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ORIGINAL ARTICLE

Left Ventricular Function and Geometry of Children with Chronic Kidney Disease (CKD) in a Resource-Poor Setting of Africa

Fonction et Géométrie du Ventricule Gauche des Enfants Atteints de Maladie Rénale Chronique (MRC) dans un Contexte Africain Pauvre En Ressources

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ABSTRACT

BACKGROUND: Chronic Kidney Disease (CKD) is a multi-systemic clinical condition characterized by an irreversible deterioration of renal function that invariably progresses to end-stage renal disease (ESRD). Cardiovascular affectation portends morbidity and mortality in chronic kidney disease.

OBJECTIVE: The aim of the study was to compare the prevalence of changes in function, and geometry of the left ventricle in children with CKD and their controls.

METHODOLOGY: This was a descriptive cross-sectional study. Children aged 6 to 17 years with features suggestive of CKD along with age and sex-matched apparently healthy controls seen at the University of Nigeria Teaching Hospital, Enugu were enrolled consecutively. Blood samples werecollected for baseline investigations and e-GFR, followed by trans-thoracic two-dimensional echocardiography to assess the left ventricular function and geometry. Data was analysed using the statistical package for social sciences (SPSS) version 17.0. Simple frequencies and proportions, Student's t-test and chi-square were applied appropriately. P value at <0.05 was significant.

RESULTS: Out of 9,419 children aged 6-17 years seen within the study period in the hospital, 24 met the criteria for CKD. The incidence rate was 5 cases per million child population per year. Mean age was 12.33 ± 4.24 years, with a male to female ratio of 2:1. Left ventricular hypertrophy (LVH), eccentric LVH and Left ventricular dilatation (LVD) were seen in 50.0%, 33.3% and 41.7% of subjects respectively. Left ventricular diastolic dysfunction and left ventricular systolic dysfunction occurred in 37.5% and 8.3% subjects, respectively.

CONCLUSION: Prevalence of left ventricular geometry and function abnormalities was high in subjects. Intervention measures are advocated. **WAJM 2022; 39(10): 1095–1103.**

Keywords: Left ventricular function, Left ventricular geometry, Chronic kidney disease, Children.

RÉSUMÉ

CONTEXTE: La maladie rénale chronique (MRC) est un état clinique multisystémique caractérisé par une détérioration irréversible de la fonction rénale qui évolue invariablement vers l'insuffisance rénale terminale (IRT). L'atteinte cardiovasculaire est un facteur de morbidité et de mortalité dans la maladie rénale chronique.

OBJECTIF: Le but de l'étude était de comparer la prévalence des changements de la fonction et de la géométrie du ventricule gauche chez les enfants atteints d'IRC et chez les témoins.

MÉTHODOLOGIE: Il s'agissait d'une étude descriptive transversale. Des enfants âgés de 6 à 17 ans présentant des caractéristiques suggérant une IRC, ainsi que des témoins apparemment sains, appariés par l'âge et le sexe, vus au University of Nigeria Teaching Hospital, Enugu, ont été inscrits consécutivement. Des échantillons de sang ont été prélevés pour les examens de base et l'e-GFR, suivis d'une échocardiographie trans-thoracique bidimensionnelle pour évaluer la fonction et la géométrie du ventricule gauche. Les données ont été analysées à l'aide du progiciel statistique pour les sciences sociales (SPSS) version 17.0. Les fréquences et proportions simples, le test t de Student et le chi-carré ont été appliqués de manière appropriée. La valeur P à <0,05 était significative.

RÉSULTAT: Sur les 9 419 enfants âgés de 6 à 17 ans vus à l'hôpital pendant la période d'étude, 24 répondaient aux critères de l'IRC. Le taux d'incidence était de 5 cas par million d'enfants par an. L'âge moyen était de 12,33 ± 4,24 ans, avec un rapport hommes/femmes de 2:1. Une hypertrophie ventriculaire gauche (HVG), une HVG excentrique et une dilatation ventriculaire gauche (DVG) ont été observées chez 50,0 %, 33,3 % et 41,7 % des sujets respectivement. Une dysfonction diastolique du ventricule gauche et une dysfonction systolique du ventricule gauche ont été observées chez 37,5 % et 8,3 % des sujets, respectivement.

CONCLUSION: La prévalence des anomalies de géométrie et de fonction du ventricule gauche était élevée chez les sujets. Des mesures d'intervention sont préconisées. **WAJM 2022; 39(10): 1095–1103.**

Mots clés: Fonction ventriculaire gauche, Géométrie ventriculaire gauche, Maladie rénale chronique, Enfants.

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INTRODUCTION

Chronic Kidney Disease (CKD) is a multi-systemic clinical condition characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease (ESRD). Chronic Kidney Disease is common in children older than 6years and now poses a serious public health challenge with increasing incidence, threatening to reach epidemic proportion over the next decade.[1,2] Worldwide, and especially in developed countries, CKD is a growing problem, with the associated cardiovascular disease contributing largely to the mortality.[3,4] Most of the patients in sub-Saharan Africa and other developing countries succumb early to this disease burden because of lack of treatment for both CKD and the associated cardiovascular abnormalities.[5–6] Mortality is about 30 times higher in patients with CKD than age matched population, contributed mainly by cardiovascular factors with higher figures from Africa.[5–7]

Cardiovascular disease often begins much earlier before ESRD sets in and patients with reduced kidney function are more likely to succumb on account of this complication.[8] There is a paucity of local studies on cardiovascular abnormalities in children with CKD in the sub-region. We therefore set out to study the prevalence and pattern of left ventricular function as well as the left ventricular geometry of this group of children in our sub-region. A good knowledge of this can be compared with findings from other parts of the world and could inform some interventional programmes which will reduce mortality in the group, a reduction in the overall child mortality and ultimately contribute to realization of MDG goal 4.

MATERIALS AND METHODS

Study Area

The study was carried out at the Paediatric Nephrology Clinic of the Children Out-Patient department (CHOP) and the Echocardiography room of the University of Nigeria Teaching Hospital (UNTH), Ituku-Ozalla, Enugu, South-East, Nigeria. The hospital serves as a major referral centre to the surrounding health facilities in the South-Eastern Nigeria and beyond. The Paediatric Nephrology clinic of UNTH offers services to patients from the catchment area of the hospital which is predominantly Enugu, South-East, Nigeria, with a population of 3.3 million (3,267,837) and children constitute 40% of the population.[9] All children with features of renal disorder are referred to the Paediatric Nephrology Clinic.

Ethical Clearance was obtained from the Independent Hospital Research and Ethical Committee (IHREC) of the UNTH and written informed consent and assent were obtained from parents and patients, where applicable.

Study Design

This was a descriptive, cross-sectional study of children aged 6 to 17 years with history, physical findings, and laboratory/ imaging findings suggestive of kidney disease lasting up to 3 months without any clinical features suggestive of primary cardiovascular disease (both congenital and acquired) and selected age and sex matched controls who were enrolled consecutively for the study.

Patient Recruitment

At first, a screening urinalysis, using the reagent strip Medi-Combi 10 test strips manufactured by Machery-Nagel D-52313 Duren, Germany, was done for the controls while the subjects were patients with clinical, laboratory features and diagnosis of CKD attending the renal clinic. Subjects aged 6 to 17 years with present or past history and findings suggestive of renal disease or structural urinary tract abnormality, as well as persistent significant proteinuria (1+ or more) or haematuriafor at least 3 months, irrespective of the estimated glomerular filtration rate (GFR) were included. Age and sex matched controls were drawn from the children out-patient clinic. The controls were children with normal urinalysis, eGFR more than 90mls/min/ $1.73m^2$, haemoglobin $\geq$ 10g/dl and no present or past medical history or physical examination findings suggestive of either renal, cardiac or any other chronic diseases like sickle cell disease etc. Children less than 6 years or more than 17 years of age; children 6–17 years with acute renal failure (duration of kidney insult less than 3 months); children with history and clinical features suggestive of preexisting cardiac condition e.g. congenital heart disease (CHD), endomyocardial fibrosis (EMF), rheumatic heart disease etc; children with history and clinical features suggestive of sickle cell anaemia and patients that have undergone Kidney Transplant(KT) were excluded from the study. A written informed consent was obtained from the selected subjects and controls. On enrolment, basic blood investigations like serum, electrolytes urea and creatinine, haemoglobin level and genotyping were obtained from each subject and age and sex matched control. The eGFR was calculated for each subject and control using the Schwartz formula.[10] The eGFR was used in the staging of CKD in subjects and expected to be normal in the controls. The samples were then sent immediately to the chemical pathology and haematology laboratories of the University of Nigeria Teaching Hospital (UNTH), ItukuOzalla, Enugu for prompt analysis and entry of values in the proforma. A transthoracic two-dimensional, M-mode, pulsed-wave, continuous-wave and colour-flow Doppler echocardiography using SONOSCAPE SSI-5000, 2007 model with 3.5Hz transducer probe, were acquired with the subjects lying on the left lateral position. After two dimensional studies and M-mode measurements, left ventricular mass (LVM) was calculated using the *anatomically validated formula*: LVM (gm) = 1.05(specific gravity of ventricular muscle) X { [Left ventricular end- diastolic dimension(LVEDd) + Left ventricular posterior wall thickness (LVPW) +Inter- ventricular septal thickness (IVS)] 3 – Left ventricular end diastolic dimension (LVEDd)3}.[11,12] Left ventricular mass index (LVMI) was calculated by dividing the left ventricular mass (LVM) by the body surface area (BSA) and relative wall thickness (RWT) as $PW/(LVEDd^2)$.[12] Left ventricular hypertrophy was defined in absolute terms in children as LVMI $\geq$ $124.21 g/m^2$ for both males and females, and increased RWT if $\geq$ 0.45. Eccentric left ventricular hypertrophy: Presents with high LVMI and low RWT (< 0.45), with dilated internal ventricular dimensions;

Concentric left ventricular hypertrophy: Presents with high LVMI and high RWT (>0.45). In this case, wall thickness is increased in the presence of normal internal ventricular diameter. It is more associated with increased incidence of cardiovascular events; while Concentric remodelling presents with high RWT and normal LVMI. Trans-mitral early diastolic (E) and late diastolic (A) wave peaks were obtained, as well as the isovolumic relaxation time (IVRT) and E-wave deceleration time (DT), which were obtained using the pulsed-wave Doppler and each of these could be used in assessing left ventricular diastolic function. In this study, impaired relaxation with E/A ratio less than1.2 signifies left ventricular diastolic dysfunction.[13] Note must however be taken that even if the various indices of LV diastolic function were measured, the interpretation of results is complex and unequivocal evidence of LV diastolic dysfunction is difficult to obtain by non-invasive methods.[14]

The left ventricular systolic function was assessed using the ejection fraction and the fractional shortening. Once the IVS, LVEDd, LVESd and the LVPW measurements were taken on the M-mode, the echocardiography machine automatically generated these parameters: EF (%), FS (%), LVEDV, LVESV and SV. Left ventricular mass (LVM) and left ventricular mass index (LVMI) were calculated manually by substituting all the measured parameters in their formulae. Determination of left ventricular dilatation (LVD) for age and sex were done with the aid of a nomogram on M-mode echocardiographic measurements on healthy infants and children by Kampmann, *et al.*[15] Subjects with detected abnormal left ventricular geometry from the study were followed up at the Paediatric Cardiology and Paediatric Nephrology units of the hospital with possible intervention. They were also enrolled for interval echocardiography reviews.

Data Analysis

The data collected were analysed using the statistical package for social sciences (SPSS) version 25. Simple frequencies and proportions (percentages) were used for comparison of demographic data. Student's t-test was used to compare pairs of means of parametric variables like left ventricular end diastole dimension (LVEDd) and other M-mode measurements between the study and control groups. Frequencies of non-parametric variables like left ventricular hypertrophy (LVH), left ventricular diastolic dysfunction etc were compared between the subjects and controls using Chi-squared test corrected by Yates' method, where necessary. Level of significance was regarded as less than 0.05 (< 0.05) at 95% confidence interval.

RESULTS

During the eight-month period of the study, nine thousand, four hundred and nineteen (9,419) paediatric patients within the age group 6–17 years were seen at UNTH Children Emergency (CHER), Children Outpatient Clinic and all the Paediatric Consultant Clinics of the University of Nigeria Teaching Hospital, giving approximately five (5) new cases per million child population per year and a prevalence of 18.4 per million children population with the mean age of 12.33 ± 4.24 years. There were 16 males and 8 females in both study and control groups, with male to female ratio of 2:1 (Table 1).

Twenty- one (87.5%) of the subjects (21) were in socioeconomic class 3 to 5 while all the controls were of socio-economic class 1 to 4 using Oyedeji's classification[16] (Figure 1).

Table 2 shows the stages of the patients with CKD at enrolment. Patients in stage I CKD were nine (37.5%) in number, 4 (16.7%) were in stage 5 while 2(8.3%) were in stage 3.The mean values of the measured and calculated echo parameters like LVEDd, fractional shorting (FS%), LVESd, LVPW, LVM, LVMI, RWT, A- wave velocity, ejection fraction (EF%) and E/A for subjects and controls are as shown in the Table 3A &B.

Comparisons of the left ventricular geometry and functional abnormalities detected in subjects and controls are

Table 1: Age and Sex Distribution of Subjects and Controls

	Subjects			Controls		
	Male n (%)	Female n (%)	Total	Male n (%)	Female n (%)	Total
6–8	2 (8.3)	5 (20.7)	7 (29.1)	2 (8.3)	5 (20.7)	7 (29.1)
9–11	2 (8.3)	1 (4.2)	3 (12.5)	2 (8.3)	1 (4.2)	3 (12.5)
12–14	3 (12.5)	1 (4.2)	4 (16.7)	3 (12.5)	1 (4.2)	4 (16.7)
15–17	9 (37.5)	1 (4.2)	10 (41.7)	9 (37.5)	1 (4.2)	10 (41.7)
Total	**16 (66.7)**	**8 (33.3)**	**24 (100.0)**	**16 (66.7)**	**8 (33.3)**	**24 (100.0)**

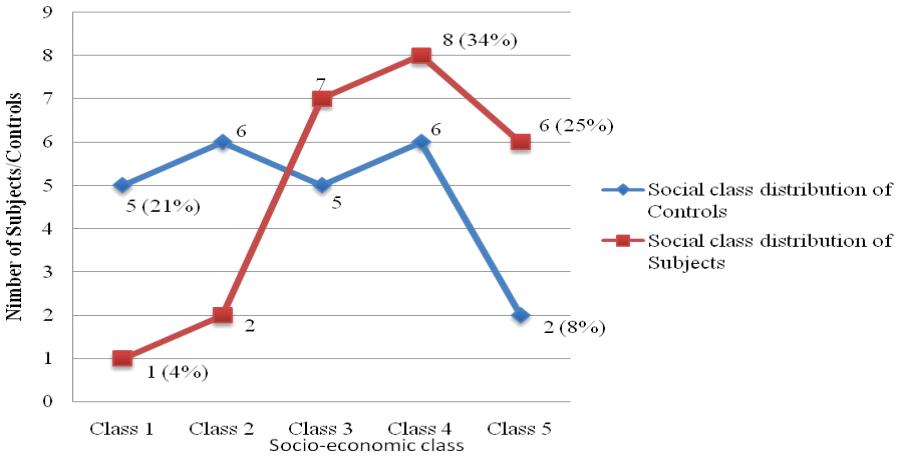

Fig. 1: Social Class Distribution of Study Population.

Table 2: Distribution of CKD Stages in Subjects

CKD Stage (eGFR in mls/min/1.73m^2)	N	Percentage (%)
Stage 1 (>90)	9	(37.5)
Stage 2 (60–89)	6	(25.0)
Stage 3 (30–59)	2	(8.3)
Stage 4 (15–29)	3	(12.5)
Stage 5 (< 15)	4	(16.7)
Total	**24**	**(100.0)**

Table 3A: Echocardiographic Measurements of Subjects and Controls [M-mode echo]

Parameter (Unit)	Subjects Mean ± 2SD [n = 24]	Controls Mean ± 2SD [n = 24]	t-value	p-value
LVESd (cm)	3.19 ± 0.90	2.77 ± 0.60	1.89	0.07
LVEDd (cm)	4.77 ± 0.86	4.66 ± 0.74	0.48	0.63
FS (%)	37.17 ± 12.35	40.13 ± 6.77	1.03	0.31
LVEDV (mls)	122.69 ± 59.14	111.76 ± 46.69	0.71	0.48
LVESV (mls)	41.47 ± 30.71	27.14 ± 13.31	**2.10**	**0.04***
SV (mls)	74.37 ± 33.77	84.62 ± 37.40	1.00	0.33
EF (%)	65.58 ± 12.14	75.75 ± 7.23	**3.53**	**<0.01***

Table 3B: Echocardiography Measurements of Subjects and Controls [M-mode echo] cont'd.

Parameter (Unit)	Subjects Mean ± 2SD [n = 24]	Controls Mean ± 2SD [n = 24]	t-value	p-value
IVS (cm)	0.83 ± 0.36	0.61 ± 0.16	**2.68**	**0.01***
LVPW (cm)	0.85 ± 0.25	0.65 ± 0.11	**3.65**	**<0.01***
LVM (gm)	176.43 ± 94.23	117.37 ± 50.08	**2.70**	**0.01***
LVMI (gm/m2)	138.09 ± 64.06	83.45 ± 16.63	**4.04**	**<0.01***
RWT (cm/cm)	0.4033 ± 0.24	0.2842 ± 0.06	**2.38**	**0.02***
IVRT (sec)	0.08 ± 0.03	0.07 ± 0.01	1.48	0.15
DT (sec)	0.15 ± 0.05	0.14 ± 0.04	0.80	0.44
E (cm/sec)	84.19 ± 18.17	88.90 ± 12.73	1.04	0.30
A (cm/sec)	60.91 ± 25.39	45.90 ± 9.59	**2.71**	**0.01***
E/A ratio	1.58 ± 0.67	2.02 ± 0.42	**2.73**	**0.01***

➢ * = Significant.

shown in Table 4. There were a high proportion of subjects (50%) with left ventricular hypertrophy (LVH) and 33.3%had eccentric LVH. Left ventricular dilatation was documented in 10 (41.7%) subjects. Left ventricular diastolic dysfunction was noted more than left ventricular systolic dysfunction in 37.5% and 8.3% subjects respectively.

Table 5 showed that 50% of subjects with LVH were equally distributed amongst male and female subjects. Eccentric LVH was the commonest geometry in 33.3% subjects of which 75% was seen in males. Concentric remodelling was observed in 3 (12.5%) subjects, occurring more in females (66.7%).However, there was no significant difference between the distribution of the different LVH geometries in the subjects and amongst both sexes.

Table 6 depicts the relationship between the stages of CKD and left ventricular function in the subjects. Statistically significant relationship was noted with left ventricular diastolic function ($p<0.05$). Considering the relationship between the stages of CKD and left ventricular geometry in subjects (Table 7), only left ventricular hypertrophy ($p<0.05$) had significant relationship with stages of CKD. One of the subjects in CKD stage 5 met the criteria for dilated cardiomyopathy (DCM).

DISCUSSION

The overall case incidence rate of CKD in children aged 6–17 years in this study was five (5) new cases per million-child population per year and the prevalence of 18.4 per million age-related populations (MARP). This value is comparable to 14.9 per MARP reported by Odetunde, *et al*[17] in the earlier study done in the same center. The prevalence obtained in this study is lower when compared to the reports from Chilean survey of 42.5 per MARP,[18] Jordan report of 51 per MARP1,[1,19] Italian Italkid project of 74.7 per MARP[1,3,5] and United States renal data system (USRDS) report of 82 per MARP,[1,20] and could be explained by the fact that these studies were extensively done to obtain data all over the index country from both hospital-based and population-based studies with wide coverage giving a better representation of the country's population unlike the skewed coverage of this hospital-based study.

The mean age for CKD of 12.33 ± 4.24 years in this studyis in conformity with earlier studies by several authors who worked on similar age group.[21–23] Chronic glomerulopathies caused by infective agents, a number of which pass through nephrotic phase and renal scarring due to repeated urinary tract infections are common in the West African sub-region. Most of these processes take some time to evolve and may explain the relatively higher prevalence of CKD and its associated cardiovascular abnormalities in the older age group noted in this study. On the other hand, Ahamadzadeh[24] in his study of South-western Iranian children aged 3 months to 16 years, documented a lower mean

Table 4: Comparison of left Ventricular Geometry and Function Abnormalities detected in Subjects and Controls [M-mode; 2-D& Doppler Echo]

Echo Cardiovascular Abnormality	Subjects 24(100%)	Controls 24 (100%)	χ_y^2	p-value
Left Ventricular Dilatation (LVD)	10 (41.7)	1 (4.2)	**7.55**	**<0.01***
LV Systolic dysfunction	2 (8.3)	0 (0.0)		
LV Diastolic dysfunction	9 (37.5)	0 (0.0)		
Left Ventricular hypertrophy (LVH)	12 (50.0)	0 (0.0)	–	–
• Concentric LVH	4 (16.7)	0 (0.0)	–	–
• Eccentric LVH	8 (33.3)	0 (0.0)	–	–
Concentric remodelling	3 (12.5)	0 (0.0)	–	–

* = *Significant.*

Table 5: Prevalence of Left Ventricular Hypertrophy and Geometric Patterns in Subjects

LVH Defining Parameter	All (n = 24) (%)	Male (n = 16) (%)	Female (n = 8) (%)	P-value*
LVMI(g/m²)i.e. LVM/BSA (g/m²)	12(50.0)	8(50.0)	4(50.0)	0.667
Geometric pattern**				
Eccentric hypertrophy	8(33.3)	6 (75.0)	2(25.0)	0.432
Concentric hypertrophy	4(16.7)	2(50.0)	2(50.0)	
Normal	9(37.5)	7(77.8)	2(22.2)	
Concentric remodeling	3(12.5)	1(33.3)	2(66.7)	

*LV, Left Ventricle; LVMI, Left Ventricular Mass Index; LVM, Left Ventricular Mass; BSA, Body Surface Area. *Chi-square; **Geometric pattern determined LVH defined by LVM/ BSA i.e. LVMI with a cut-off of 124.21g/m² for both sexes.[37]*

Table 6: Relationship between Stages of CKD and LV function in Subjects

S/No	LV Function	CKD Staging					χ^{2}**	P-value
		Stage 1 (>90) (%)	Stage 2 (60–89) (%)	Stage 3 (30–59) (%)	Stage 4 (15–29) (%)	Stage 5 (<15) (%)		
1.	**LV Systolic function**						5.450	0.244
	Systolic Dysfunction	0 (0.0)	0 (0.0)	0(0.0)	1(33.3)	1(25.0)		
	Normal	9(100.0)	6(100.0)	2(100.0)	2(66.7)	3(75.0)		
	Total	9(100.0)	6(100.0)	2(100.0)	3(100.0)	4(100.0)		
2.	**LV Diastolic function**						18.792	**0.016***
	Impaired Dysfnx	2(22.2)	1(16.7)	0(0.0)	2(66.7)	3(75.0)		
	Restrictive Dysfnx	2(22.2)	0(0.0)	2(100.0)	0(0.0)	1(25.0)		
	Normal fnx	5(55.6)	5(83.3)	0(0.0)	1(33.3)	0(0.0)		
	Total	9(100.0)	6(100.0)	2(100.0)	3(100.0)	4(100.0)		

age of 4.20 ± 3.60 years as the modal age for CKD. This is explained by the fact that this latter study noted high prevalence of congenital urologic malformations (50.4%) followed by hereditary nephropathies (17.2%), among others as the main causes of CKD. Though this study noted more females in the age group 6-8 years, there is generally a preponderance of male subjects in this study and this is consistent with the trend reported inprevious studies.[21,24–27] The reason for this general male preponderance is not clear, but could be genetically determined as the life-style factors seen in adults are not applicable to children. On the contrary, Arúnas, *et al*[28] in Vilinius, Lithuania, noted female preponderance of CKD with male: female ratio of 1:1.6 in children aged 1–18 years. The reason for sex difference was not adduced in the study. The distribution of our CKD stages with more (37.5%) of stage 1 could be as a result of Nephrotic Syndrome cases contributing more of the CKD cases using the NKF-KIDOQI definition.[29–31] However, this observation varied slightly from same centre study done earlier than this study where we looked at retrospective review of documented CKD cases over 5 years.[32] The retrospective study had more of glomerulonephritis contributing to CKD with stages 4 and 5 seen in 44.9% of cases as against 29.2% of stages 4 and 5 observed in this study. Similar to this index study, a longer duration of retrospective review over 12years in Southwest, Nigeria corroborated with Nephrotic syndrome contributing more to CKD (64.0%) in their series.[33] Another Southwestern Nigerian study that retrospectively reviewed CKD cases over 9 years noted very high contribution of glomerulonephritis (90.26%) but interestingly a high prevalence of CKD stage 1 of 45.5%, with combined stages 4 and 5 CKD of 21.4%[34] similar to our index study of 35.5% and 29.2% respectively.

The specific LVH prevalence of 50.0% documented in this study is similar to the report by Nashwa and co-workers[26] in Australia, in a similar group of patients and also to that by El-Husseini and co-workers[21] in Egypt in post-transplant patients. However, this prevalenceis

Table 7: Relationship between Stages of CKD and Left Ventricular Geometry in Subjects

S/No	LV Geometry	CKD Staging					χ^2**	P-value
		Stage 1 (>90) (%)	Stage 2 (60–89) (%)	Stage 3 (30–59) (%)	Stage 4 (15–29) (%)	Stage 5 (<15) (%)		
1.	**Left Ventricular Dilatation (LVD)**						4.508	0.342
	Dilated LV	3(33.3)	3(50.0)	0(0.0)	1(33.3)	3(75.0)		
	Normal for LVD	6(66.7)	3(50.0)	2(100.0)	2(66.7)	1(25.0)		
	Total	9(100.0)	6(100.0)	2(100.0)	3(100.0)	4(100.0)		
2.	**Left Ventricular Hypertrophy (LVH)**						9.887	**0.042***
	LVH	3(33.3)	4(66.7)	1(50.0)	3(100.0)	4(100.0)		
	Normal for LVH	6(66.7)	2(33.3)	1(50.0)	0(0.0)	0(0.0)		
	Total	9(100.0)	6(100.0)	2(100.0)	3(100.0)	4(100.0)		
3.	**Dilated Cardiomyopathy (DCM)**	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(25.0)	–	–*

high compared to 16–31% reported in similar groups of patients by some authors from Cincinnati, United States of America and Canada.[35,36] The relative high prevalence of LVH in this study could be attributed to factors such as poor standard of health services, low level of health awareness, drug abuse and use of herbal concoctions, poor health-seeking behaviour and extreme poverty, all of which could be a contributor to the late presentation and late initiation of appropriate therapy seen amongst most of the patients with CKD in the West African sub region. Most of the cases that present late are often complicated with fluid over-load, which further increase the risk of LVH,[37]especially eccentric left ventricular hypertrophy found predominant (33.3%) in this study. This finding could further be attributed to lower rate of dialysis and ultrafiltration obtained by children with CKD in the sub region when compared to their counterparts in the developed countries of the world. Eccentric left ventricular hypertrophy as seen in the subjects is supported by Weaver, *et al*[36] who noted a positive association between LV mass index (LVMI) and cardiac output in children with CKD in United States of America. On the other hand, concentric left ventricular hypertrophy, which occurs due to excessive pressure on the ventricular muscles, as seen in fewer (16.7%) subjects has been associated with increased incidence of cardiac ischaemia and sudden death.[36,38] There are varying reports as to whether eccentric or concentric LVH is more common in these group ofchildren.[36–39] Generally, reports from the developed part of the world show more of concentric hypertrophy,[36,38] which could be because they can afford chronic dialysis and ultra-filtration with resultant marked reduction in volume overload. This is not an absolute finding as some other authors in Europe and America documented predominance of eccentric LVH.[21,37,39,40–43] The study by Matteucci, *et al*[41]noted similar distribution and prevalence of the different LVH geometries in similar group of children. Their finding of predominant eccentric LVH (21.0%), followed by concentric LVH (12.1%) and then concentric remodelling (10.2%) closely corroborates with the finding of this study. On the contrary however, while we noted no sex discrimination in the development of LVH, Matteucci, *et al*[41] noted statistically significant male preponderance ($p<0.005$). This observed difference could be as a result of the difference in sample size (133 Vs 24), the slightly younger subjects compared to index (3–18 years) and the fact that end stage CKD (stage 5) were excluded in their study.The high prevalence of left ventricular dilatation (LVD) noted in this study was similar to the reports of Parekh et al in the USA and El- Hussenini, *et al* in Egypt.[21,44] Left ventricular dilatation if persistent and progressive could result in dilated cardiomyopathy (as seen in one subject) and subsequent left ventricular pump failure (systolic dysfunction) as seen in a few 2 (8.3%) subjects.

The trend noted in this study of a higher prevalence of left ventricular diastolic dysfunction as against left ventricular systolic dysfunction is now a common finding in children with CKD. This has been observed by previous workers.[23,35,45] This observation is in contrast to adults in whom left ventricular systolic dysfunction is more frequent and often associated with early cardiac failure and decreased survival.[46,47] The reason for this higher prevalence of diastolic dysfunction in children has been attributed to high levels of serum cystatin C and high left ventricular mass index in this group of children.[48] Furthermore, children with CKD are known to have decreased aerobic capacity even in early stages of the illness. Maximal aerobic capacity (VO_2 max) represents the cardiovascular system's ability to take up, distribute, and utilize oxygen to perform work during maximal exercise. Lower VO_2 max has also been shown to predict left ventricular diastolic dysfunction in this group of patients even in the phase of normal left ventricular systolic function.[49] Abnormal left ventricular diastolic function in children is observed even with early to late trans-mitral flow velocity ratio (E/A) not being less than 1.0,[46,50] thus the cut off value of less than 1.2 used in this study.[13] Trans-mitral Doppler velocities in children are unfortunately affected by several factors including left atrial pressure and preload,[21,47] which is particularly important as most of the children with CKD are often hypervolaemic.

Our study noted an increasing trend in the proportion of subjects developing left ventricular systolic dysfunction as the stage of CKD worsens, but however the difference across the CKD stages was not statistically significant ($p>0.05$). This finding could be because most of our

subjects belonged to CKD stages 1 and 2. Study done at Cincinnati on children with chronic renal insufficiency (CRI)[51] with lower stages of CKD where they used more complex method of both FS and heart rate-corrected velocity of circumferential fibre shortening (VCF) as left ventricular performance revealed significantly higher left ventricular performance and contractility in CRI and dialysis subjects compared to controls. They further noted that as dialysis progress, the LV systolic function drops. A similar study in North-central Nigeria by Peter, *et al*[52] with similar sample size and more of early stages of CKD like index study (66.7% in stage 1 with 0.0% stage 2) also noted statistically significant LV systolic dysfunction. This may be explained by our using a lower value of EF(<40%) to define LVSD as against <50% used by Peter, *et al.*[52] However, while Brady, *et al*[51] noted that LVSD is more with dialyzed subjects, Peter, *et al*[52] noted it more in undialyzed subjects with 14.3% of stage 1 disease having LVSD. The statistically significant LVDD noted in this study as CKD disease stage progresses is corroborated by other workers.[21,46,53,54] In comparison with controls, LVDD was found to be significantly more in CKD subjects in both Peter, *et al*[54] study and index work (both $p<0.05$), though it was not looked at across the stages of CKD. The subjects in the South-eastern Nigeria showed more LVDD than the Northern subjects as contrary to 4 (19.1%) total LVDD with 2(9.5%) each of impaired and restrictive pattern, we noted a total of 13 (54.2%) subjects with LVDD, 8 (33.3%) impaired and 5 (20.8%) restrictive pattern. The reason for this observation is not so clear. It could be partly contributed by the younger age group (3–14 years) studied in the North. The south-eastern subjects could be more oedematous with more challenge of volume overload. The causes of CKD in the Northern series were not highlighted in the study. We noted that as the CKD stages progresses to end-stage, abnormal cardiac geometry like left atrial dilatation, left ventricular dilatation, left ventricular hypertrophy and dilated cardiomyopathy ensures. The statistically significant left ventricular geometry change associated with worsening stages of CKD is left ventricular hypertrophy (LVH) $p< 0.05$. Peter, *et al*[54] noted similar trend with the observed LVH cases in CKD stages 4 and 5 only. In our series, LVH was noted in all the CKD stages with highest proportion of 100% each observed in CKD stages 4 and 5. Sarkozy, *et al*[55] demonstrated a genetic predisposition to this via pro-hypertrophic micoRNA-212 elaborated by patients with CKD. Some studies have shown that LVDD is an independent predictor of LVH in children with CKD.[21,27,37,47,48] Other independent predictors of LVH include anaemia and young age.[27]

CONCLUSION

We arrived at the following conclusions:

1. The case incidence rate of CKD in children aged 6–17 years in Enugu, South-east Nigeria is presently five (5) new cases per million-child population per year with a prevalence of 18.4 per million age-related populations (MARP).
2. Compared to controls, children with CKD showed statistically significant reduction in left ventricular systolic and left ventricular diastolic function.
3. Compared to controls, children with CKD exhibited significantly higher values in LVESV, IVS, LVPW, LVM, LVMI, RWT.
4. Compared to control group, the statistically significant left ventricular geometry observed were left ventricular dilatation (LVD) and left ventricular hypertrophy (LVH). The dominant geometric type of LVH noted in subject was eccentric LVH. One subject in CKD stage 5 was noted to have developed dilated cardiomyopathy.
5. When the heart function and LV geometry was compared across the stages of CKD in subjects, left ventricular diastolic dysfunction and LVH significantly got worse as the stage of CKD progresses to end-stage disease (CKD stage 5).

RECOMMENDATIONS

We therefore recommend the following:

1. Early detection strategies for cardiovascular complication by instituting echocardiography screening early in the course of the disease in all children with CKD, with follow-up interval echo-cardiography as the illness progresses for comparison.
2. Early intervention in children with CKD at risk of developing left heart function and geometry abnormalities with agents like ACE-inhibitors or ARBs, heart-specific beta blockers ± oral inotropes for improved cardiac function and cardiac remodeling.
3. Primary prevention of CKD and its burden by intensifying principles of preventive nephrology, especially mass health education and promotion, the screening for microalbuminuria and proteinuria for at risk children and as routine outpatient/preschool entry tests.

REFERENCES

1. Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. *Pediatr Nephrol.* 2007; **22:** 1999–2009.
2. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and deranged kidney function in the adult US population: third National Health and Nutrition Examination Survey. *Am J kidney Dis.* 2003; **41:** 1–12.
3. Sanjeev G. Chronic kidney Disease. eMedicine specialties: paediatrics-general medicine-nephrology.http://emedicine.medscape.com/article/984358. updated: Jun 21, 2011.
4. Lysaght MJ. Maintenance dialysis population dynamics: current trends and long term implications. *J Am Soc Nephrol.* 2002; **13:** 37–40.
5. Ardissino G, Dacco V, Testa S, Bonaudo R, Claris-Appiani A Taioli E, *et al.* Epidemiology of chronic renal failure in children: data from the Italkid project. *J Pediatr.* 2003; **111:** 382–387.
6. Esbjorner E, Berg U, Hansson S. Epidemiology of chronic renal failure in children: a report from Sweden 1986–1994. *Pediatr Nephrol.* 1997; **11:** 438–442.
7. Anochie I, Eke F. Chronic renal failure in children a report from Port Harcourt, Nigeria (1985–2000). *Pediatr Nephrol.* 2003; **18:** 692–695.

8. Chavers BM, Shuling L, Collin AJ, Herzog CA. Cardiovascular disease in pediatric chronic dialysis patients. *Kidney Int.* 2002; **62:** 648–653.
9. National Population Commission, Enugu, Nigeria. Provisional census figures. *Official Gazette.* 2007; **24:** B–185.
10. Vogt BA, Avner ED. Renal Failure. In: Behrman RE, Kliegman RM, Jenson HB (eds.) Nelson Textbook of Pediatrics (18th Ed.) Philadelphia, E Saunders Company, 2007: 2206–2214.
11. Levy D, Savage DD, Garrison RJ, Anderson KM, Kannel WB, Castelli W. Echocardiographic criteria for left ventricular hypertrophy: the Framingham Heart Study. *Am J Cardiol.* 1987; **59:** 956–960.
12. Brandão AA, Pozzan R, Albanesi Filho FM, Brandã AP. Role of anthropometric indexes and blood pressure as determinants of left ventricular mass and geometry in adolescents. *Hypertension.* 1995; **26:** 1190–1194.
13. Feigenbaum H. Echocardiography. Philadelphia. Lea and befiger. 4th ed. 1986: 622.
14. Arodiwe EB, Ulasi IV, Ijoma CK, Ike SO. Left ventricular diastolic function in a predialysis patient population. *West Afr J Med.* 2010; **29:** 225–229.
15. Kampmann C, Wiethoft CM, Wenzel A, Stolz G, Betancor M, Wippermann CF, *et al.* Normal values of M mode echocardiographic measurements of not more than 2000 healthy infants and children in Central Europe. *Heart.* 2000; **83:** 667–672.
16. Oyedeji GA. Socio-economic and cultural background of hospitalized children in Ilesha. *Nig J Paediatr.* 1985; **12:** 111–117.
17. Odetunde OI, Okafor HU, Uwaezuoke SU, Ezeonwu BU, Adiele KD, Ukoha OM. Chronic kidney disease as seen in a tertiary hospital in Nigeria: Enugu south-east Nigeria Report. *Niger J of Clin Pract.* 2014; **17:** 196–200.
18. Lagomarsimo E, Valenzuela A, Cavagnaro F, Solar E. Chronic renal failure in pediatrics Chilean survey. *Pediatr Nephrol.* 1999; **13:** 288–291.
19. Hamed RMA. The spectrum of chronic renal failure among Jordanian children. *J Nephrol.* 2002; **15:** 130–135.
20. U.S. renal data system, USRDS 2007 (19th) Annual data report: Atlas of end-stage renal disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD. Available at: http://www.usrds.org/2007/pdf/00_intro_07.pdf. accessed: August 20, 2010.
21. El-Husseini AA, Sheashaa HA, Hassan NA, El-Demerdash FM, Sobh MA, Ghoneim MA. Echocardiographic changes and risk factors for left ventricular hypertrophy in children and adolescents after renal transplantation. *Pediatr Transplant.* 2004; **8:** 249–254.
22. Pecoits-Filho R, Barberato SH. Echocardiography in chronic kidney disease: Diagnostic and Prognostic implications. *Nephron Clinical Practice.* 2010; **114:** 242–247.
23. Bello AK, Peters J, Rigby J, Rahman AA, Nahas ME. Socioeconomic status and chronic kidney disease at presentation to a renal service in the United Kingdom. *Clin J Am Soc Nephrol.* 2008; **3:** 1316–1323.
24. Ahamadzadeh A. Chronic kidney disease in South-Western Iranian children. *Iran J Paediatr.* 2009; **19:** 147–153.
25. Mitsnefes MM, Kimball TR, Kartal J, Witt SA, Glascock BJ, Khouray PR, *et al.* Cardiac and vascular adaptation on paediatric patients with chronic kidney disease: Role of calcium-phosphorus metabolism. *J Am Soc Nephrol.* 2005; **16:** 2796–2803.
26. Nashwa MS, Bahia HM, Fatina IF. Prevalence of viral infection among Egyptian children with end stage renal disease. *Aust J Basic Appl Sci.* 2009; **3:** 3479–3491.
27. The National Paediatric Hospital experience Hanoi Vietnam. Chronic kidney disease in children. Available at: http://www.Sciencia .org/Stories/130620/ html. Accessed: June 10, 2011.
28. Arúnas M, Vilija C, Marija J, Augustina J. Left ventricular geometry in children with chronic renal failure. *Medicina (kaunas).* 2005; **41:** 5–11.
29. National kidney foundation. K/DOQI clinical practice guildlines for chronic kidney disease: evaluation, classification, and stratification. *Am J kidney Dis.* 2002; **39:** 1–266.
30. Whyte DA, Fine RN. Chronic kidney disease in children. *Pediatrics in Review.* 2008; **29:** 335–341.
31. Kopple JD. National Kidney foundation K/DOQI clinical practice guildlines for nutrition in chronic renal failure. *Am J kidney Dis.* 2001; **37:** 566–570.
32. Odetunde OI, Okafor HU, Uwaezuoke SU, Ezeonwu BU, Adiele KD, Ukoha OM. Chronic kidney disease as seen in a tertiary hospital in Nigeria: Enugu south-east Nigeria Report. *Niger J of Clin Pract.* 2014; **17:** 196–200.
33. Adekanmbi AF, Ogunlesi TA, Oba-Daini OO, Ayeni VA. Chronic Kidney Disease in Nigerian Children: Challenges of Management. *African J Paed Nephrol.* 2018; **5:** 1–5.
34. Olowu WA, Adefehinti O, Aladekomo TA. Epidemiology and Clinico-pathologic outcome of pediatric chronic kidney disease in Nigeria, a single center study. *Arab J Nephrol Transplant.* 2013; **6:** 105–113.
35. National Institute for Health and Clinical Excellence. Urinary tract infection in children: diagnosis, treatment and long-term management. *NICE Clin Guideline.* 2007; **54:** 1–30.
36. Weaver DJ, Kimball TR, Koury PR, Mitsnefes MM. Cardiac output and associated left ventricular hypertrophy in paediatric chronic kidney disease. *Paediatr Nephrol.* 2009; **24:** 565–570.
37. Mitsnefes M, Kimball T, Kartal J, Witt S, Glascock B, Khoury P, Daniels C. Progression of left ventricular hypertrophy in children with early chronic kidney disease: 2-year follow-up study. *Paediatr.* 2006; **149:** 671–675.
38. Huting J. Mitral valve calcification as an index of left ventricular dysfunction in patients with end stage renal disease on peritoneal dialysis. *Chest.* 1994; **105:** 383–388.
39. Mitsnefes MM. Cardiovascular disease in children with chronic kidney disease. *Adv Chronic Kidney Dis.* 2005; **12:** 397–405.
40. Shroff R. Monitoring Cardiovascular risk factors in children on dialysis. *Perit Dial Int.* 2009; **29:** 173–175.
41. Matteucci MC, Wuhl E, Picca S, Mastrostefano A, Rinelli G, Romano C, *et al.* Left ventricular geometry in children with mild to moderate chronic renal insufficiency. *J Am Soc Nephrol.* 2006; **17:** 218–226.
42. Badawy A, Nigm DA, Ezzat GM, Gamal Y. Interleukin 18 as a new inflammatory mediator in left ventricular hypertrophy in children with end-stage renal disease. *Saudi J Kidney Dis Transpl.* 2020; **31:** 1206–1216.
43. Cho H, · Choi HJ, · Kang HG, · Ha IS, Cheong HI, Han KH, *et al.* Influence of the Method of Definition on the Prevalence of Left-Ventricular Hypertrophy in Children with Chronic Kidney Disease: Data from the Know-Ped CKD Study. *Kidney Blood Press Res.* 2017; **42:** 406–415.
44. Parekh RS, Carrol CE, Wolfe RA, Port FK. Cardiovascular mortality in Children and young adults with end-

stage Kidney disease. *J Pediatr.* 2002; **141:** 191–197.
45. Drozdz, D, kordon Z, Pietrzyk JA, Drozdz M, Rudzinski A, Zachwieja K. The assessments of heart function in children with kidney disease (CKD). *Pol MerkurLekarski.* 2008; **24:** 98–100.
46. Johnstone LM, Jones CL, Grigg LE, Wilkinson JL, Walker RG, Powell HR. Left ventricular abnormalities in children, adolescents and young adults with renal disease. *Kidney Int.* 1996; **50:** 998–1006.
47. Mitsnefes MM. Cardiovascular complications of paediatric chronic kidney disease. *Pediatr Nephrol.* 2008; **23:** 27–39.
48. Mitsnefes M, Kimbal T, Kartal J, Katchman T, Mishra J, Devarajan P. Serum cystatin C and left ventricular diastolic dysfunction in children with chronic kidney disease. *Paediatr Nephrol.* 2006; **21:** 1293–1298.
49. Weaver DJ, Kimball TR, Knilans T, Mays W, Knecht SK, Gerdes YM, *et al*. Decreased Maximal Aerobic Capacity in Pediatric Chronic Kidney Disease. *J Am Soc Nephrol.* 2008; **19:** 624–630.
50. ImpactEDnurse. Mean Arterial Pressure. http://www. Impactednurse. com/ Retrieved 2010-12-25.
51. Brady TM, Schneider MF, Flynn JT, Cox C, Samuels J, Saland J, *et al.* Carotid Intima-Media Thickness in Children with CKD: Results from the CKiD Study. *CJASN.* 2012; **7:** 1930–1937.
52. Peter ID, Aliyu I, Asani MO, Obiagwu PN, Igwe OO, Bode-Thomas F. Left ventricular systolic dysfunction in paediatric chronic kidney disease patients. *Res Cardiovascular Med.* 2019; **8:** 79–83.
53. ImpactEDnurse. Mean Arterial Pressure. http://www. Impactednurse. com/ Retrieved 2010-12-25.
54. Peter ID, Asani MO, Aliyu I, Obiagwu PN. Left ventricular mass, geometry patterns and diastolic myocardial performance in children with chronic kidney disease. *J Clin Sci.* 2018; **15:** 55–59.
55. Sárközy, M., Gáspár, R., Zvara, Á, Siska A, Kovari B, Szucs G, *et al.* Chronic kidney disease induces left ventricular overexpression of the pro-hypertrophic microRNA-212. *Sci Rep.* **9:** 1302 (2019). https://doi.org/10.1038/s41598-018-37690-5.