Prevalence of Microalbuminuria among secondary school children

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Abstract

Background: Microalbuminuria is an early sign of kidney and cardiovascular damage. Therefore, early detection in asymptomatic individuals may be helpful in preventing deterioration in renal function.

Methods: We carried out a cross-sectional study of 820 secondary school students aged 10 - 19 years from September to November 2008. The urine samples of 615 (75.0%) without overt proteinuria and haematuria were tested for microalbuminuria using the micral test strips. Values of greater than 20mg/L were considered positive.

Results: There were 299 (48.6%) males and 316 (51.4%) females, with a M:F ratio of 1:1.1. The prevalence of microalbuminuria as seen in 214 of the students was 33.2%. It was significantly higher in females (45.3%), obese subjects (35.4%), those with hypertension (70.6%), those with positive family history of hypertension (59.5%), and diabetes mellitus (46.4%). Microalbuminuria was found in 1 of the 2 subjects who had features of DM and in one subject with sickle cell anemia. **Conclusion:** The prevalence of microalbuminuria in Nigerian adolescents is high. We recommend routine screening for microalbuminuria in adolescents for early detection and prevention of renal damage.

Key words: microalbuminuria, obesity, hypertension, children, Nigeria

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Introduction

Microalbuminuria is a subclinical condition that is associated with high morbidity and mortality.^{1,2} It is the excretion of very small amounts of albumin in urine, slightly in excess of 20 microgram per minute (ig/min).³ Microalbuminuria is an early sign of damage to the kidneys and cardiovascular system.^{1,4,5} It has been found to be highly prevalent in several disease conditions in adults^{2,6}, as well as in children and adolescents. ^{7,8,9,10} The major identified causes of microalbuminuria include diabetes mellitus (DM)^{7,11,12}, hypertension^{1,13}, sickle cell anaemia (SCA)⁹, Human Immunodeficiency Virus (HIV) infection¹⁰, and obesity.¹⁴

The prevalence of microalbuminuria in the general population is reported to be 10 - 15%.⁶ In the Netherlands¹, microalbuminuria was found in 12.1% of apparently healthy adults in the general population. In the United States of America (USA), Jones et al ¹⁵ reported a lower prevalence of 7.8% in the general population of children, adolescents, and adults. In Africa, there is paucity of data on the

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Dr Augustina N Okpere Department of Pediatrics University of Port Harcourt Teaching Hospital PMB 6173 Port-Harcourt, Rivers State, Nigeria Telephone: +234-8059150818 E-mail: anokpere@yahoo.com prevalence of microalbuminuria in the general population of children. In Nigeria, Ibadin et al¹⁶ reported a 19% prevalence of microalbuminuria among healthy adolescents and young adult offsprings (aged 10-24years) of hypertensive parents in Benin City.

In diabetic patients, microalbuminuria predicts the development of overt diabetic nephropathy^{5,17}, while in hypertensive patients, it is associated with cardiovascular events such as myocardial ischaemia and stroke. ^{1,13} It is also an early sign of sickle cell nephropathy in patients with SCA.⁹ In non-diabetic and non-hypertensive subjects, presence of microalbuminuria is associated with increased levels of athrogenic factors and an increase in cardiovascular morbidities and mortalities.¹⁸

Individuals with microalbuminuria may have a rapid progression to overt proteinuria, progressive deterioration in renal function, and development of end stage renal disease (ESRD) later in life.^{2,19} For primary prevention of ESRD, nephrologists are focusing on early detection of microalbuminuria in asymptomatic individuals, so that appropriate interventions can be commenced early to prevent further deterioration in renal function.^{19,20,21}

This study was carried out to determine the prevalence of microalbuminuria and factors associated with microalbuminuria in the general population of adolescents, and also to improve on the paucity of data from Africa.

Methods

A cross-sectional study was done over a period of eight weeks, between September 29th to November 10^{th} 2008 in twelve secondary schools in Port Harcourt City, the capital of Rivers State of Nigeria. Rivers State is located in the South-South geo-political zone of Nigeria. It is a major industrial center in Nigeria and the regional headquarters of the petroleum sector. Twelve secondary (eight private and four public) schools and 864 students aged 10 – 19 years were selected using multi-staged sampling technique, from the fifty-two secondary schools in Port Harcourt City. The sample size was calculated from the formula²²:

$$n = \underline{Z^2(pq)}_{d^2}$$

Where n is the desired sample size; Z is the standard normal deviate, usually set at 1.96 which corresponds to the 95% confidence level, so that $Z^2 = 3.8416$; p is the prevalence of microalbuminuria; 19.0% was the prevalence of microalbuminuria in healthy adolescents and young adults in a study conducted in Benin City, Nigeria¹⁶; therefore p is equal to 0.19; q is 1 - p and d is the degree of accuracy desired, set at 0.04 so that d^2 is equal to 0.016. Therefore,

$$n = \frac{3.8416 (0.190 \ge 0.810)}{0.0016} = 369.5$$

A total of 820 students were however recruited for the study to give allowance for design effect and attrition. The following exclusion criteria were used: students who had been involved in vigorous exercise or competitive sport twelve hours prior to the study, students with fever at the time of study or a history of febrile illness two weeks pior to the study, students with signs and symptoms suggestive of pre-existing renal disease, female students who were menstruating and within one week of cessation of menses at the time of study, those with history of vaginal discharge, and male students with history of urethral discharge.

Ethical clearance was obtained from the Research and Ethics Committee of the University of Port Harcourt Teaching Hospital (UPTH). Permission was also obtained from the Rivers State Ministry of Education, principals of the selected schools, as well as the selected students and their parents/guardians.

The study was carried out on school days in the various schools. For each student, a detailed history was obtained including the bio-data; symptoms such as fever, body swelling, dysuria,

polyuria, polydipsia, polyphagia, weight loss and bone pains; medical history to identify causes of microalbuminuria as well as family history of diabetes mellitus or hypertension. The social class of each subject was determined using the social classification described by Oyedeji²³ based on the profession and educational level of both parents. A brief physical examination checking for facial or leg oedema, temperature, weight, height, and blood pressure was performed in an enclosed room or the school's clinic where available. The Body Mass Index (BMI) for each subject was calculated as weight $(kg)/height (m^2)$. The nutritional status of the subjects was calculated using the BMI percentile charts for age and sex according to the United States Centers for Disease Control and Prevention 2000 growth charts²⁴. A subject was classified as obese when the BMI was equal to or greater than the 95th percentile. Those whose blood pressures were elevated on the first day where re-checked the next day. Hypertension was defined as blood pressure greater than or equal to the 95th percentile for age, sex and height.²⁵

After the clinical examination, each subject voided about ten milliliters (mls) of spot urine into a 20mls universal container (A) which had been previously labeled with the subject's study number. Five milliliters of the urine was then withdrawn using a 5mls syringe into a second universal bottle (B) which had also been previously labeled with the subject's study number.

A dipstick urinalysis was performed on the urine sample on container A to test for protein, leucocytes, blood, nitrite, and glucose using the Combi-Screen^R .10SL manufactured by Macherey Nagel MN, Germany with Lot number 56704. The urinalysis was considered positive when any of the components was positive. Positive nitrite and leukocyte esterase were considered suggestive of urinary tract infection; presence of glycosuria in the presence of polyuria, polyphagia or polydipsia was suggestive of diabetes mellitus. However, the diagnosis of diabetes mellitus was not confirmed with a fasting blood sugar level because the investigators were not permitted to collect blood samples from the students. Also, in line with this, the students were not screened for HIV infection. The results were entered into a proforma attached to the questionnaire

The urine samples in container B of those subjects who were negative for proteinuria and blood on dipstick urinalysis were tested immediately for microalbuminuria using the Micral-test strips manufactured by Roche, USA with Lot number 28989833. There were four colour blocks on the micral test strip vial (0, 20, 50, 100 milligram per liter (mg/L)) reflecting the categories of albumin concentrations. A reading of 20mg/L and above was considered positive for microalbuminuria.

All adolescents with abnormal urine finding, obesity and hypertension were referred to the pediatric nephrology/endocrine unit of the University of Port Harcourt Teaching Hospital (UPTH) for further evaluation.

Data analysis

Data from the study wereanalysed using the computer programme Epidemiological Information Software (EPI – INFO) version 6.04 and the Statistical Package for Social Sciences (SPSS) version 15.0. The Chi- square analysis, student's t test and one-way analysis of variance (ANOVA) were used where appropriate to test proportions. Pearson's correlation was used to measure association. In all cases, a p value of < 0.05 was regarded as statistically significant.

Results

Of the 820 students, 194 (23.7%) had overt proteinuria and 11 (1.3%) had haematuria on dipstick urinalysis and were excluded from further analysis. The remaining 615 (75.0%) students formed the study population. Table 1 shows the characteristics of the study population. There were 299 (48.6%) males and 316 (51.4%) females giving, a male to female (M:F) ratio of 1:1.1. They were aged 10-19 years (mean 13.6 \pm 2.2 years). Majority (66.2%) of the subjects were aged 10-14 years. The mean age of the male subjects was 14.0 \pm 2.3 years, while that of the females was 13.2 \pm 2.0 years. The difference was statistically significant (t = 4.040; p = 0.000). Majority of the students were in private school and belonged to social class I as shown in table 1.

Prevalence of microalbuminuria

Out of the 615 students analysed, 214 subjects had microalbuminuria, giving a prevalence of microalbuminuria as 33.2%. They comprised 61 (29.9%) males and 143 (70.1%) females. The proportional prevalence of microalbuminuria was significantly higher in females (chi sqaure = 42.803; p = 0.000). Table 2 shows the characteristics of the subjects with and without microalbuminuria. Microalbuminuria was present in all the different age groups.

Table 1: Characteristics of the study population

Parameter	Num	ber %
Sex		
Male	299	48.6
Female	316	51.4
Age group		
10-14years	407	66.2
15-17years	177	28.8
18-19years	31	5.0
School typ	e	
Private	366	59.5
Public	249	40.5
Social class	s	
Ι	234	38.1
II	71	11.5
III	122	19.8
IV	179	29.1

The mean age of the subjects with microalbuminuria was 13.6 \pm 1.9 years, while that of those without microalbuminuria was 13.6 ± 2.3 years; the difference was not statistically significant (t = -0.464; p = 0.643). The proportional prevalence of microalbuminuria was significantly higher in the age group 15-17 years and lowest after the age of 17 years (chi sqaure = 13.937; p = 0.001). The proportional prevalence of microalbuminuria was higher in students in the public school. This was however not statistically significant (chi sqaure = 0.889; p = 0.346). Furthermore, social class did not affect the prevalence of microalbuminuria (chi sqaure = 2.408; p = 0.661). The mean weight and BMI of subjects with microalbuminuria (48.6 \pm 1.3kg and 19.7 \pm 3.7 respectively) were higher than those without microalbuminuria (47.1 \pm 11.1 and 19.2 \pm 3.4 respectively). However, the difference was not statistically significant (t = 1.500; p = 0.134 and t = 1.544; p = 0.123 respectively).

Factors associated with microalbuminuria in adolescents

Obesity

Obesity was identified in 65 (10.6%) of the subjects. Of these, 23 (35.4%) had microalbuminuria. The proportional prevalence of microalbuminuria was significantly higher in the obese subjects compared to those without obesity (chi square = 0.16; p = 0.669), as shown in table 3.

Parameter	Microalbuminu	ria	Total (%)	p value	
	Positive (%)	Negative (%)		-	
Age group					
10-14years	137 (33.7)	270 (66.3)	407 (100)		
15-17years	66 (37.3)	111 (62.7)	177 (100)	0.001	
18-19years	1 (3.2)	30 (96.8)	31 (100)		
Sex					
Male	61 (20.4)	238 (79.6)	299 (100)		
Female	143 (45.3)	173 (54.7)	316 (100)		
School type	2				
Private	116 (31.7)	250 (68.3)	366 (100)		
Public	88 (35.3)	161 (64.7)	249 (100)		
Social class					
Ι	71 (30.3)	163 (69.7)	234 (100)		
II	27 (38.0)	44 (62.0)	71 (100)	0.645	
III	45 (36.9)	77 (63.1)	122 (100)		
IV	58 (32.4)	121 (67.6)	179 (100)		
V	3 (33.3)	6 (66.7)	9 (100)		

Table 2: Characteristics of the study subjects with and without Microalbuminuria

Hypertension

Blood pressure was elevated in 17 (2.8%) subjects. Twelve (70.6%) of the subjects with hypertension had microalbuminuria. The proportional prevalence was significantly higher in those with elevated blood pressure compared to those with normal blood pressure (chi square = 11.042; p = 0.001).

Possible diabetes mellitus

Two (0.3%) subjects had features of diabetes mellitus. One of these (50%) had microalbuminuria. The difference was however not statistically significant (chi square = 0.256; p = 0.613).

Sickle Cell Anaemia (SCA)

The haemoglobin genetope of only 11 (1.8%) students were obtained. Two (18.2%) of these had genotype SS while the remaining 9 (81.8%) students had genotype AA. Microalbuminuria was present in 1 (50%) of the 2 (18.2%) students with SS genotype.

Family history of hypertension

Family history of hypertension was obtained from 42 (6.8%) of the subjects of which 25 (59.5%) had microalbuminuria. There was significantly higher prevalence of microalbuminuria in subjects with positive family history of hypertension compared to those without family history of hypertension (chi square2 = 14.122; p = 0.000) as shown in table 3.

Only 1 (2.4%) of the students with a family history of hypertension had high blood pressure.

Family history of diabetes mellitus

Family history of diabetes mellitus was obtained from 56 (9.1%) subjects, and 26 (46.4%) had microalbuminuria. There was significantly higher prevalence of microalbuminuria in subjects with positive family history of diabetes mellitus, compared to those without family history of diabetes mellitus (chi square = 4.885; p = 0.027 respectively). However, there was no significant difference in the subjects whether the hypertension, or diabetes mellitus existed in the mother, father or other relations (chi square = 0.502; p = 0.809 and chi square = 4.374; p = 0.224 respectively).

Table 3: Factors associated with Microalbuminuria adolescents

Parameter	Microalbuminuria		Total (%)	p value	OR (95% CI)	
	Positive(%) Negativ			-		
Obesity	23 (35.4)	42 (64.6)	65 (100)	0.689	1.116 (0.651 - 1.913)	
Non-obese	181 (32.9)	369 (67.1)	550 (100)			
Hypertension	12 (70.6)	5 (29.4)	17 (100)	0.001	0.197 (0.680 - 0.567)	
Normal BP	192 (32.1)	406 (67.9)	550 (100)			
Possible DM	1 (50)	1 (50)	2 (100)	0.554		
No features of DM	203 (33.1)	401 (66.9)	613 (100)			
Fx of Hypertension	25 (59.5)	17 (40.5)	42 (100)	0	3.237 (1.705 - 6.145)	
No Fx of Hypertension	179 (31.2)	394 (68.8)	573 (100)			
Fx of DM	26 (46.4)	30 (53.6)	56(100)	0.027	1.855 (1.065 - 3.230)	
No Fx of DM	178 (31.8)	381 (68.2)	559 (100)			

OR = Odds Ratio; CI = Confidence Interval; DM = Diabetes Mellitus; Fx = Family history

However, when all the associated factors of microalbuminuria were subjected to further logistic regression analysis, only hypertension (adjusted odds ratio (OR) = 5.393; 95% confidence interval [CI] =

1.791 - 16.236) and diabetes mellitus (adjusted OR = 5.390; CI=0.310 - 0.939) were significantly associated with microalbuminuria as shown in table 4.

Table 4:	Crude and	adjusted	odds	ratios	for	Microa	lbuminuria	in	adolescents
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OR (95% CI)	OR (95% CI)
1.116 (0.651 - 1.913)	0.859 (0.474 - 1.555)
0.197 (0.680 - 0.567)	0.177 (0.570 - 0.552)
2.020 (0.126 - 32.455	0.931 (0.555 - 15.776)
3.237 (1.705 - 6.145)	1.374 (0.736 - 2.566)
1.855 (1.065 - 3.230	3.098 (1.548 - 6.198)
	$\begin{array}{c} 1.116 & (0.651 - 1.913) \\ 0.197 & (0.680 - 0.567) \\ 2.020 & (0.126 - 32.455) \\ 3.237 & (1.705 - 6.145) \\ 1.855 & (1.065 - 3.230) \\ \end{array}$

DM = Diabetes Mellitus; OR = Odds ratio; CI = Confidence interval.

Discussion

The study noted a higher prevalence of microalbuminuria at 33.2% compared to the 19% reported by Ibadin et al¹⁶ in Benin City, Nigeria and the 7.8% reported by Jones et al¹⁵ in the United States of America. The lower prevalence reported by Ibadin et al¹⁶ may be due to the exclusion of subjects with obesity and hypertension from the study while that reported by Jones et al¹⁵ may be due to the larger sample size and the wide variation in the ages of the study population. In contrast, the prevalence of microalbuminuria in this study is much lower than the 61.0% prevalence reported by Unuigbe et al²⁶ among medical students in Benin City. The higher prevalence reported by Unuigbe et al 26 may be attributed to the fact that the subjects were older (25 - 35 years) and hence more likely to have microalbuminuria.27,28

The finding of a significantly higher genderspecific prevalence of microalbuminuria in females (45.3%) compared to males (20.4%) is similar to the findings recorded by Jones el al¹⁵ in the USA, who reported a gender specific prevalence of 9.7% in females and 6.1% in males in the general population. The higher prevalence of microalbuminuria in females has also been reported among children with sickle cell anaemia (SCA) by Dharnidharka et al¹³ in the USA. The cause of the gender disparity in favour of females cannot be readily explained. In contrast, Ibadin et al¹⁶ reported a higher prevalence in males (20.8%) compared to females (16.7%). The authors suggested that the gender disparity may be attributed to under-representation of females in hypertensive disease in the general population.

In this study, the age-specific prevalence of microalbuminuria was significantly higher in subjects aged 15-17 years, compared to the younger subjects aged 10-14 years. This is similar to the findings reported by Unuigbe et al²⁶ in Benin City, Jones el

al¹⁵ in the USA and by Marsenic et al²⁹ and McBurney at al³⁰ among childern with sickle cell amaenia in the USA. They reported a positive correlation between microalbuminuria and age. The present study therefore supports previous reports that microalbuminuria increases with increasing age.

The higher prevalence of microalbuminuria in obese subjects compared to their counterparts who had normal weight is similar to the findings recorded by Unuigbe et al.²⁶ They reported a positive correlation between microalbuminuria and body mass index (BMI). Similarly, Diercks et al¹ in the PREVEND study conducted in Australia and Valensi et al14 in the USA reported a strong association between obesity and microalbuminuria. Obesity is strongly associated with microalbuminuria.³¹ It is a well documented risk marker for progressive renal function loss in patients with renal disease.³¹ With the rising global epidemic of obesity in children and adolescents^{32,33} and ESRD³⁴, the exact role of obesity in renal disease requires further evaluation. In contrast, Hwang et al²⁷ reported an inverse relationship between microalbuminuria and BMI. They reported a higher prevalence of microalbuminuria in nonobese subjects. The authors could not explain the reason for the negative correlation between microalbuminuria and obesity.

The high prevalence of microalbunimuria in subjects with elevated blood pressure is similar to the findings reported by Unuigbe et al²⁶, Jones et al¹⁵, and Diercks et al¹ in the general population. They reported a positive correlation between microalbuminuria and hypertension in the study subjects. In the present study, the 59.5% prevalence of hypertension in subjects with family history of hypertension was significantly higher than 31.2% prevalence in those without family history of hypertension. In consonance with this, Ibadin et al¹⁶ reported a 19.0% prevalence of microalbuminuria in off-springs of hypertensive parents and a lower 8.0% prevalence in the control group who were subjects of normotensive parents. Unuigbe et al²⁶ also reported a positive correlation between microalbuminuria and family history of hypertension in Benin City. The findings of this study may suggest that children with family history of hypertension have increased predisposition to microalbuminuria. Some authors have reported that microalbuminuria is linked to the pathogenesis of hypertension and serves as a predictor of hypertension in normotensive individuals.^{16,26,35} While Ibadin et al¹⁶ reported a higher prevalence in subjects with paternal history of hypertension, in the present study, the prevalence of microalbuminuria did not vary significantly whether the hypertension existed in the mother or father.

The 46.4% of microalbuminuria in subjects with family history of diabetes mellitus (DM) is much higher than the 31.8% prevalence in those without family history of DM. This is similar to the findings recorded by Unuigbe et al²⁶ who reported a higher prevalence of microalbuminuria in subjects with family history of diabetes. Although none of the subjects in the present study were known diabetic patients, microalbuminuria was present in one of the subjects with polyuria, polyphagia and glycosuria. Microalbuminuria is a chronic microvascular complication of DM.⁵ It predicts the development of incipient nephropathy in diabetic subjects.^{5,17} The findings of this present study may suggest that microalbuminuria probably predates clinical diagnosis of DM and where there is a family history of diabetes, it can be used as a tool to identify those at risk of developing DM and nephropathy later in life.

Sickle cell anaemia is a well documented risk factor for microalbuminuria.⁹ However, the exact relationship between microalbuminuria and sickle cell anaemia could not be established in the present study as the haemoglobin genotype of all the subjects was not known. However, one of the two known sickle cell anaemia patients had microalbuminuria. The subject was normotensive and did not have family history of hypertension and diabetes mellitus.

The limitations of this study were the inability to identify and exclude students with orthostatic proteinuria and physiologic proteinuria due to routine physical activity such as trekking to school.

Conclusion

The prevalence of microalbuminuria in adolescents aged 10 to 19 years is high. The proportional prevalence was significantly higher in female subjects compared to the male subjects. The factors associated with microalbuminuria were obesity, hypertension, family history of hypertension and diabetes mellitus, and sickle cell anaemia. We recommend routine screening of adolescents for microalbuminuria for early detection and prevention of renal damage.

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