prevalence of microalbuminuria (MA)

Parameter	MA positive	MA negative	Number (%)	p value
Obesity	28 (63.6)	16 (36.4)	44 (100)	< 0.001
Normal weight	89 (31.7)	192 (68.3)	281 (100)	0.476
Overweight	23 (59.0)	16 (41.0)	39 (100)	0.005
Underweight	36 (16.4)	184 (83.6)	220 (100)	0.864

confidence level was set at 95% and level of significance at $p < 0.05$.

RESULTS

Five hundred and eighty four subjects with a mean age of 13.9 ± 2.4 years were recruited. The males were 263 (45%). The mean age of males and females were 13.8 ± 2.4 years and 14.0 ± 2.3 years respectively. Of the 584 subjects recruited for the study, 176 had microalbuminuria with an overall prevalence of 30.1%

Furthermore, prevalence of MA increased significantly with increasing age, with the highest prevalence among the age group 16 to 18 years (72/149; 48.3%), p = 0.005, $p < 0.01$. Other details are shown in Table 1.

Of the 44 obese subjects, 28 (63.6%) had MA which was higher than the prevalence of MA

Table 4. Relationship between blood pressure recordings in subjects and prevalence of microalbuminuria

Blood pressure	Microalbuminuria Positive	Microalbuminuria Negative	n (%)	p value
Systolic BP				
Normal	85 (19.9)	343 (80.1)	428 (100)	
Prehypertension	36 (50.7)	35 (49.3)	71 (100)	
Hypertension	55 (64.7)	30 (35.3)	85 (100)	< 0.001
Diastolic BP				
Normal	166 (29.2)	402 (70.8)	568 (100)	
Prehypertension	2 (28.6)	5 (71.4)	7 (100)	
Hypertension	8 (88.9)	1 (11.1)	9 (100)	< 0.001

among the normal weight subjects 89/281 (31.7%) ($p < 0.001$). Similarly, the proportion of overweight subjects who had MA (23/39; 59%) was significantly higher than the proportion of normal weight subjects (89/281; 31.7%), (p = 0.005, $p < 0.01$) as shown in Table 3.

Out of the 85 subjects with systolic hypertension, 55 (64.7%) had MA and this was about three times higher than the prevalence of MA among subjects

Table 5. Correlation of occurrence of microalbuminuria with subjects' socio-demographic characteristics and cardiovascular diseases' risk factors

Variable	R	p value
Gender	0.038	0.462
Age	0.292	0.011
Body mass index	0.710	0.001
Systolic blood pressure	0.884	0.001
Diastolic blood pressure	0.190	0.029
Weight	0.790	0.004
Height	-0.097	0.190
Waist circumference	0.475	0.005
Hip circumference	0.005	0.904
Waist to hip ratio	0.328	0.002

Table 6. Logistic regression of occurrence of microalbuminuria (MA) and subjects' socio-demographic characteristics / cardiovascular disease risk factors

Variable	B	aOR	95% CI		p value
			Lower	Upper	
Age	0.103	1.108	1.007	1.219	0.035
Obesity	1.579	4.849	1.124	20.913	0.034
Overweight	1.279	3.594	1.184	10.174	0.024
Systolic hypertension	0.955	3.097	1.903	5.042	0.001
Diastolic hypertension	0.238	0.788	0.362	1.716	0.549
Waist circumference	0.271	0.763	0.531	1.095	0.142
Hip circumference	0.243	1.275	0.949	1.712	0.106
Weight	0.243	1.275	0.949	1.712	0.106

with normal systolic blood pressure readings 85/428 (19.9%). Similarly, the prevalence of MA among subjects with systolic pre-hypertension 36 / 71 (50.7%) was higher when compared with subjects with normal systolic blood pressure 85 / 428 (19.9%), $p < 0.001$. Furthermore, the prevalence of MA amongst subjects with diastolic hypertension 8 / 9 (88.9%) was significantly higher when compared with subjects who had normal diastolic blood pressure 166 / 568 (29.2%) and those within the diastolic pre-hypertensive category 2 / 7 (28.6%), $p < 0.001$ **(**Table 4).

There was a strong positive correlation between subjects' weight, body mass index and systolic blood pressure with the occurrence of MA ($r = 0.790$, $p = 0.004$, $p < 0.01$; $r = 0.884$**,** $p = 0.001$, $p < 0.01$**;** $r = 0.710$; $p = 0.001$, $p < 0.01$) respectively. Similarly, waist circumference and waist to hip ratio had weak to moderate positive correlation with the development of microalbuminuria **(**$r = 0.475$, $p = 0.005$, $p < 0.01$; and $r = 0.328$, $p = 0.002$, $p < 0.01$**)** respectively. Furthermore, subjects' age and diastolic blood pressure had significant, positive (but weak) correlation with occurrence of MA **(**$r = 0.292$**,** $p = 0.011$, $p < 0.05$**;** $r = 0.190$, $p = 0.029$, $p < 0.05$) respectively (Table 5).

The logistic regression of selected cardiovascular risk factors against occurrence of MA revealed that the independent predictors of microalbuminuria were older age, being obese, overweight and being hypertensive (systolic). The adjusted odds ratio (aOR) showed obese subjects have five-fold risk of MA [aOR 4.849, (95% CI 1.124, 20.913)], and overweight subjects have a fourfold increase in the risk of MA [aOR 3.594, (95% CI 1.184, 10.174)]. Besides, subjects with systolic hypertension had threefold MA [(aOR 3.097, 95% CI 1.903, 5.042)] as shown in Table 6.

DISCUSSION

In the study, the prevalence of MA was 30.1%, and this is comparable to the values of 33.2% and 37.5% reported by previous workers among secondary school students in Nigeria.[15,19] However, it was higher than the prevalence of 19.0% reported among normotensive, non-obese offspring's of hypertensive parents in Benin[3] and 10.1% among healthy subjects in South Africa.[20] The higher prevalence in the current study may be related to the study population as all categories of adolescent were included in contrast to the study in Benin which excluded hypertensive and obese adolescents, a group in which higher prevalence of MA has been reported.[19] The lower prevalence reported in the South African study may be due to the ages of the subjects (6 to 9 years), as it has been demonstrated that prevalence of MA is very low in young children.[21] The observation is further corroborated by the demonstrated age-related increase in prevalence of MA in this study.

In this study, the prevalence of MA was highest among late adolescent age group (16 to 18 years) and this is in keeping with earlier reports among adolescents from USA[22] and Enugu[23] respectively. This further corroborates previous observations that the prevalence of MA increases with increasing age.[15,19,24] The prevalence of MA among obese subjects was 63.6% which is higher than the values of 7.9% and 10.1% reported by Park et al[25] and Burgert et al[26] among similar cohorts in Korea and United States of America respectively. The high prevalence noted in the current study may be due to rise in the global prevalence of obesity in both developing and developed world in the recent past[27]. Besides, MA has been found to be more common in black population when compared with white population.[28] In an earlier study in Nigeria, Okpere et al[29] found a prevalence rate of 35.4% among obese adolescents.

The prevalence of MA among hypertensive subjects in this study was 64.7% and this is comparable to the 58% prevalence rate recorded by Assaidi et al[30]. However, it is higher than the 20% prevalence reported by Seeman et al[14] in Czech Republic. The discrepancies in the prevalence could be due to differences in methods and the criteria for patients' selection. Also, in the Czech study, not all the recruited subjects had hypertension as some of the subjects were in the pre-hypertension category (BP 90-95th percentile), a group in whom lower prevalence of MA has been reported and corroborated in this study. This study also shows a positive correlation between MA and weight, systolic blood pressure and BMI, which is consistent with the report of other researchers.[19,26] The prevalence of obesity and overweight among the subjects in this study were 7.5% and 6.7% respectively, which were higher than the corresponding values of 3.3% and 1.4% noted in north western part but lower than the 9.4% and 13.8% reported in south western part of the country. The increasing incidence of obesity and overweight may be due to adoption of western lifestyle and diets such as use of calorie drinks, beverages and snacks.

The study shows obesity, overweight, hypertension and older age were associated with increased risk of development of MA. Similar findings were observed by other researchers.[29,30] This may be due to the effect of chronic low-grade inflammation that causes widespread derangement in endothelial function, thereby resulting in excessive leakage of albumin seen in obese and overweight subjects.

CONCLUSIONS

Our study shows a high prevalence of MA among secondary school students in Ilorin, Nigeria. Besides, three of every five obese adolescents had MA. The CVDs risk factors predictive of MA are overweight, obesity, systolic hypertension and older age. We therefore recommend routine screening for MA in overweight / obese adolescents either as part of School Health services or routine clinic evaluation aimed at ultimately curtailing the emergence of CVDs. Routine blood pressure check in adolescent is advisable as it would facilitate early identification and improved case management of ensuing pre-HTN and HTN.

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