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Trends in the Epidemiology of Severe Pediatric Non-surgical Renal Disorders in Ibadan Nigeria: A Marked Increase in the Incidence of Acute Kidney Injury

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Authors' contributions

This work was carried out in collaboration between all authors. Author AOA designed the study and was involved in the data generation, data analysis and in manuscript writing. Author ADA was involved in data generation and manuscript writing. Author OOO participated in data generation and manuscript writing while author JY was involved in data analysis and manuscript writing. All authors read and approved the final manuscript.

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ABSTRACT

Background: Renal disorders are increasingly being recognized as major contributors to morbidity and mortality. Variability in their pattern in different populations and regions of the world and changes occurring with time have been demonstrated. We aimed to determine the current trends in the pattern of severe non-surgical childhood renal disorders at our Centre and compare the findings with previous studies.
Methodology: A descriptive analytical study was carried out on consecutive incident cases of non-surgical renal disorders aged 14 years and below, managed in the Pediatric Nephrology Unit of the

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University College Hospital, Ibadan, Nigeria. Two separate time periods were studied.
Results: A total of 869 incident cases of severe non-surgical disorders were admitted during the study periods. There was an increase in the hospital incidence from 1.5 to 2.2 per 100 pediatric admissions and in the average yearly admission from 43 to 103. The crude annual incidence increased from 42 per million age-related population (PMARP) to 86 (PMARP) at the end of the two study periods. The most remarkable increase occurred with Acute Kidney Injury, which showed a 6.5-fold rise and was the most common cause of renal morbidity and mortality in children encountered in the study. Interventional measures resulted in early detection, prompt treatment and reduced mortality.
Conclusion: The study has shown an increase in the incidence of severe childhood renal disorders in Ibadan, with Acute Kidney Injury being the leading non-surgical renal disorder. A significant decline in case fatality rates was demonstrated in recent years.

Keywords: Paediatric; non-surgical renal disorders; acute Kidney injury; glomerulonephritis; nephrotic syndrome; chronic kidney disease; Ibadan Nigeria; Africa.

1. INTRODUCTION

One of the earliest reports on the pattern of childhood renal disorders in Sub-Saharan Africa emanated from our Center and the authors pointed out that, contrary to previous assumptions, childhood renal disease was common in our part of the world [1]. Their studies and those of workers from East Africa [2], West Africa [3] and South Africa [4,5] and studies from multiracial countries [6,7], have shown the variability in the pattern of renal disorders in different populations of the world. It has also been demonstrated that within the same geographical region, renal disease patterns may differ from place to place and from time to time [8-14]. Since genetic factors, life style modifications, socioeconomic and environmental factors influence the pattern of renal disorders, [15] it is pertinent to review disease patterns from time to time in a dynamic world. Detecting changing trends may be needful in planning appropriate healthcare delivery and ensuring a better disease outcome.

1.1 Aims and Objectives

To appraise the current trends in the pattern of severe non-surgical childhood renal disorders in the Paediatric Nephrology Unit (PNU) of the University College Hospital (UCH), Ibadan, Nigeria and compare the findings with previous studies.

2. PATIENTS AND METHODS

2.1 Ethics Statement

Ethical clearance was obtained from the University of Ibadan/University College Hospital, Ibadan Joint Ethical Committee for this study. The patients' individual data were anonymized and not traceable to them in this study.

2.2 Research Design

This is a descriptive analytical study based on patients' data collected prospectively over two time periods (1989-1998 & 2007-2013). These were time periods when Paediatric nephrologists were available with fairly regular services being offered and accurate data were kept. Patients' demographic and clinical data as well as investigation results were analyzed. The UCH, Ibadan is the only referral center in the city of Ibadan for severe renal cases; hence it is assumed that data recruited from the hospital would be representative of the epidemiological pattern in the city.

2.3 Study Population

Consecutive incident patients with severe non-surgical renal disorders, aged 14 years and below, admitted into the PNU of the UCH, Ibadan were studied.

2.3.1 Inclusion criteria

All non-surgical renal disorders that required admission into the Paediatric Nephrology Unit.

2.3.2 Exclusion criteria

- Surgical cases such as Posterior urethral valves, even when they had complicating medical issues.
- Non-severe non-surgical renal cases that were treated in Out-patient Clinics or discharged home from the Paediatric Emergency Unit.
- Pre-renal acute renal failure.

2.4 Investigations

Investigations routinely carried out on these patients were dipstick urinalysis, urine microscopy / culture / sensitivity, serum electrolytes, urea and creatinine, full blood count, hemoglobin electrophoresis, blood film for malaria parasites. In more recent years, Hepatitis B & C screening, human immunodeficiency virus (HIV) screening, abdominal ultrasonography were routinely done and other investigations were as dictated by the provisional diagnosis such as timed and spot urine protein estimation, creatinine clearance, lipid profile, renal biopsies, ASO titer, micturating cysto-urethrogram (MCUG) and renal scintigraphy. All laboratory tests were carried out using standard laboratory procedures. Chest radiography, electrocardiography, echocardiography, Doppler studies, Computerized tomography (CT) scan and Magnetic resonance imaging (MRI) were carried out when indicated.

2.4.1 Definitions of terms

The diagnosis of the renal disorders was based on standard case definitions as stated below:

1. Nephrotic syndrome (NS) was diagnosed in the presence of a combination of massive proteinuria (proteinuria of 3^+ and above on dipstick urinalysis with a 24-hour urinary protein of >40 mg/m^2/ hour), hypoalbuminemia (serum albumin of <25 g/L), edema and hyperlipidemia [16].
2. Acute Kidney Injury (AKI). Only patients with Kidney Disease Improving Global Outcome (KDIGO) Stage III or Pediatric RIFLE (pRIFLE) Failure Stage were included in the study i.e. sudden and rapid deterioration of kidney function manifesting as oliguria of <0.3 ml/kg/hour for more than 24 hours or anuria of >12 hours or tripling of baseline creatinine or serum creatinine greater than 353.6 µg/dl or initiation of renal replacement therapy, or a decrease in eGFR to <35 ml/min per 1.73 m^2 [17]. RIFLE is an acronym of Risk, Injury, and Failure; and Loss; and End-stage kidney disease used in staging AKI.
3. A diagnosis of Chronic Kidney Failure (Stage 5 CKD): was made when the GFR less than 15ml/min/1.73m^2 or need for dialysis in patients with clinical or radiologic features of background chronic kidney disease [18].
4. Acute Nephritic Syndrome or Acute glomerulonephritis (AGN) was diagnosed in children manifesting with sudden onset of features of glomerular injury, which include hematuria, mild to moderate proteinuria, hypertension, edema, oliguria and varying degrees of renal insufficiency [19].
5. Primary Hypertension (HTN) was diagnosed in the presence of blood pressure measurements that are equal to or greater than the 95th percentile for age, gender and height, where no secondary causes could be found [20].
6. The diagnosis of a primary urinary tract infection (UTI) was made in the presence of significant bacteriuria [21,22] and was was not secondary to any structural or functional defect.

2.5 Data Analysis

Data generated from the study were entered in Microsoft Excel spreadsheet and later transferred to STATA 12 for analysis. Data cleaning was done and baseline demographic characteristics of the participants were analyzed. Median and corresponding interquartile ranges for continuous variables were presented and proportions of the categorical variables were computed. According to the 2006 national census, Ibadan, the capital city of Oyo State, had a population of 2,560,573 and the population of children aged ≤14 years was 949,639[23]. The population of Ibadan was 1,835,300 in 1991 and that of children aged ≤14 years was 768,105. The population growth rates and necessary variables were used to calculate the incidence rates. Incidence rate of renal disorders was presented over both time periods of interest (1989-1998 and 2007-2013), with age and sex specific incidence rates also presented. Standardization was not done because age and sex distribution over both time periods were similar. Case fatality rates were also reported. The proportions of the various renal syndromes over the two time periods were compared using the two-sample Proportion z test. *P*-value < 0.05 was deemed significant.

3. RESULTS

Two time periods were selected for this study; 1989 – 1998 (Time I) and 2007–2013 (Time II). Over the course of the selected years, there were 46,354 pediatric admissions – 23,530 (50.8%) during Time I and 22824 (49.2%) during Time II. Thirteen thousand, seven hundred and

forty seven (58.4%) boys and 9783 (41.6%) girls were admitted into the Department of Paediatrics during Time I and 13,326 (58.4%) boys and 9498 (41.6%) girls during Time II.

Table 1 shows the base-line characteristics of the study population. Overall, there were 869 children admitted with severe non-surgical renal disorders, with 361 (41.5%) in Time I and 508 (58.5%) in Time II. The median age of children in Time I was 8 years (IQR: 4–11) while that of children in Time II was 7 years (IQR: 3-10), p = 0.027; There was no statistical significant difference in gender between the 2 time periods.

3.1 Incidence of Renal Disorders

Eight hundred and sixty-nine children were admitted for severe non-surgical renal disorders during the study period, making the cumulative incidence 1.9 per 100 pediatric hospital admissions. There was a significant increase in incidence of renal admissions over the two time periods, with 361 (1.5 per 100 pediatric admissions) cases from Time I and 508 (2.2 per 100 pediatric admissions) from Time II (p-value <0.01).

The yearly incidence rate showed a steady increase (Fig. 1). The 2013 figures translate to a crude annual incidence of 86 per million age-related population (PMARP) compared with 46 (PMARP) crude annual incidence in 1998 (Fig. 1). Fig. 2 shows the pattern of annual admissions for severe pediatric non-surgical disorders. There was a sharp rise in pediatric non-surgical renal admissions in 1990 & 1991; followed by a sharp decline in the first period. Period II showed a steady and progressive increase in pediatric renal admissions.

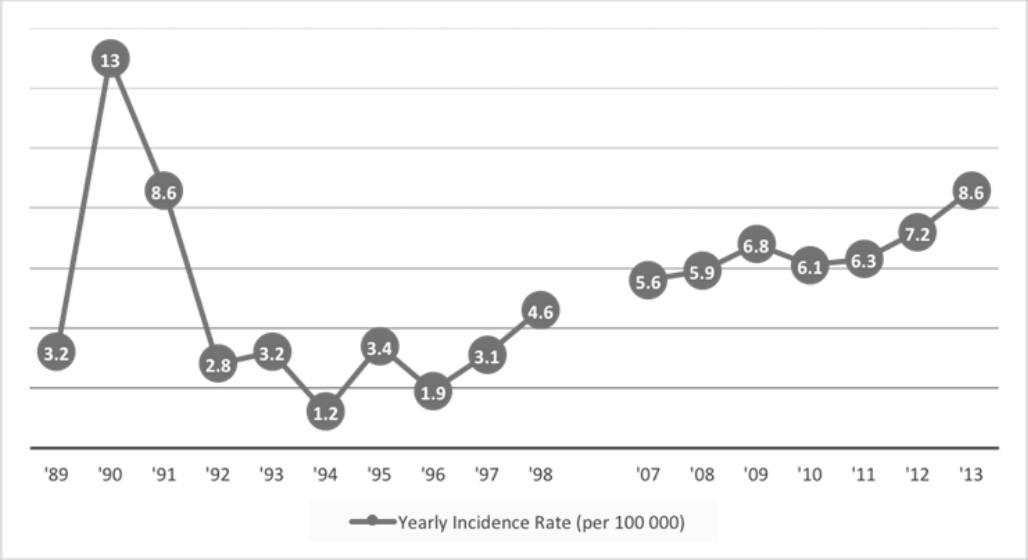

Fig. 1. Yearly Incidence rate over the two time periods

Table 1. Baseline characteristics of patients with severe non-surgical renal disorders

	Time I	Time II	p-value
Number (%)	361 (41.5%)	508 (58.5%)	
Median age (range) (yrs)	8 (4 – 11)	7 (3 – 10)	0.027
Age group			
< 5 yrs	94 (26.1%)	170 (33.5%)	0.045
5 – 9 yrs	131 (36.4%)	179 (35.2%)	
≥ 10 yrs	135 (37.5%)	159 (31.3%)	
Gender			
Male	185 (51.3%)	280 (55.1%)	0.259
Female	176 (48.7%)	228 (44.9%)	

Time I= 1989-1998; Time II: 2007-2013

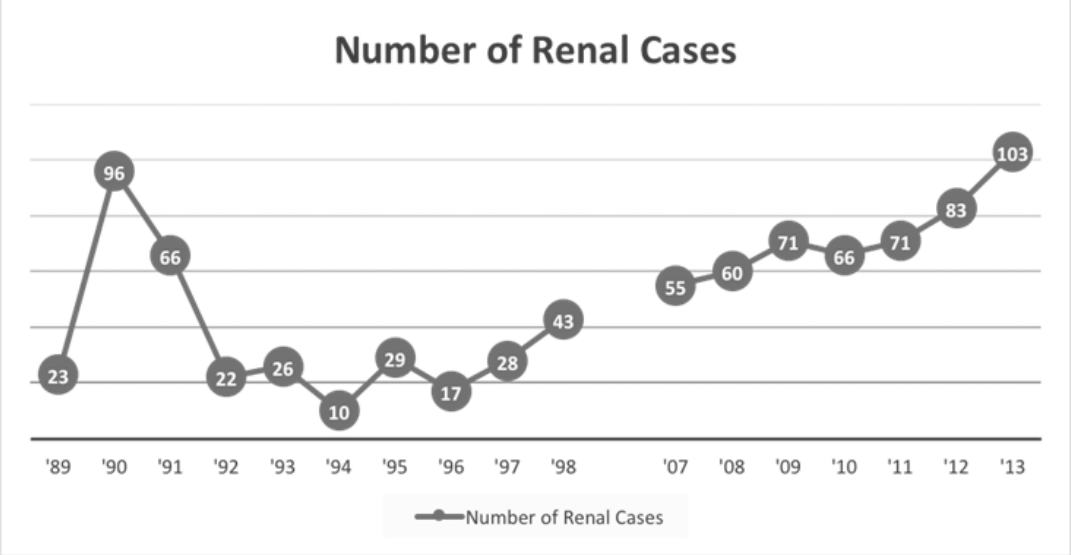

Fig. 2. Pattern of annual admissions for severe non-surgical renal disorders over the study period

Comparing renal syndromes per 100 renal admission over the two time periods, the incidence of Acute Kidney Injury (AKI) was much higher in Time II compared with Time I ($p < 0.001$), while nephrotic syndrome and acute nephritic syndrome showed reduction in their percentage contributions ($p < 0.001$). (Table 2) Fig. 3 shows the incidence pattern of these renal syndromes over time. It demonstrates that since the late 1990s, the incidence of nephrotic syndrome and that of acute nephritic syndrome have been fairly stable while the incidence of acute kidney failure has been increasing. Age specific incidence of renal disease shows that for most of the period of interest, the oldest age group (10-14 years) had the highest, and children aged less than 5 years had the least incidence of non-surgical renal disease, with the incidence in children <5 years increasing in the last 2 years (Fig. 4).

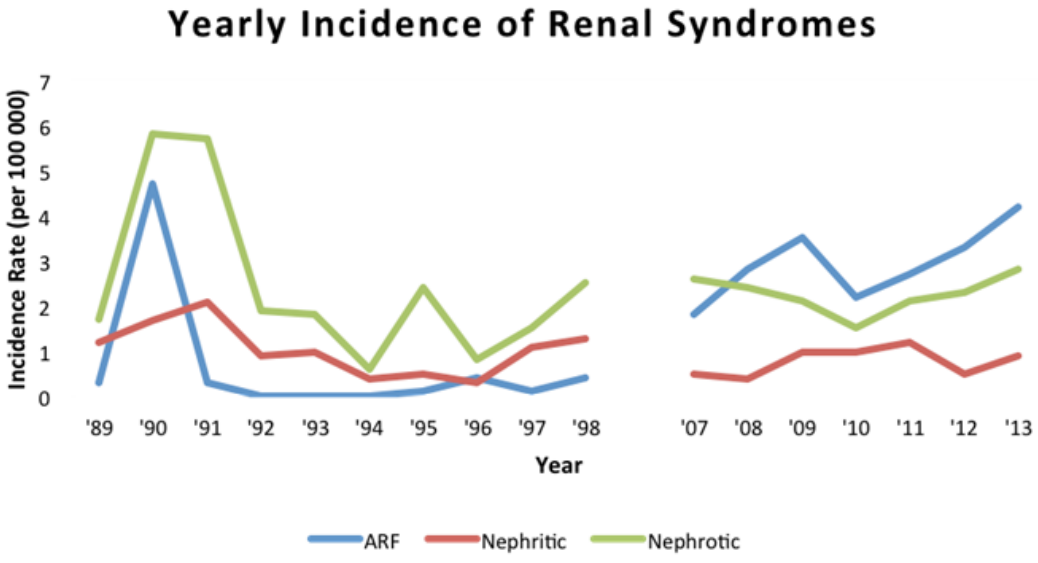

Fig. 3. Yearly incidence of renal syndrome

There was a significant increase in incidence of AKI in all age groups between Time I and Time II, more marked in the lower age groups, especially the under-5s with significant reduction in incidence of nephrotic syndrome and AGN between Group I and Group II. Nephrotic syndrome occurred more commonly in children over 5 years of age (Table 3).

Table 4 compares the clinical conditions associated with Acute Kidney Injury requiring dialysis in the different time periods.

Fig. 5 shows the sex distribution in renal disorders during the study periods; with a higher incidence in males.

3.2 Patient Outcomes

Overall, there was a significant reduction in the overall case fatality rate from pediatric non-surgical renal disorders from 18.8% in Time I to 13.8% in Time II (p=0.047). There was a decrease in case fatality rates of various renal syndromes with only AGN showing a slight

Table 2. Incidence of renal syndromes per renal admission in both time periods

	Time I	Time II	Z	p-value
Acute kidney failure	49 (13.6%)	225 (44.3%)	-9.6	<0.001
Chronic kidney failure	20 (5.5%)	33 (6.5%)	-0.6	0.543
Acute nephritic syndrome	86 (23.8%)	59 (11.6%)	4.8	<0.001
Nephrotic syndrome	200 (55.4%)	172 (33.9%)	6.3	<0.001
Others (HTN, UTI, PKD)	6 (1.7%)	19 (3.7%)	-1.7	0.082

Time I = 1989-1998; Time II = 2007-2013

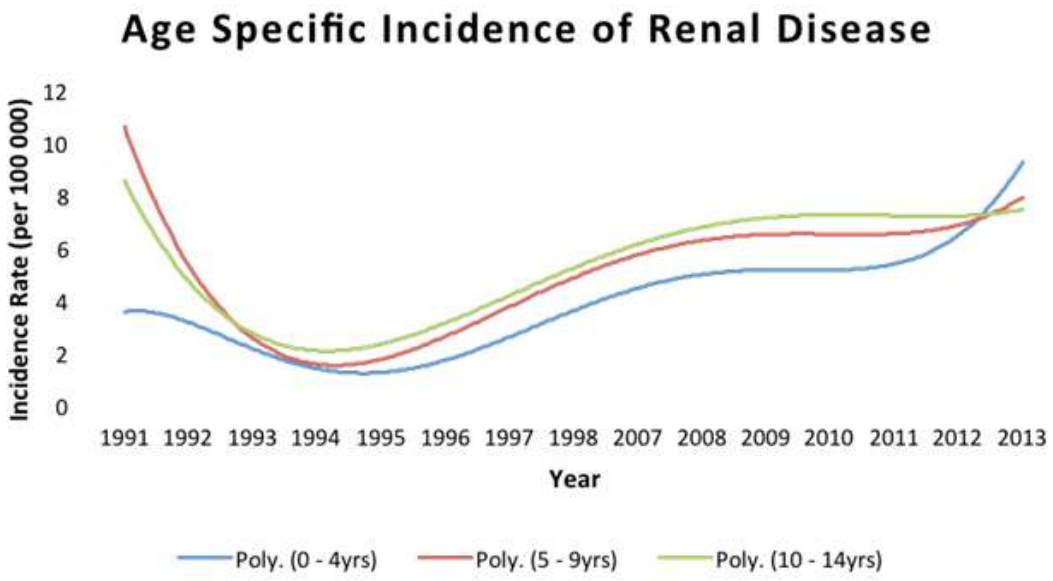

Fig. 4. Age-specific incidence of renal disease

Table 3. Proportion of renal syndromes in participants

	0 – 4 yrs		5 – 9 yrs		10 – 14 yrs	
	Time I	Time II	Time I	Time II	Time I	Time II
AKI (failure stage)	28 (29.8%)	103 (60.6%)	6 (4.6%)	78 (43.6%)	15 (11.1%)	44 (27.8%)
NS	33 (35.1%)	42 (24.7%)	92 (70.2%)	66 (36.9%)	74 (54.8%)	64 (40.2%)
AGN	30 (31.9%)	10 (5.9%)	30 (22.9%)	25 (14.0%)	26 (19.3%)	24 (15.1%)
CKD (stage 5)	1 (1.1%)	6 (3.5%)	2 (1.5%)	5 (2.8%)	17 (12.6%)	22 (13.8%)
Others	2 (2.1%)	9 (5.3%)	1 (0.8%)	5 (2.8%)	3 (2.2%)	5 (3.1%)

Table 4. Comparing Clinical conditions associated with Acute Kidney Injury requiring dialysis in the different time periods

Diagnosis	1990-1999 n (%)	2006-2013 n (%)
Intravascular hemolysis with Haemoglobinuria	2 (8.7)	30 (37)
Septicemia	2 (8.7)	21(26)
Acute glomerulonephritis (AGN)	10 (43.5)	9 (11.1)
Gastroenteritis	-	3 (3.7)
Hemolytic uremic syndrome	1 (4.3)	3 (3.7)
Severe Malaria (excluding 5 with IVH)	-	3 (3.7)
Diethylene glycol poisoning	4 (17.4)	7 (8.6)
Malignancies	4 (17.4)	3 (3.7)
Others	-	2 (2.5)
Total	**23 (100)**	**81 (100)**

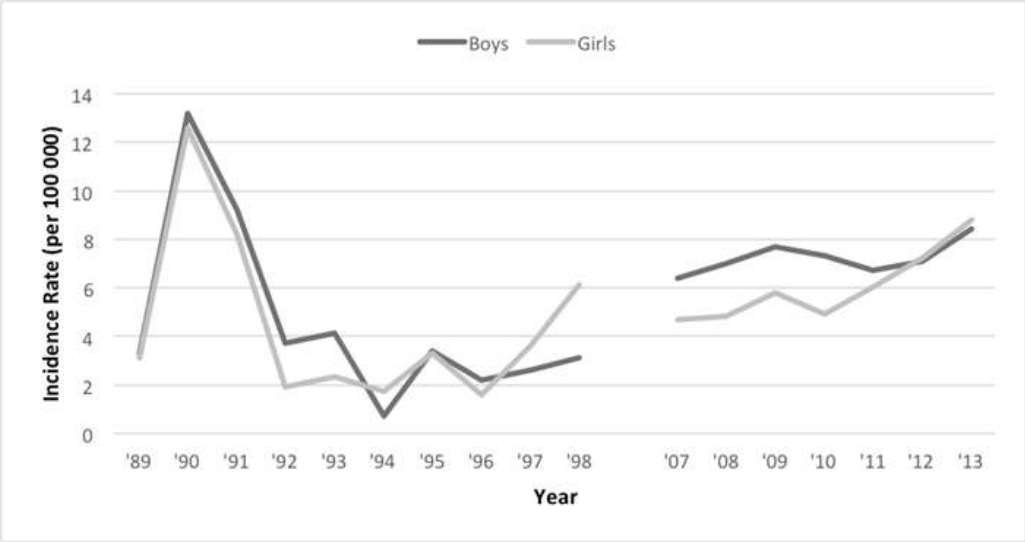

Fig. 5. Sex specific incidence for renal disease

increase in case fatality rate. In Time II, the case fatality rates for AKI, NS, AGN and Stage 5 CKD were 19.6%, 8.1%, 6.6% and 18.4% respectively whereas in Time I they were 63.3% (including patients dying from an epidemic of diethylene glycol poisoning), 10%, 5.8% and 21.2% respectively. Excluding deaths from the epidemic, the case fatality rate was 26.9%. AKI was the leading cause of mortality over both time periods. There were reductions in the contributions of NS, AGN and CKF to the overall renal mortalities.

4. DISCUSSION

This study has evaluated the hospital incidence of severe non-surgical childhood renal disorders in Ibadan, Nigeria. This showed an overall upward trend with an increase in the hospital incidence from 1.5 to 2.2 per 100 pediatric admissions and an increase in the average yearly admission from 43 to 103. The crude annual incidence increased from 42 per million age-related population (PMARP) to 86 (PMARP) at the end of the two study periods. The most remarkable is the increase in the incidence of AKI which showed a 6.5-fold rise. This finding is in keeping with the global trend of increase in the incidence of AKI both in children and adults [24,25]. This increase in hospital incidence is probably real, as it has occurred despite the increased number of centers now offering nephrology services to children in the Southwestern (SW) part of Nigeria in particular, and the country in general.

The incidence of renal disease from this study cannot be reliably compared with most studies from Nigeria, which were not strictly incidence studies and included surgical renal disorders

[9-11]. However, the more recent studies from Lagos [26] and Jos [27] have also shown an increase in the incidence of AKI. Probable explanations for this increase include early detection of AKI by optimal use of the RIFLE/AKIN/KDIGO criteria for diagnosing AKI in our Unit, and increased referral to our center as health workers became aware that dialysis was being offered to children and adolescents. Data comparing the AKI patients that received dialysis (Table 4) shows that between 1990-1999 and 2006-2013, Intravascular haemolysis with haemoglobinuria and Sepsis increased as major causes of severe AKI, while AGN reduced in prevalence. HUS, however, has remained uncommon. Most of the causes of AKI were infection- related, and this finding is in keeping with previous reports from centres in Nigeria [9,11,26,27]. The Intravascular haemolysis was mainly associated with malaria and G6PD deficiency, while some were inexplicable. Prior use of anti-malarial drugs might result in false negative results for malaria parasites and therefore under-diagnosis of malaria in our setting. Intensified efforts in controlling infections and infestations will go a long in reducing these occurrences.

Although AKI contributed the highest mortality, a gradual reduction in mortality was observed over the years. It is important to note that 2 epidemics of AKI secondary to diethylene glycol poisoning occurred in Nigeria during the study periods and some of the patients were managed in our Centre. The first occurred in August/September 1990 when twenty-three affected children presented, with almost 100% mortality as detailed by Osinusi et al. [28]. This explains the upsurge in the incidence of AKI during that period. The second occurred between August and December 2008; thirteen patients presented to us very late from Lagos with almost 100% mortality. The second epidemic was however associated with greater public awareness and more health institutional support for the treatment of AKI.

Between 2007 and 2013, the case fatality rate for AKI fell to 19.6% despite the contribution of the diethylene poisoning epidemic. Excluding the mortalities from the epidemic, the case fatality rate dropped to 14.7%. A relatively new meta-analytical study of world incidence of AKI quoted mortality of AKI in children to be 13.8% [25], which is similar to our recent experience. Some of the reduction in mortality in AKI was achieved through intense efforts put in place to ensure dialysis despite the irregular availability of standard dialysis consumables in our country. These included improvisation of materials e.g. utilizing fenestrated nasogastric tubes as peritoneal dialysis catheters and instant constitution of dialysis fluid.

Nephrotic syndrome (NS) has remained a major cause of renal morbidity and mortality in paediatric patients in Ibadan but it is no longer the leading entity. In the 1960s, and up till 1998 as shown in this study, NS and AGN were the predominant pediatric non-surgical renal disorders seen in our center (Table 5). Although, AKI now leads, NS remains the most common chronic glomerular disease in our cohort and is consistent with reports from other parts of Nigeria and many parts of the world [1,7,11,28].

With regards to AGN, our data indicate that in contrast to the findings in the Northern [9,27] and Eastern [14,11] parts of Nigeria, the contribution of AGN to paediatric kidney disease burden in Ibadan was relatively small and this is in keeping with the declining incidence of childhood AGN in developed countries of the world [29]. The average annual hospital admission of AGN in Lagos, Southwest Nigeria [26], is however similar to our findings in this study (Table 5). Though the reason for the zonal differences may not be clear, it may probably be due to differences in socio-economic and climatic conditions.

Concerning chronic kidney failure from non-surgical renal disorders, the average annual hospital admission rates, though still low, showed a slight increase. A report of paediatric end-stage renal failure as seen in our Centre that included patients with Congenital anomalies of the kidney and the urinary tract (CAKUT), gave an average annual incidence of 6.6, in children 14 years and below [30]. Community-based studies should provide more accurate answers to the incidence and prevalence of CKD in Nigerian pediatric population.

The low incidence of UTI is not surprising as UTI in Nigeria is managed by both trained and untrained personnel. Antibiotics are easily bought from road-side vendors, patent medicine dealers and over the counter and may suppress the symptoms while damage progresses. Intensive public health education is needed to reverse this trend.

Table 5. Comparison of average annual hospital renal admissions from Ibadan, Enugu and Lagos

Kidney diseases	Ibadan (1959-1963)[1]	Ibadan (1989-1998) present study	Ibadan (2007-2013) present study	Enugu (1984-1996)[14]	Lagos (2008-2011)[26]
N/S	31.2	20	25	26.6	18.3
AGN	4.4	8.6	8.4	20.9	8
AKI	-	5	32	4.7	16
CKD	2.2	2	4.7	1.9	3.5
UTI	1.4	0.5	2.6	3.7	2.8

**. p <0.05*

The available manpower and facilities in a center dictate the pattern of referral. This study was performed in time periods in Nigeria when facilities for renal care were inadequate. The following efforts were however put in place to improve local care of renal diseases: Training of trainers through international collaborations; widening of the scope of the medical students' curriculum in Pediatric Nephrology; improvisation of materials for patients' management and increasing awareness of kidney diseases through our regular World Kidney Day activities. These interventional measures have indeed contributed to the improved outcome.

5. CONCLUSION

This study has shown an increase in the incidence of childhood non-surgical renal disorders in Ibadan, with AKI being the leading entity. A decline in case fatality rates was demonstrated in recent years. We opine that a further increase in awareness of kidney diseases in the community and easier access to treatment modalities will further improve outcomes.

CONSENT

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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