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Original Article

Estimated Glomerular Filtration Rate in Apparently Healthy School Children in Uyo, Nigeria, Using the Updated Schwartz Formula

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Abstract

Background: Glomerular filtration rate (GFR) is the best indicator of renal function in children and adolescents. It is usually estimated in patients with renal diseases especially end stage renal disease without consideration of the possibility of its derangement in the general population, who may be asymptomatic. We set out to estimate GFR in a population of school children using the validated updated Schwartz formula (2009) to determine those with levels below ⩽ 60ml/min/1.73m^2 and document the factors associated with it.

Subjects and Methods: It was a cross-sectional study in children and adolescents drawn from a primary and a secondary school in a semi-urban community of Uyo local government area (LGA) of Akwa-Ibom State, Nigeria, over a three-month period (June 2017 to August 2017).Anthropometric, social and laboratory parameters were determined using standard methods while GFR was estimated using the updated Schwartz formula.

Results: Two hundred children aged between four to seventeen years with a male to female ratio of 1:1.8 constituted the study population. The mean and median eGFR were 82.8±17.7ml/min/1.73m^{2}and 81.0 ml/min/1.73m^2 respectively. The percentage of children and adolescents with eGFR ⩽ 60ml/min/1.73m^{2}was 10.0%. Female gender and a large waist circumference were the factors that were significantly associated with reduced eGFR.

Conclusion: The percentage of apparently healthy school children and adolescents with eGFR< 60 ml/min/1.73m^2 in our locale is high.We recommend a regular community based screening of children for CKD using this simple method.

Keywords: eGFR, children, Schwartz, female gender, waist circumference, Nigeria

Introduction

Glomerular filtration rate (GFR) is known and widely accepted as the best overall indicator of renal function and kidney disease progression in children and adolescents.[1]Serum creatinine is the most commonly used method of measurement of GFR because it is simple, convenient and practical but less accurate because of the influence of non-GFR determinants such as muscle mass which increases with age in children. However, in recent times, cystatin C has been suggested as a more sensitive marker of renal function.[2]

Community based studies [3,4]of estimated GFR of apparently healthy school children are sparse as most studies are hospital based, done mostly in sick children like sickle cell anaemia and renal disease patients and then comparing with controls. Gheissarie*etal*[3] obtained a mean eGFR of 99.6±19ml/min/1.73m^2 while a mean eGFR of 129.4±23.1ml/min/1.73m^{2}was reported from Turkey.[4] Nigerian studies have also reported mean eGFR of 112±31ml/min/1.73m^2, 126.6±20.2ml/min/1.73m^2 and 60±34.4ml/min/1.73m^{2}respectively from different

parts of the country in healthy controls of studies of sickle cell anaemia patients.[5-7]

GFR has been reported to increase with increasing age [5,8] with boys having higher values than girls.[9]Sharma *et al*[10]did not show any correlation between body mass index (BMI) and eGFR while some other studies showed increased BMI to be associated with reduced eGFR.[11-12] In various adult studies, hypertension[13-16]and lower social class[17-21] were associated with low eGFR. In a nationwide survey of healthy children and adolescents in Iran, dyslipidaemia was associated with reduced eGFR.[22]

Our aim in this study was to apply the updated Schwartz formula (2009) among apparently healthy school children in order to assess their renal function by estimating their GFR, and then determine the percentage of children with eGFR<60ml/min/1.73m^2. The associations if any between some physical, social and laboratory parameters with eGFR was determined.

Subjects and methods

This was a cross-sectional study conducted among children and adolescents drawn from a primary and a secondary school in a semi-urban community of Uyolocal government area (LGA) of Akwa-Ibom State, Nigeria, over a three-month period from June 2017 to August 2017. The community was selected from one out of four clans of the LGA by simple random sampling method. It has three primary schools and one secondary school. The primary school used was also selected by random sampling method. A total of one hundred subjects were selected from each school, seventeen from each class (there are six classes per school) giving a total study population of two hundred children. Selection of the children was by balloting technique.

Informed consent was obtained from the parents and assent from children aged 7 years and older after the details of the study objectives, procedures and potential benefits were explained to them. Approval was also sought and obtained from the State Ministry of Education.

A team of trained medical personnel were responsible for data collection, ranging from demographic and clinical data (age, gender, height, weight, waist circumference, social class, BMI, blood pressure) to collection of blood samples for serum creatinine estimation. The height and weight were measured using a stadiometer and calibrated scale respectively recorded to one decimal point. Waist circumference was measured to the nearest 0.1cm at the midpoint between the bottom of the rib cage and the top of the iliac crest at the end of exhalation.

Body mass index (BMI) was calculated and the World Health Organization(WHO) charts of BMI for age and gender were used as reference standards. Subjects with BMI equal to or greater than the 5th percentile and less than the 85th percentile were considered to have a normal BMI; those with BMI above the 95th percentile were classified as obese while those with BMI between 85th and 95th percentile were classified as overweight.

Social class was determined using the Oyedeji socioeconomic classification scale,[23] which is categorised into five classes and for the purposes of this study, I,II were regarded as high social class, III as middle social class while IV and V were classified as belonging to the low socioeconomic class. The blood pressure was measured using the mercury sphygmomanometer with an appropriate sized cuff for age. The subject was in a sitting position with the right upper arm placed on a table after the subject has been allowed to rest for at least 15 minutes before the procedure.

An average of three BP readings was used for each child. The technique of BP measurement adopted was as described by the 4th Task Force on Blood Pressure Control in Children.[24]Serum creatinine was measured by a senior laboratory scientist at the Department of Chemical Pathology of the University of Uyo Teaching Hospital, Uyoby the enzymatic colorimetric method using Randx Reagent from Randox Laboratory Ltd, United Kingdom.

To calculate the GFR for each subject, the "updated" Schwartz formula[4] was used as follows: GFR (ml/min/1.73m^2) = 0.413 x ht(cm) /serum creatinine (mg/dl) According to the estimated GFR, CKD was defined as GFR<60ml/min/1.73m^2.

Statistical analysis

Continuous values are expressed as mean + standard deviation(SD) and categorical variables are presented as numbers (percentage). Statistical analyses were carried out using the SPSS software version 25. Chi square *P*-value < 0.05 was considered to be statistically significant and Fishers Exact Test was used for cells with numbers less than five.

Results

Two hundred children aged between four to seventeen years were recruited into the study, with 81(40.5%) aged between 10-14 years. There were 72 (36.0%)males;with a male to female ratio of approximately 1:1.8. Eighty-eight (44.0%) children belonged to social class III. The socio-demographic information of the children is shown in table 1.

Table 2 shows that the mean age was 12.4 ± 3.6 years while the mean weight and mean height were 37.7 ± 12.9 kilograms and 144.1 ± 17.3 centimetres respectively. The waist circumference ranged from 47.0 to 96.0 centimetres, with a mean of 62.7 ± 7.4 centimetres. The systolic blood pressure ranged from 66 to 163 mmHg while that of the diastolic blood pressure was 33-100 mmHg. The median systolic and diastolic blood pressures were 103.0 mmHg and 65.0 mmHg respectively.

The minimum estimated glomerular filtration rate was 42.5mls/min/1.73m^2. Twenty (10.0%) children had eGFR<60ml/min/1.73m^2.The relationship of some physical parameters and eGFR as depicted in table 3 shows that more females significantly had higher eGFR (p=0.0001) than males and a large waist circumference was also significantly associated with low estimated GFR (p=0.003). There was no significant association between eGFR and age (p=0.091), body mass index (p=0.941) and both systolic and diastolic blood pressures at p=0.772 and p=0.750 (Fishers Exact Test) respectively.

Table 4 shows the relationship between social factors and eGFR. Low eGFR was noted in children from the lower social classes III and IV but this was not statistically significant (p=0.353). There was no significant association between a positive family of chronic kidney disease and low eGFR (p=0.080).

The estimation serum levels of certain laboratory parameters and their relationships with GFR are shown in table 5. The estimated GFR did not show any significant relationship with serum creatinine and urea: p=0.090 and 0.646(Fisher's Exact Test) respectively, as only few children had elevated serum levels of creatinine and urea. The lipid profile also did not show any relationship with eGFR. None of the patients with low eGFR had hypercholesterolaemia (p=0.0194, Fisher's Exact Test). Only 11% of the patients had derangement of others parameters of the lipid profile but there was no statistical significance: serum triglycerides, p=0.350 (Fisher's Exact Test), serum HDL, p=0.382 (Fisher's Exact Test), serum LDL, p=0.111 (Fisher's Exact Test) and serum VLDL, p=0.395 (Fisher's Exact Test) respectively.

Table 1: Socio-demographic parameters of the children

Parameter		Number	Percentage
Gender	Female	128	64.0
	Male	72	36.0
Age group (years)	0-4	5	2.5
	5-9	40	20.0
	10-14	81	40.5
	⩾15	74	37.0
Social class	I	13	6.5
	II	38	19.0
	III	88	44.0
	IV	55	27.5
	V	6	3.0
	Total	200	100.0

Table 2: Physical parameters of the children

Parameter	Minimum	Maximum	Mean	Median	Standard deviation	Variance
Age (years)	4	17	12.4	13.0	3.6	12.8
Weight (kilograms)	13.0	72.0	37.3	39.0	12.9	165.6
Height (centimetres)	100.0	182.0	144.1	148.0	17.3	299.4
Waist circumference (centimetres)	47.0	96.0	62.7	63.0	7.4	54.7
Systolic blood pressure(mmHg)	66	163	103	103	15.6	244.3
Diastolic blood pressure(mmHg)	33	100	64.9	65	11.2	125.1

Table 3: Relationships of physical parameters and eGFR (ml/min/1.73m^2)of the children

Variables	eGFR<60 ml/min/1.73m^2 No (%)	eGFR ⩾60 ml/min/1.73m^2 No (%)	Total No (%)	*P* value
Age (years)				
0-4	1(0.5)	4(2.0)	5(2.5)	0.091
5-9	8(4.0)	32(16.0)	40(20.0)	
10-14	6(3.0)	75(37.5)	81(40.5)	
⩾15	5(2.5)	69(34.5)	74(37.0)	
Gender				
Male	3(1.5)	125(62.5)	128(64.0)	**0.0001***
Female	17(8.5)	55(27.5)	72(36.0)	
Waist circum-Ference				
40-60	13(6.5)	62(31.0)	75(37.5)	**0.003***
>60-80	6(3.0)	117(58.5)	123(61.5)	
>80-100	1(0.5)	1(0.5)	2(1.0)	
Body mass Index				
Underweight	1(0.5)	8(4.0)	9(4.5)	0.940
Normal	19(9.5)	171(85.5)	190(95.0)	
Overweight/obese	0(0.0)	1(0.5)	1(0.5)	
Systolic blood pressure (mmHg)				
60-120	18(9.0)	158(79.0)	176(88.0)	0.772
121-180	2(1.0)	22(11.0)	24(12.0)	
Diastolic blood pressure (mmHg)				
30-75	16(8.0)	151(75.5)	167(83.5)	0.750**
>75	4(2.0)	29(24.5)	33(16.5)	
Total	20(10.0)	180(90.0)	200(100.0)	

*=Significant values **=Fisher's exact test

Table 4: Relationship between social parameters and eGFR (ml/min/1.73m^2)of the 200 children

Variables		eGFR<60 ml/min/1.73m^2 No (%)	eGFR⩾60 ml/min/1.73m^2 No (%)	Total No (%)	*P* value
	I	0(0.0)	13(6.5)	13(6.5)	0.353
	II	5(2.5)	33(16.5)	38(19.0)	
	III	6(3.0)	82(42.0)	88(44.0)	
	IV	8(4.0)	47(23.5)	55(27.5)	
	V	1(0.5)	5(2.5)	6(3.0%)	
Family history of CKD	None	20(10.0)	143(71.5)	163(81.5)	0.080
	Positive	0(0.0)	16(8.0)	16(8.0)	
	Unknown	0(0.0)	21(10.5)	21(10.5)	
	Total	20(10.0)	180(90.0)	200(100.0)	

CKD=chronic kidney disease

Table 5: Relationships between laboratory parameters and eGFR (ml/min/1.73m^2) of the 200 children.

Variables		eGFR<60 ml/min/1.73m^2 (%)	eGFR⩾60 ml/min/1.73m^2 (%)	Total (%)	*P* value
Serum urea (mmol/l)	2.0-7.0	18(9.0)	177(88.5)	195(97.5)	0.646**
	>7.0	2(1.00)	3(1.5)	5(2.5)	
Serum creatininine (µmol/l)	50-115	20(10.0)	179(89.5)	199(99.5)	0.900**
	>115	0(0.0)	1(0.5)	1(0.5)	
Serum cholesterol (mmol/l)	3.5-6.5	20(10.0)	165(82.5)	185(92.5)	0.194**
	>6.5	0(0.0)	15(7.5)	15(7.5)	
Serum triglycerides (mmol/l)	0.4-2.0	19(9.5)	160(80.0)	179(89.5)	0.350**
	>2.0	1(0.5)	20(10.0)	21(10.5)	
SerumHDL (mmol/l)	<0.9	9(4.5)	70(35.0)	79(39.5)	0.382**
	⩾0.9	11(5.5)	110(55.0)	121(60.5)	
Serum LDL	1.5-3.5	11(5.5)	128(64.0)	139(69.6)	0.111**
	⩾3.5	9(4.5)	52(26.0)	61(30.5)	
Serum VLDL	0.4-0.6	8(4.0)	62(31.0)	70(35.5)	0.395**
	⩾0.6	12(6.0)	118(59.0)	130(65.5)	
	Total	20(10.0)	180(90.0)	200(100.0)	

HDL=High density lipoprotein LDL=Low density lipoprotein VLDL=Very low density lipoprotein **=Fisher's Exact Test

Discussion

The appropriate and accurate methods of measurement of GFR require the use of exogenous substances such as inulin, Cr51-EDTA, iohexol and iothalamate for the determination of renal clearance, but these methods are time consuming, very expensive, invasive and impractical for daily clinical practice in children. Consequently, measuring serum concentrations of endogenous markers of renal function like creatinine or the low molecular weight protein cystatin C is used routinely to estimate GFR.[25]

The updated Schwartz formula has been validated in children with normal renal function for use in determining the eGFR for children and adolescents.[26-27] It has been described as the "best creatinine based-GFR equation for all children" by the United States National Kidney Disease Education Program (NKDEP).[28] In this study, using this formula, the mean and median eGFR of 82.8±17.7ml/min/1.73m^2 and 81.0±17.7ml/min/1.73m^2 respectively is lower than 99.6±19.7ml/min/1.73m^2 and 98.5±19.7ml/min/1.73m^2 obtained by Gheissari *et al*[3] in a study of 712 healthy Iranian children aged between seven and 18 years, and a mean of 129.4±23.1ml/min/1.73m^2 among a population based field study of 3622 children aged 5-18 years in Turkey.[4] In Nigeria, Okoro and Onwuameze[5] obtained a mean GFR of 112±31ml/min/1.73m^2 while Ibitoye *et al*[6] reported a mean of 126.6±20.2ml/min/1.73m^2 among children in Sokoto, north western Nigeria. This later study's value was from a control group of children with Hb genotype AA. On the contrary, our values are higher than the 60±34.4ml/min/1.73m^2 reported by Ocheke[7] in Jos, north central Nigeria in a prospective study of 100 Hb AA patients who served as controls in a study of estimated GFR in sickle cell anaemia patients. These differences may be as a result of differences in the characteristics of the sampled populations. Sharma AP *et al*[29] and Filler G[30] in their studies have documented that the demographic and the clinical status of a population can significantly affect the accuracy of eGFR obtained using the formula. This also may probably explain why we obtained a higher prevalence (10.0%) of CKD when compared with the 1.3% reported in the Iranian study[4] and 0.26% in another Turkish study.[31]

Our study's lack of a significant association between increased eGFR and age contrasts with the findings of previous studies[5,8] who reported that there's a linear increase of eGFR with age between 1 year and 14 years. Females had a higher eGFR in this study, different from the findings of Koulouridis *et al*[9] where boys showed higher eGFR rates than girls but agrees with the findings from a community based Iranian study[22] of healthy children and adolescents like ours where females had higher eGFR than males. Body mass index (BMI) also did not have an effect on the eGFR in this study, although a larger waist circumference (which could be a marker of obesity),was significantly associated with a lower eGFR. This could be because most of the study participants had a normal BMI. This was a similar finding by Sharma *et*al[10] who documented that eGFR did not have a significant correlation with BMI in their study of 240 children. However, theirs was a cystatin C based study and the children had kidney diseases compared to the apparently healthy children in the index study. On the contrary, some studies[11-12,32] have reported increased BMI to be consistently associated with reduced eGFR. Kawamoto *et al*[11] study was in adults that were community-dwelling healthy persons while Miliku *et al.*[12] studied a large population of 6 year olds, therefore the narrow age category and the larger sample size could explain the findings. The systolic and diastolic blood pressures had no association with the eGFR in this study as compared to various adult studies that found hypertension to be associated with low eGFR.[13-16]

The relationship between socioeconomic status and eGFR has not been studied extensively in children as compared to adults. We did not find any significant association between the two in our study as also noted in the CKid study in children,[17] althoughchildren in social class III and IV had lower eGFR. In contrast, many adult studies report lower socioeconomic status to be associated with decreased kidney function.[18-21]

It has been documented that family history of end stage renal disease is an important risk factor for the subsequent development of nephropathy. This has been linked to certain genetic loci e.g. familial focal segmental glomerulosclerosis is linked to the 1q25-31, 11q21-22 and 19q13 loci in different families.[33] In the present study however, eGFR was not significantly associated with a family history of chronic kidney disease. Maybe, a lack of a proper understanding of the meaning of renal disease as information obtained from the subjects could explain

this.

In our study, the lipid profile not showing any relationship with eGFR contrasts the findings of other authors who documented that dyslipidaemia was associated with a decrease in eGFR.[9-11] Most likely these changes occur at the late stages of chronic kidney disease (CKD) but majority of our subjects were apparently healthy.

In conclusion, 10.0% apparently healthy children had eGFR< 60ml/min/1.73m^2. They were referred to the tertiary health facility in the State, where they are being followed up by the Paediatric Nephrologist. This finding suggests that there are a lot of asymptomatic children with impaired renal function, who would not present to the hospital until late. Female gender and a large waist circumference were the only factors that were significantly associated with a reduced eGFR.

We recommend a regular community based screening of children for CKD using this simple method. A larger, nationwide population based study and a longitudinal study of the subjects with low eGFR to see their outcome is desirable in future.

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Authors' contributions
Ikpeme EE conceived the study and wrote the manuscript. Dixon-Umo OT analysed the data and wrote up the results section. Okpokowouruk FS and Akpan MU actively participated in the data collection.

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