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Renal Doppler values in healthy Nigerian children: Anthropometric variations

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The rising morbidity and mortality from end-stage renal disease (ESRD) among children in sub-Saharan Africa and Nigeria is now a primary health concern. Due to this, an accurate, simple, affordable, non-invasive method for early diagnosis of renal diseases in children is needed to prevent progression to ESRD. In this prospective, cross-sectional study among children with no evidence of clinical and pathologic abnormalities, we investigated the intrarenal Doppler indices and their relationship with participants' demographics. One hundred and thirty-one children with no clinical or laboratory pathologic abnormalities from age 3 to 10 years, and a total of 262 kidneys were evaluated. Significant statistical differences exist in the pulsatility index (PI), resistivity index (RI), and acceleration time (AT) among the different age groups of the studied children population. Children aged 2 to 3 years had statistically significant higher PI (mean = 0.99, 95% CI of mean = 0.95; 1.04) than in children aged 7 to 8 years and 9 to 10 years (mean = 0.88, 95% CI of mean = 0.83; 0.94). The RI showed similar trend, while AT was also significant but in the opposite direction. Age, weight, and height showed significant correlations with PI, RI, AT, and Systolic/Diastolic ratio(S/D). Age and weight also had correlations with renal lengths. This study thus revealed that normative data for each age group were reasonably similar to those from other parts of the world. Intra-renal PI, RI, and S/D declines with age but stabilize at 6 to 8 years. The parameters showed dependency on age, weight, and height in normal healthy children.

Key words: Healthy children, Doppler, renal disease, reference values.

INTRODUCTION

Recently, early diagnosis of renal health status in children has been the focus because of complications, like chronic renal disease, that may result from improperly treated acute kidney injury cases either from delayed diagnosis or lack of affordable treatment options. Chronic kidney disease (CKD), the end of the spectrum of renal diseases, is a significant health problem throughout the world with increasing incidence and prevalence (Brück et al., 2015; Neuen et al., 2017; Ladapo et al., 2014). The prevalence of the early stages of CKD to CKD stage II in children is about 18.5-58.3 per million children globally (Gulati, 2018) with a steady rising incidence in recent years, especially in developing countries (Coresh and Jafar, 2015; Thomas et al., 2015). The burden of renal

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disease is, however, more common in black individuals with about three times higher incidence of CKD or progression rate to End Stage Renal Diseases (ESRD) than in white individuals (Bock et al., 2019). The differences may be due to; genetic susceptibility (Lipkowitz et al., 2013), socioeconomic problems, and limited access to medical care. Other causes of childhood renal damage in sub-Saharan Africa (SSA) include schistosomiasis, post-infectious glomerulonephritis, HIV-related nephropathy, malaria, and sickle cell disease (Halle et al., 2017; Anigilaje et al., 2019; Asinobi et al., 2014).

The resultant ESRD has, therefore, become a significant cause of morbidity and mortality among children in sub-Saharan Africa, with a high mortality rate recorded in Nigeria (Anigilaje et al., 2019; Ademola et al., 2019).

Given the high morbidity and mortality associated with renal disease and the enormity of resources needed for treatment, particularly in low-income settings, there is need for a simple, affordable, non-invasive but accurate method for early diagnosis of early renal diseases in children.

Among other investigative modalities, Doppler sonography of the renal arteries has emerged as a non-invasive technique to evaluate the renal blood flow and impedance, which are both affected in renal diseases. Additionally, the steady technological improvement in recent years, increasingly affordable, and portability of new ultrasonographic scanners has now made Doppler ultrasound (DUS) a frequently used screening tool in patients with suspected renal diseases (Choi et al., 2017; Hansen et al., 2016; Gameraddin, 2019). Doppler sonography provides a non-invasive high-quality method of evaluation of the main renal and intrarenal blood flow, and also allows measurements of blood flow velocity and changes that are important in the evaluation of several kidney diseases (Correas et al., 2016; Spatola and Andrulli, 2016). These measurements include estimates of peak systolic velocity (PSV), end-diastolic velocity (EDV), time-averaged maximum velocity (TAM) and the commonly used Doppler indices; Pulsatility index (PI) and resistance index (RI) and systolic/diastolic velocity (S/D) ratio (Drelich-Zbroja et al., 2018; Oglat et al., 2018). The RI and the PI provide reliable information about blood flow and resistance that is not affected by the effect of variation in vessel angulation and size (Oglat et al., 2018).

Researchers in other climes have documented age related dependency of the renal Doppler indices in children. While Kuzmic et al. (2000) reported that children younger than six years of age have a RI higher than the standard upper limit value of RI (0.7) in adults. Other studies also showed that intrarenal RI serves prognostic and therapeutic implications (Maksoud et al., 2019; Lai et al., 2016). Furthermore, renal RI, PI, and SD ratio have been found useful in the detection of acute rejection of kidney allograft and acute tubular necrosis (Meier et al., 2017; Bagheri et al., 2019).

In pediatric nephrology, Doppler investigation has diagnosed several renal and reno-vascular diseases and other conditions. A previous study among Nigerian children with acute falciparum malaria documented that acute falciparum malaria may affect the renal vessel diameter and intra-renal blood flow indices (Adekanmi et al., 2015). A study by Shokeir et al. (1997) also showed that in children with equivocal obstructive uropathy, the RI could differentiate obstructive from non-obstructive cases. Although there are several studies on Doppler velocimetry changes in abnormal renal conditions (Lai et al., 2016; Meier et al., 2017; Bagheri et al., 2019; Shokeir et al., 1997; Esther and Kim, 2016), there is still a lacuna in the knowledge of the physiological and anatomical factors that contribute to renal blood flow patterns and changes (Viazzi et al., 2014). Thus, having a baseline reference values for intrarenal arterial Doppler parameters will be necessary to determine abnormal renal Doppler changes in children with renal pathology (Sigirci et al., 2006). There is no data on the reference values of renal indices amongst children, particularly in sub-Sahara Africa, to our knowledge. There is a need for standard reference Doppler indices of the renal flow that may serve as a baseline for recognition of abnormal renal Doppler indices and by inference renal disease among Nigerian children with no otherwise known clinical or laboratory pathologic abnormalities.

METHODOLOGY

For this study, we obtained ethical approval from our Institution's Ethical Review Committee. A total of one hundred and thirty-one healthy school-age children, aged from 3 to 10 years, comprising of 77 girls and 56 boys. Consent was sought from the school authorities of the selected nursery and primary school in a major city in Southwest Nigeria and, more importantly, from the parents/caregivers through letters written through the school authorities. Those pupils whose parents/caregivers gave consent participated in the study. A convenience sampling method was adopted to achieve a relatively even spread in terms of age and gender.

Healthy children with no history or symptomatology of chronic illness, those without ongoing symptoms of febrile illness on clinical examination or recent history of febrile illness were selected. The height of participants was measured in centimeters while standing erect against a stadiometer.

While the children's weights were measured with a bathroom weighing scale that has been zero balanced and recorded in kilograms, each child had about 5 ml of venous blood for laboratory tests for malaria parasite, hemoglobinopathy, and renal function tests. Children included in the study had no febrile illness, no recent history of febrile illness, negative malaria parasite test, Haemoglobin AA genotype, normal range electrolyte, urea, and creatinine levels and ultrasonographically normal kidney at the first scans. Those with deranged electrolyte, urea, and creatine and renal anomalies on renal ultrasound were exempted but referred to the appropriate unit at the University College Hospital, Ibadan, for expert management.

Doppler Ultrasonography of selected participants was carried out

Table 1. Characteristics of the study population.

Variable	Mean ± SD	Median (IQR)	Min - Max
Age in years	6.02 ± 2.11	6.0 (4.0 - 8.0)	3.0 - 10.0
Weight (kg)	19.6 ± 5.11	19.0 (15 - 23)	11.0 - 32.0
Height (m)	1.12 ± 0.14	1.12 (1.01 - 1.23)	0.82 - 1.37
Length right kidney	7.39 ± 0.89	7.37 (6.75 - 8.01)	4.67 - 9.50
Length left kidney	7.85 ± 0.85	7.80 (7.26 - 8.44)	5.78 - 10.0
Serum urea	23.9 ± 6.09	23.0 (19.0 - 29.0)	15.0 - 41.0
Serum creatinine	0.60 ± 0.21	0.60 (0.45 - 0.70)	0.20 - 1.2

in the prone /semi decubitus position using a portable Colour Doppler Micromax Sonosite Inc. Bothell, WA, USA ultrasound scanner with a 3.5 to 5 MHz convex transducer. All children were scanned during quiet breathing by the same radiologist, to exclude interobserver error. No sedative agent was administered in this study.

All subjects had an initial scan to document the renal size, position, and parenchymal echogenicity. Furthermore, those with normal renal sonographic features enrolled. With the aid of Colour flow sonography, the main renal vessels were localized, and the renal artery and vein diameter of three measurements recorded in centimeters. After that, we applied the spectral Doppler, and the mean of 3 wave patterns recorded as flow velocities for each kidney. Similarly, we interrogated the interlobar intrarenal arteries with a duplex scan, and spectral wave-pattern generated for each artery. The peak systolic, diastolic, the systolic/diastolic velocity ratio (S/D ratio), pulsatility index (PI), and resistant index (RI) were then automatically generated or traced manually in appropriate cases. The average of three waveforms Doppler parameters was recorded and used for statistical analysis.

Data analysis

The data generated was entered and analyzed using the Statistical Package for Social Sciences (SPSS) software version 23 (SPSS inc. Chicago, IL, USA.). Tables, means ± standard deviation, median and interquatile range (IQR) were used to present the results of the anthropometric characteristics, the renal vessels, and Doppler parameters. We employed the one-way analysis of variance using appropriate post-hoc test to explore the mean differences in Doppler velocimetry and the main renal artery and vein dimensions between age groups. Also, Pearson's correlation was used to determine the correlation between renal Doppler velocimetry and age height and weight, respectively. P-value < 0.05 were considered statistically significant.

RESULTS

A total of one hundred and thirty-one children participated in this study. As shown in Table 1, the mean age of participants was 6.02 ± 2.11 years, with an average weight of 19.6 ± 5.11 kg. The height of participants ranges from 0.82 m to 1.37 m, with a mean height of 1.12 ± 0.14 m. 56 (42.7%) were males, while females constitute 57.3% (75/131).

Evaluation of the main renal vein and arteries in Table 2 showed that there was statistically significant difference

in the kidney main vein diameter among age groups of healthy children participants. Participants from age 9 to 10 years had statistically significant larger left renal vein diameter (mean = 0.74, 95% CI of mean = 0.67; 0.81) than in children who were 7 to 8 years old (mean = 0.63, 95% CI of mean = 0.57; 0.68), children aged 5 to 6 years (mean = 0.62, 95% CI of mean = 0.57; 0.67) and children aged 3 to 4 years (mean = 0.59, 95% CI of mean = 0.55; 0.64) respectively p=0.006.

There was a statistically significant difference in PI among age groups of healthy children in this study p = 0.002. Participants that were 2 to 3 years old had statistically significant higher PI (mean = 0.99, 95% CI of mean = 0.95; 1.04) than in children whose ages were from 7 to 8 years (mean = 0.91, 95% CI of mean = 0.87; 0.94) and children from age 9 to 10 years (mean = 0.88, 95% CI of mean = 0.83; 0.94) respectively. Similarly, there was a statistically significant difference in RI among age groups of healthy children in this study p<0.001. Participants that were 2 to 3 years old had statistically significant higher RI (mean = 0.63, 95% CI of mean = 0.61; 0.64) than in children between the ages of 7 to 8 years (mean = 0.59, 95% CI of mean = 0.58; 0.61) and children between ages 9 to 10 years (mean = 0.56, 95% CI of mean = 0.53; 0.59) respectively. There was also a statistically significant difference in AT among the age groups of healthy children studied, p=0.010. Participants between the ages of 2 to 3 years had statistically significant lower AT (mean = 63.1, 95% CI of mean = 55.8; 70.3) than in children from age 7 to 8 years (mean = 82.7, 95% CI of mean = 70.9; 94.5). (Table 3)

Age in years showed statistically significant correlations with EDV (r = 194, p = 0.029), kidney PI (r = -0.335, p<0.001), RI (r = -0.429, p<0.001), AT (r = 0.245, p=0.005), S/D (r = -0.247, p=0.005) and renal length (r = 0.657, p<0.001). (r = -0.211, p=0.016), kidney RI (r = -0.381, p<0.01), kidney AT (r = 0.197, p=0.024), kidney S/D (r = -0.204, p=0.021) and kidney length (r = 0.627, p<0.001) showed correlation with weight. Also, there was statistically significant correlation between height and intra-renal PI (r = -0.215, p= 0.014), RI (r= -0.307, p<0.001), and AT (r = 0.236, p = 0.007) respectively (Table 4).

Table 2. Main renal artery and vein dimensions versus age group among the study population.

Renal vessel diameter	3 to 4 years (Grp1) Mean (95% CI for the mean)	5 to 6 years (Grp2) Mean (95% CI for the mean)	7 to 8 years (Grp3) Mean (95% CI for the mean)	9 to 10 years (Grp4) Mean (95% CI for the mean)	p-value	Post Hoc test
Right renal artery (cm)	0.49 (0.45; 0.53)	0.54 (0.49; 0.59)	0.51 (0.47; 0.55)	0.57 (0.51; 0.62)	0.063	
Left renal artery (cm)	0.51 (0.47; 0.55)	0.54 (0.50; 0.58)	0.53 (0.49; 0.57)	0.59 (0.55; 0.63)	0.075	
Right renal vein (cm)	0.59 (0.54; 0.64)	0.62 (0.58; 0.67)	0.63 (0.58; 0.69	0.71 (0.65; 0.77)	0.023	Grp1<Grp4
Left renal vein (cm)	0.59 (0.55; 0.64)	0.62 (0.57; 0.67)	0.63 (0.57; 0.68)	0.74 (0.67; 0.81)	0.006	Grp1, Grp2 and Grp3< Grp4
Renal vessel flow						
Right renal artery velocity (cm/s)	88.0 (78.3; 97.7)	96.0 (87.7; 104.3)	103.5 (92.9; 114.0)	100.1 (92.3; 107.8)	0.137	
Left renal artery velocity (cm/s)	89.6 (80.7; 98.5)	99.4 (89.3; 109.4)	95.0 (85.2; 104.8)	103.5 (96.0; 110.9)	0.208	
Right renal vein velocity (cm/s)	33.4 (29.2; 37.7)	35.6 (31.6; 39.6)	41.0 (35.1; 46.9)	37.1 (31.8; 42.4)	0.122	
Left renal vein velocity (cm/s)	35.8 (31.3; 40.4)	38.0 (34.0; 42.1)	36.9 (33.1; 40.7)	38.3 (34.1; 42.5)	0.832	

Table 3. Intrarenal Doppler parameters versus age group among the study population.

Doppler parameter	Age groups of children in years				p-value	Post Hoc test
	3 to 4 (Grp1) Mean (95% CI for the mean)	5 to 6 (Grp2) Mean (95% CI for the mean)	7 to 8 (Grp3) Mean (95% CI for the mean)	9 to 10 (Grp4) Mean (95% CI for the mean)		
TAM	16.7 (14.5; 18.9)	17.1 (15.4; 18.7)	18.3 (16.5; 20.2)	17.7 (15.4; 20.0)	0.627	
PSV	55.4 (49.3; 61.4)	56.1 (51.2; 60.9)	58.3 (53.4; 63.2)	58.4 (51.2; 65.7)	0.817	
EDV	19.7 (17.4; 22.0)	22.9 (19.3; 26.5)	22.7 (20.6; 24.9)	24.0 (21.2; 26.8)	0.133	
PI	0.99 (0.95; 1.04)	0.95 (0.90; 0.99)	0.91 (0.87; 0.94)	0.88 (0.83; 0.94)	0.002	Grp1>Grp3 and Grp4
RI	0.63 (0.61; 0.64)	0.60 (0.58; 0.62)	0.59 (0.58; 0.61)	0.56 (0.53; 0.59)	<0.001	Grp1>Grp3 and Grp4
AT	63.1 (55.8; 70.3)	79.0 (69.9; 88.2)	82.7 (70.9; 94.5)	80.6 (69.0; 92.2)	0.010	Grp1<Grp3
S/D	2.88 (2.69; 3.07)	2.59 (2.43; 2.75)	2.64 (2.46; 2.82)	2.47 (2.21; 2.73)	0.019	Grp1>Grp4

TAM= Time-averaged flow velocity mean, PSV = peak systolic volume, EDV= end-diastolic volume, PI- Pulsatility index, RI= resistivity index, AT= Acceleration time, S/D= Systolic/ Diastolic ratio.

DISCUSSION

Renal disease can cause morphological and physiological changes in the kidney. The knowledge of the normal limits of renal features like renal size and renal Doppler velocimetry in healthy children would be useful for identifying abnormal conditions in children. In this current study, we sonographically evaluated the left and right kidneys of healthy children aged 3 to 10 years. Previous reports on renal arteries documented the artery diameter to be between 0.5 to 0.6 cm (Tuncay et al., 2011). This was confirmed by findings from this study which showed a main renal artery mean range of (0.49 cm, 95% CI of mean: 0.45 cm; 0.53 cm) to (0.57 cm, 95% CI of mean: 0.51 cm; 0.62 cm) on the right and (0.51 cm, 95% CI of mean: 0.47 cm;

Table 4. Correlation between anthropometric measurements and Doppler parameters.

Variable	Age (years)		Weight (kg)		Height (m)	
	Correlation coefficient (r)	p-value	Correlation coefficient (r)	p-value	Correlation coefficient (r)	p-value
Kidney Length	0.657	<0.001	0.627	<0.001	0.675	<0.001
TAM	0.127	0.156	-0.131	0.141	0.010	0.914
PSV	0.103	0.250	-0.132	0.137	0.011	0.903
EDV	0.194	0.029	-0.009	0.917	0.055	0.534
PI	-0.335	<0.001	-0.211	0.016	-0.215	0.014
RI	-0.429	<0.001	-0.381	<0.001	-0.307	<0.001
AT	0.245	0.005	0.197	0.024	0.236	0.007
S/D	-0.247	0.005	-0.204	0.021	-0. 111	0.212

TAM= Time-averaged flow velocity mean, PSV = peak systolic volume, EDV= end-diastolic volume, PI- Pulsatility index, RI= resistivity index, AT= Acceleration time, S/D= Systolic/ Diastolic ratio.

0.55 cm) to (0.59 cm, 95% CI of mean: 0.55 cm; 0.63 cm) on the left among the various age groups.

In this present study, although no significant difference exists between the main renal artery diameter among the various age groups, the age of subjects and the main renal artery showed a statistically significant correlation (r= 0.173; p=0.049). This observation indicates an increase in arterial diameter with age, in line with the report of Chiaganama et al. (2013) of a 0.4 mm increase in renal artery diameter observed after 20 years, and that of Turba et al. (2009) that reported a 1 mm increase in renal artery diameter per decade.

The main renal vein diameter among older children was significantly larger than in younger children (right, p = 0.023; left, p = 0.006), we presume this may be due to the corresponding increase in sizes of the renal vessels as the kidneys increases in size with age.

In concordance with a previous study, there was a significant correlation between age and renal artery flow velocity (r = 0.192, p=0.026) (Deeg et al., 2003). Deeg et al. (2003) reported a mean renal artery flow velocity of (51.5±13.4 cm/s) in infants, (71.3±13.5, in toddlers (80 ±18 cm/s) in school-age children and (80.7±13.7) in adolescents which is similar to our current study.

Previous studies have shown that renal Doppler indices in healthy children are significantly dependent on age (Kuzmic et al., 2000; Viazzi et al., 2014; Murat et al., 2005; Lin and Cher, 1997). In this current study, there was a negative correlation between age and RI (r = −0.429; p < 0.001), PI (r = −0.335; p < 0.001) and S/D ratio (r = -0.247, p=0.005). This may be related to increases in renal size with age, causing an increase in vascular diameter, cross-sectional area (Viazzi et al., 2014; Gudinchet et al., 1994). Furthermore, height and body weight also had statistically significant negative correlation with RI (height r = -0.307, p<0.001; weight -0.381, p<0.001), PI (height r = -0.215, p=0.014; weight r = -0.211, p=0.016) and S/D (weight r = -0.204, p=0.021) respectively in this present study. All healthy children

above 64 months had RI values below 0.7. The renal Doppler RI values in healthy children six years and above in this current study were also under the normal upper limit value of RI (0.70) seen in adults.

In contrast, Kuzmic et al. (2000) reported a decreasing renal RI from childhood that increases above 0.7 with age and later dropped to adult level at approximately six years of age, and therefore proposed the utilization of 0.70 RI as a threshold value for the increased renal vascular resistance in adults and children over six years of age. Sığırcı et al. (2006) and Murat et al. (2005) both in Turkey, reported younger ages of 54 and 42 months for RI to reduce to adult level respectively while Lin and Cher (1997), and Vade et al. (1993) in Turkey reported older ages of 128 and 120 months for RI to reduce to adult level respectively. Although there was a consistent reduction in RI with increasing age in this study, the values were consistently not up to RI of 0.7 seen in adults. More studies are needed to validate this result that the RI in Nigerian children does not reach the 0.7 thresholds.

Also, results from our study showed that the mean PI declined with increasing age and stabilized at eight years, similar to findings by Lin and Cher (1997), which reported a decline in the value of PI with increasing age in healthy children and then stabilized at 102 months. Sığırcı et al. (2006) reported a mean acceleration time of 89.2 ± 32.4 (unit) in children 1–6 years and 103 ± 26.5 (unit) in children 6–12 years having a significant positive correlation with age (r = 0.370). Acceleration time also had a statistically significant positive correlation with age in our study. However, the mean acceleration time values were 63.1 (55.8; 70.3) in children 3 to 4 years, 79.0 (69.9; 88.2) in children 5 to 6 years, 82.7 (70.9; 94.5) in children 7 to 8 years and 80.6 (69.0; 92.2) in children 9 to 10 years, which was lower than those reported by Sığırcı et al. (2006).

Taken together, the lower intrarenal Doppler values (RI, PI, and AT) in healthy Nigerian children, compared with

figures from studies in other climes, maybe due to racial differences.

Conclusion

In healthy Nigerian children, the intra-renal Doppler reference values are comparable to values btained in children in other parts of the world. Whilst the Doppler parameters varies with age, weight, and height, the maximum intrarenal RI value in Nigerian children does not exceed 0.7. Healthy normal Nigerian children intra-renal PI, RI, and S/D values decline with age and stabilizes at age 6 to 8 years.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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