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Risk factors for chronic kidney disease in children attending pediatric outpatient clinic in federal medical center Asaba

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Abstract

Introduction: In Nigeria, chronic kidney disease (CKD) incidence in children ranges between 2-6 cases per annum. Management of CKD which includes dialysis and renal transplant (renal replacement therapy) is not easily obtainable and affordable in our environment. Identifying patients with increased risk and prompt treatment aimed at risk reduction, slow down the progression. Consequently, screening for early detection therefore becomes inevitable, even individuals who appear normal should be screened for modifiable CKD risk factors such as proteinuria, hypertension and obesity.
Objectives: To screen for risk factors for CKD in children attending paediatric outpatient clinic in Federal Medical Center Asaba.
Methods: It was a cross-sectional descriptive study in which all the children 3-16 years, attending the children outpatient clinic, and have satisfied the inclusion criteria were screened for proteinuria, hypertension and obesity, in the month of June 2014.
Results: A total of 298 children: 153 (51.3%) males and 145 (48.7%) were screened. Children (3-9 years) comprise 74.2% (221/298) while adolescents (10-16 years) were 25.8% (77/298), with a male to female ratio of 1:1.1. The median age of the children was 6 years and a range of 3-16 years. Risk factors for CKD (proteinuria, hypertension and obesity) were detected in 15.8% (47/298) children. The respective proportion of those with proteinuria, hypertension and obesity was 3.0% (9/298), 3.7% (11/298), 10.1% (30/298) and the presence of the risk factors for CKD has no age or gender predilection.
Conclusion: Risk factors for CKD exist in asymptomatic children, obesity being the most common.

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Introduction

The burden of renal disease in Nigerian children is becoming enormous with prevalence rate ranging from 1.1%-4.5% and those documented were urinary tract infection (UTI), acute glomerulonephritis (AGN) and nephrotic syndrome (1-4). These renal diseases culminate to chronic kidney disease (CKD) if not detected early and managed promptly. CKD is defined as abnormalities of kidney structure or function, present for 3 months, with implications for health (5). Markers of kidney damage include GFR <60 ml/min/1.73m^2, abnormalities in the composition of the blood or urine, or abnormalities in imaging tests (5). In Nigeria, CKD incidence in children ranges between 2-6 cases per annum (6,7). People with CKD risk are defined by estimated GFR ≥90 ml/min/1.73 m^2 with CKD risk factors (5). Once CKD is established, it progresses and becomes irreversible, because the adaptive hyperfiltration of the surviving nephrons leads to a vicious cycle of nephron loss (5). Identifying patients with increased risk and prompt treatment aimed at risk reduction, slow down the progression (5). Management of CKD which includes dialysis and renal transplantation is not easily obtainable and affordable in our environment. Preventive nephrology becomes the only feasible and reasonable approach to curbing the menace of renal disease. Consequently, screening for early detection therefore becomes inevitable, even individuals who appear normal should be screened for such modifiable risk factors for CKD; proteinuria, hypertension and obesity (5).

The prevalence of isolated proteinuria in as-

Core tip
The risks of chronic kidney disease (CKD) exist in asymptomatic children and these can be detected early and preventive measures instituted.

ymptomatic children 5-15 years old in Nepal was 3.5% (8) and 0.2% on second screening and in Egypt (9), 0.1% of persistent proteinuria was documented in those 6-13 years of age on second screening.

Hypertension has been identified as being common in children especially in adolescents; 5.4% in Enugu Nigeria (10) and 5.7% in Ludhiana India (11). In preschool age (3-5 years), the prevalence of hypertension was 1.9% in Enugu Nigeria (12), while in Surat India it was 6.5% in 6-18 years children population (13). Hypertension was reported in 21% of children 8-13 years of age in Texas (14) while in Ohio, it was 3.6% in children 3-18 years of age (15).

Obesity is also on the increase although such findings were largely on adolescent population. In Enugu Nigeria, children 3-5 years of age have a prevalence of 0.5% (12), 1.7% in 2-15 years age group (16) and 1.9% in those 11-18 years of age (10). Similar studies in Nigerian adolescents documented 1.4% in Sokoto (17), 5% in Abeokuta (18) and 9.4% in Lagos (19).

Proteinuria follows adaptive hyperfiltration of the surviving glomeruli with increase in single nephron glomerular filtration rate (SNGFR) sequel to glomerular injury from any etiology (20). Accumulation of protein within the mesangium leads to mesangial hyperplasia, infiltration of monocytes/macrophages with elaboration of mediators of chronic inflammation and fibrosis (notably transforming growth factor β, IL-6, fibroblast growth factor), further sclerosis occurs, more nephrons are lost and a vicious cycle of increasing glomerular blood flow and hyperfiltration. Uncontrolled systemic hypertension can cause arteriolar nephrosclerosis and hyperfiltration (20). Glomerulopathy in form of focal segmental glomerulosclerosis occurs in obesity sequel to glomerular hyperperfusion and hyperfiltration from afferent arteriolar vasodilatation mediated by hyperinsulinemia (a marker of a reduced insulin sensitivity) (21). Insulin also increases the effects of angiotensin II on mesangial cells thus contributing to hypertension, raised intraglomerular pressure, exacerbation of proteinuria, induction of intrarenal inflammatory cytokines and growth factors, and apoptosis (21)with resultant fewer functioning nephrons and increase in SNGFR (20). Burden of CKD can be reduced by reduction in proteinuria, hypertension and obesity (5,13).

This study will provide the basis for screening apparently healthy children in the community.

Patients and Methods

This study was carried out in the FMC Asaba, located in Asaba, the capital of Delta State. The FMC, Asaba is one of the tertiary hospital facilities in the state with multidisciplinary departments and carters for patients from Delta and Anambra states.

It was a descriptive study in which all the children 3 to 16 years attending children outpatient clinic, and have satisfied the inclusion criteria (not a known CKD patient) were enrolled, over a month period (June 2014). The children were stratified into 4 groups: 3-5 years (preschool), 6-9 years (childhood), 10-13 years (early adolescence) and 14-16 years (middle adolescence). The care giver provided such information as age, sex, presenting complaints etc were obtained using the case record form. Weight, height and blood pressure were measured and documented. Random urine sample was collected from each subject and analyzed using the Multistix; urinalysis reagent strip, Mission® Expert (ACON Laboratories, Inc San Diego, USA) batch number 1150537502 with sensitivity and specificity of 95% and 99% respectively.

The subjects were given a universal container to collect their urine. Urinary dipstick was used to screen the urine for protein (22). Significant proteinuria with dipstick was defined as 1+ of proteinuria on urine dipstick if the specific gravity is ≤1.015 or 2+ of proteinuria if the urine specific gravity is >1.015(23). For accurate interpretation of proteinuria with urinary dipstick, children with axillary temperature ≥38°C were excluded (24) so also those with alkaline urine, glycosuria (25), and UTI (using the same urinary dipstick) (26). The urine of such children were tested again after one week for re-evaluation.

Blood pressure of the subjects was measured after they were seated for at least 5 minutes, using the ACCOSON mercury sphygmomanometer (Essex CM19 5QP, DEKAMET MK.3, England) with appropriate cuff sizes. Hypertension was defined as average systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) that is 95th percentile for gender, age, and height on 3 occasions. While prehypertension in children was defined as average SBP or DBP levels that are 90th percentile but below 95th percentile or adolescents with BP levels 120/80 mm Hg (27).

Thereafter, health weighing scale and Stadiometer (RTZ-120A, HECOS, China) combined measuring instrument was used for measuring the weight and the height respectively. The weight was measured to the nearest 0.1 kg with subjects on light clothing and without footwear. The standing height was measured to the nearest 0.1 cm, with the subject's head, buttocks and heel touching the metallic measuring tape fixed horizontally on the instrument. None of the subjects had their footwear on them. The body mass index (BMI) for age and sex was computed using weight (kg)/height^2 (m^2) (28). Obesity was defined as BMI for age of 95th percentile or more using the World Health Organization (WHO) child growth standard chart (28).

Children who have no identifiable risk for CKD continued with their regular clinic appointment, whereas those with risk factors including those with non-significant proteinuria, were given appointment to visit the paediatric nephrology clinic within 1-4 weeks.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. Informed consent was obtained and the research was approved by the Ethics Committee of Federal Medical Center, Asaba.

Statistical methods

The data was analyzed using SPSS version 20 and results expressed in frequency tables. Chi-square and Fisher exact

tests (where applicable) were used to test significance of association between categorical variables. For any comparison of variable, *P* is significant at a value <0.05.

Results

A total of 298 children: 153 (51.3%) males and 145 females (48.7%) were screened (Table 1). Children (3-9 years) comprise 74.2% (221/298) while adolescents (10-16 years) were 25.8% (77/298) (Table 1), with a male to female ratio of 1:1.1. The median age of the children was 6 years and a range of 3-16 years. The mean SBP, DBP and BMI of the study population were higher in those subjects with risk factors for CKD, as shown in Table 1. Risk factors for CKD (proteinuria, hypertension and obesity) were detected in 15.8% (47/298) children, one child had all the three risk factors and one had both hypertension and obesity. The respective prevalence of those with proteinuria, hypertension and obesity was 3.0% (9/298), 3.7% (11/298) and 10.1% (30/298) as shown in Table 2. The presence of the risk factors for CKD has no gender predilection (Table 2) while those who were obese were younger (Table 3).

Proteinuria was present in 14.8% (44/298) of the children and out of this number, 35 had 1+ of proteinuria in the presence of high specific gravity either alone or in association with other confounding factors: fever, UTI, alkaline urine or glycosuria. Thus the proportion with significantly clinical proteinuria was 3.0% (9/298). Diastolic hypertension was noted in 2.7% (8/298), systolic hypertension in 0.7% (2/298) while 0.3% (1/298) had both.

Only 6 out of the 9 children with significant proteinuria were seen at follow up, 2 still had 1+ (persistent proteinuria of 0.8%, 2/298) and were to be seen after 3 months following which further investigations such as serum creatinine estimation and urine protein quantitation may be needed. Only 10 with confounding factors had a second screening and all were negative. Two with obesity are on follow up in paediatric endocrinology clinic while the rest including those with hypertension were lost to follow up.

Table 1. Demographic characteristics of the study population and CKD risk factors

General characteristics	CKD risk factors, n=47	No CKD risk factors, n=251	Total (%)
Age groups			
3-5 years	21 (44.7)	111 (44.2)	132 (44.3)
6-9 years	18 (38.3)	71 (28.3)	89 (29.9)
10-13 years	6 (12.8)	48 (19.1)	54 (18.1)
14-16 years	2 (4.3)	21 (8.4)	23 (7.7)
χ^2 (*P* value)	3.080 (0.379)		
Gender			
Male	24 (51.1)	129 (51.4)	153 (51.3)
Female	23 (48.9)	122 (48.6)	145 (48.7)
χ^2 (*P* value)	0.002 (0.967)		
Mean parameters (SD)			***P* value**
Age in years	6.6 (3.1)	7.1 (3.7)	0.347
SBP in mm Hg (SD)	93 (16)	88 (14)	0.015
DBP in mm Hg (SD)	60 (11)	56 (9)	0.009
BMI in kg/m^2	20 (4)	16 (2)	<0.0001

Abbreviations: BMI, body mass index; SBP systolic blood pressure; DBP, diastolic blood pressure; CKD, chronic kidney disease.

Table 2. Age and gender distribution of children and prevalence of different CKD risk factors

Parameters	CKD risk factors		
	Obesity, n=30	Hypertension, n=11	Proteinuria, n=9
Age group			
3-5 years	16 (53.3)	5 (45.5)	1 (11.1)
6-9 years	11 (36.7)	3 (27.3)	4 (44.4)
10-13 years	3 (10.0)	2 (18.2)	3 (33.3)
14-16 years	0	1 (9.1)	1 (11.1)
Prevalence in %	10.1	3.7	3.0
P value	0.178	0.996	0.232
Gender			
Male	15 (50.0)	6 (54.5)	3 (33.3)
Female	15 (50.0)	5 (45.5)	6 (66.7)
P value	0.877	0.829	0.272

Abbreviation: CKD, chronic kidney disease.

Discussion

Risk for CKD exists among the study population. The 3.0% prevalence for proteinuria is of considerable importance although persistent proteinuria could not be commented on categorically since only 67% of the subject came back for follow up. However, the prevalence is comparable to the 3.5% in the initial screening of school children in Nepal as reported by Parakh et al who also documented 0.2% of persistent proteinuria in the same population (8). But in comparison to the study by Bakr et al in Egyptian school children 6-13 years (9), it is quite high and the difference could be because the index study reported prevalence in initial screening while the other was on second screening (9).

The prevalence of hypertension was 3.7% which is almost the same with Hansen et al study in Ohio (3.6%) (10) although much higher when compared with 1.9% in preschool children by Odetunde et al in Nigeria (11). However, it is comparably lower than 5.4% in Nigeria by Ujunwa et al (12), 5.7% by Mohan and colleagues in India (13), both in adolescents and even much lower than 21% in preadolescents in Texas by Urrutia et al (14). This disparity may be explained by the inclusion of all children from preschool age up to middle adolescent and even the unequal distribution of the study population with less number of adolescents may be a factor. Although it seems that children contributed to the prevalence of hypertension more than the adolescents contrary to the general knowledge, it becomes pertinent that blood pressure monitoring should not be limited to adolescents alone but should be extended to children population. Another possibility is the white coat phenomenon which may have contributed to the seemingly higher contribution of children population to the prevalence of hypertension since other studies were conducted away from hospital setting. However, none of the subjects adhered to follow up making it difficult to substantiate this possibility (15).

Obesity was the most common CKD risk factor identi-

Table 3. Comparison of the mean age between children with CKD risk factors and those without CKD risk factors

Parameters	CKD risk factors					
	Obesity		Hypertension		Proteinuria	
	Yes	No	Yes	No	Yes	No
Mean age	6.1	7.2	7.2	7.1	8.8	7.0
SD	2.3	3.8	4.5	3.6	4.1	3.6
95% CI	5.20 to 6.93	6.72 to 7.62	4.18 to 10.18	6.63 to 7.47	5.66 to 11.89	6.58 to 7.42
Mean difference	-1.101		0.130		-1.774	
95% CI	-2.070 to -0.133		-2.08 to 2.34		-4.205 to 0.656	
t	-2.286		-0.115		-1.437	
P value	0.027		0.908		0.152	

Abbreviation: CKD, chronic kidney disease.

fied in 10% of the subjects. This is tremendously higher than 1.7% documented in Enugu Nigeria by Nwaiwu and Ibe who had similar study population (16). More so higher when compared with 0.5% in preschoolers (12) and a range of 1.4% to 5% (10,17,18) in adolescents, all in Nigeria. However, a similar prevalence rate of 9.4% in adolescents, was reported by Oduwole et al in Lagos (19). These show that the prevalence of obesity is increasing steadily in the society and that children and adolescent are both at risk. The existing trend in lifestyle modification towards westernization of day to day family dietary menu working in tandem with proliferation of pastry-based eatery kiosks has its contribution to this upsurge in malnutrition. The sedentary lifestyle encouraged by lack of school playground with resultant non-existent school physical exercises and the many computer-based children recreational activities have also played major roles (20-23).

Conclusion

Risk factors for CKD exist in asymptomatic children, obesity being the most common. Screening for such risk factors is recommended since they are modifiable.

Limitations of the study

This study is limited by the failure to follow up the subjects to confirm persistent hypertension and proteinuria, although effort is being made to reach them through their contact information.

Authors' contribution

BUE and IN conceived the study. IFN, IJN, OA, AA, EM and EM conducted the study and participated in the writing the primary draft. BUE edited the final paper. All authors read and sign the final manuscript.

Conflicts of interest

None to be declared.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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