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An Audit of the Use of Renal Function Tests among Paediatric Mortalities

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Authors' contributions

This work was carried out in collaboration between all authors. Author AOA conceptualized the study and working with authors ADA and OOO generated and analyzed the data. All authors were involved in the manuscript preparation and approved the final manuscript.

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ABSTRACT

Background: Acute kidney injury is a frequent and serious complication encountered in critically ill children and is an independent risk factor for mortality. Major causes of childhood mortality in our environment are conditions frequently complicated by kidney failure, yet kidney failure is conspicuously absent in many of the reports. The actual proportion of these critically ill children subjected to renal function tests is not known. In view of the low representation of kidney failure as a cause of mortality in our environment, we sought to know what proportion of critically ill/dying patients had renal functions tests done and to identify any cases of missed diagnosis.
Methods: This was a descriptive study of the mortalities in the Department of Paediatrics, University College Hospital, Ibadan, between August 2004 and May 2006, particularly those due to kidney failure. Data from the departmental mortality database collected on a weekly basis were analyzed.
Results: Out of 4,941 admissions, there were 542 mortalities (age 1day -13 years) giving a mortality rate of 11%. Low birth weight, malaria, severe perinatal asphyxia, meningitis and neonatal tetanus were the leading five causes of death. Over 80% of the mortalities were under-fives.

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Serum urea and creatinine levels were documented in only 217(40%) and 49 (9%) of the mortalities respectively. Primary analysis using ante-mortem data showed that 1.8% died from kidney failure; re-analysis based on available results of renal function tests, many obtained post-mortem, ascribed deaths related to kidney failure to at least 6%.

Conclusion: There is a low rate of utilization of renal function tests in the management of critically ill patients in our setting, which might have contributed to the under-reporting of kidney failure. There is an urgent need to improve the monitoring of renal function in at-risk and critically ill patients in order to institute/expedite appropriate treatment. Failure to apply these measures will continue to affect the under-five mortality rate in Nigeria adversely. As cerebrospinal fluid analysis is important in ruling out meningitis in Paediatrics practice, so is serum creatinine monitoring for ruling out AKI at the present, and should be ensured.

Keywords: Audit; renal function tests; paediatric mortalities; kidney failure; acute kidney injury; Ibadan; Nigeria.

1. INTRODUCTION

Acute kidney injury (AKI) previously known as acute renal failure, is a syndrome characterized by a rapid loss of the kidney's excretory function and is typically diagnosed by the accumulation of end products of nitrogen metabolism (urea and creatinine) or decreased urine output, or both [1]. AKI is a frequent and serious complication in critically ill children and has been shown to be an independent risk factor for mortality, prolonged length of intensive care unit (ICU) stay, prolonged mechanical ventilation and progression to chronic kidney disease [2-6]. The reported incidence rate of AKI in children admitted to pediatric intensive care units (PICUs) ranges from 8% to 89% [5,7-11]. A global increase in the incidence of AKI is being reported but in developing countries where a higher prevalence is expected due to poor socioeconomic and environmental factors, reliable data is sparse on the incidence, prevalence, causes and recovery from the disease [12].

Previously published reports on morbidity and mortality from Emergency Pediatric Units and Special Care Baby Units where critically ill children are managed across Nigeria [13-20], did not show AKI to be an important cause of death. The reported major causes of childhood morbidity and mortality in our environment (namely, diarrhoeal diseases, malaria, septicaemia, severe birth asphyxia and malignancies) are conditions frequently complicated by kidney failure, yet the diagnosis of kidney failure is conspicuously absent in many of such reports. The proportion of these dying children who had their renal functions evaluated and monitored is unknown. It seems therefore that the primary diseases are usually highlighted but the significant contributors to morbidity and mortality are not investigated.

Furthermore, it has been noted by Nephrologists working in our setting that most patients with kidney failure present late to hospital [21-23] and these unfortunately are just the tip of the iceberg. Many from the suburbs and rural areas do not have access to the few paediatric nephrology services available in the country. One therefore wonders at the fate of those of them who suffer from severe malaria, sepsis, gastroenteritis, pneumonia, severe birth asphyxia complicated by AKI. It is a small wonder that these children end up dying and those deaths are not reported.

Worrisome also, was our observation at our departmental mortality review meetings that many of the cases of kidney failure were only identified terminally, their confirmatory results being obtained post-mortem. This situation precluded them from receiving appropriate management and also resulted in failure in recording the kidney failure as a primary diagnosis ante-mortem.

The RIFLE (risk of renal dysfunction, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage kidney disease) criteria, paediatric RIFLE (pRIFLE) and the KDIGO (Kidney Disease: Improving Global Outcome) criteria define AKI based on changes in serum creatinine, estimated glomerular filtration rate (eGFR) or urine output [24]. Patients with AKI who present with normal urine output, or those who do not have available baseline data or repeated measurements of serum creatinine would therefore not be recognized, and the incidence of AKI would therefore be underestimated.

In view of this low representation of kidney failure (acute and chronic) as a cause of mortality in our environment, we sought to know what proportion of critically ill/dying patients had undergone renal function tests, and also to identify any cases of missed diagnoses.

It is expected that this study will draw the attention of healthcare providers to the need for adequate laboratory monitoring of renal function. The findings may also be used for historical purposes.

1.1 Aim

To determine the proportion of paediatric mortalities that underwent renal function tests (specifically serum urea, creatinine and potassium, which are considered critical within limited resources); to also determine the apparent mortality rate due to kidney failure and to re-analyze data, based on available renal function tests.

2. METHODOLOGY

This is a descriptive study focused on the mortalities in the Department of Paediatrics, University College Hospital, Ibadan and those that died of kidney failure over a study period from August 2004 to May 2006.

A regular weekly mortality review meeting chaired by the Head of Department of Paediatrics was started at the University College Hospital, Ibadan in 1965 and still holds till date. All medical personnel and senior Nursing Staff of the Department attend the meetings. On a weekly basis, all admissions and mortalities of the previous week are documented and discussed. The data documented in the departmental mortality cards include patients' demography, presenting complaints, clinical features, investigations and their results, treatment given, duration of illness, the course of the illness and cause(s) of death. Additional clinical information and laboratory results available at the mortality meetings are used to review the primary diagnoses, and final diagnoses are made.

In this study, the clinical and laboratory data of the mortalities were reviewed in order to confirm the causes of death. The results of renal function tests were extracted and analyzed. The diagnoses of the various conditions were made based on their standard definitions, predicated on the typical clinical features and the confirmatory laboratory and radiologic results. Acute Kidney Injury (Failure Stage), the equivalent of KDIGO Stage III or AKIN Stage III or pRIFLE Failure Stage was used in this study and defined as 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 [24].

A definition of Chronic Kidney Failure (Stage 5 CKD) was made when the GFR was less than 15 ml/min/1.73m^2 or need for dialysis in patients with clinical or radiologic features of background chronic kidney disease [25].

Data obtained were analyzed using the SPSS 16 for Windows software. Simple statistics of proportions and percentages were employed in the analysis.

3. RESULTS

Out of 4,941 paediatric admissions over the 21 month period, there were 542 mortalities, thus giving a mortality rate of 11%. The ages of the mortalities ranged from 1 day to 13 years and 57.4% (n= 311) were male. The age distribution among the mortalities indicated that the proportionate mortality decreased with increasing age, with 232 (42.8%) being neonates, 20.1% aged 1- 5 years while 6.5% were aged more than 10 years (Table 1).

Table 1. Age distribution of mortalities

	Freq.	Percent	Cumulative percent
0-28 days	232	42.8	42.8
I month -1 yr	115	21.2	64
1 yr -5 yrs	109	20.1	84.1
5 yrs- 10 yrs	51	9.4	93.5
>10 yrs	35	6.5	100

With regards to the duration of hospital stay, over 60% were on admission for over 24 hours. Most of the mortalities (80.3%) occurred in the first week of hospital admission with 64.2% occurring within the first 3 days of admission and 37.1% in the first 24 hours of admission (Table 2).

Among all the age groups, low birth weight, malaria, severe perinatal asphyxia, meningitis

and neonatal tetanus were the leading five diagnoses and accounted for 45.6% of the mortalities. When all the primary causes of death were ranked, chronic kidney failure (CKF) contributed 1.1% of the mortalities and was the 17th most common cause of death while AKI was the 20th most common, responsible for 0.7% of the mortalities. A total of 10 patients (1.8%) died due to CKF and AKI (Table 3).

Table 2. Duration of hospital stay

Duration of admission	No.	Percent	Cumulative percent
<1 day	201	37.1	37.1
24 hrs – ≤ 3 days	147	27.1	64.2
> 3 days – 7 days	87	16.1	80.3
> 7 days	107	18.7	100
Total	542	100	100

Table 3. Primary diagnosis in all age groups

Diagnosis	Frequency	Percentage
LBW	81	14.9
Malaria	74	13.7
Severe birth asphyxia	57	10.5
Meningitis	35	6.5
Neonatal tetanus	30	5.5
Congenital malformations	29	5.4
Malignancy	25	4.6
Pneumonia	23	4.2
Neonatal Sepsis	23	4.2
Measles	22	4.1
Septicaemia	19	3.5
Neonatal jaundice	16	3.0
Diarrhoea	15	2.8
Haemoglobinopathy	13	2.4
Severe malnutrition	11	2.0
Tuberculosis	7	1.3
Chronic kidney failure (CKF)	**6**	**1.1**
Tetanus	6	1.1
HIV	5	0.9
Acute kidney Injury (Failure stage)	**4**	**0.7**

The distribution of primary diagnoses indicated that among the neonates, low birth weight was the predominant cause of mortality, followed by perinatal asphyxia, neonatal tetanus and neonatal sepsis (Table 4).

A review of renal function tests obtained ante- and post-mortem showed that serum urea was documented in 217 (40%) and serum creatinine levels in only 49 (9%) of the mortalities. Among patients in whom serum urea was documented, 26 (12%) had serum creatinine ≥ 150 mg/dl while 13 (6.0%) had levels ≥ 200 mg/dl (Table 5).

Among the 49 patients with available serum creatinine results, 10 (20.4%) had serum creatinine ≥ 3 mg/dl (Table 6).

Table 4. Principal diagnosis in neonates (Aged 0-28 days)

Diagnosis	Frequency	Percentage
LBW	81	34.9
Severe birth asphyxia	57	24.6
Neonatal tetanus	30	12.9
Neonatal Sepsis	23	9.9
Congenital malformation	18	7.8
Neonatal jaundice	16	6.9
Pneumonia	2	0.9
Meningitis	2	0.9
Post-circumcision bleeding	1	0.4
Failure to thrive	1	0.4
Birth injury	1	0.4
Total	232	100

Table 5. Categorization of serum urea levels among patients with available results of renal function tests: 217/542 (40%)

Urea level (mg/dl)	No.	%
<70	64	29.5
70 - <100	71	32.7
100 - <150	43	19.8
150 - <200	26	12
>200	13	6
Total	217	100

Table 6. Serum creatinine levels among patients with available results of renal function tests: 49/542 = (9%)

Serum creatinine (mg/dl)	No.	%
<2	26	53.6
≥2 - 3	13	26.0
≥3	10	20.4
Total	49	100

The number of the mortalities in whom serum potassium had been estimated was 229 with 15 (6.6%) having levels greater than 6.5 mmol/dl. Taking these 6.6% along with the 6% that had serum urea of ≥200 mg/dl, this means that at least 6% of the deaths were kidney failure-related.

Going by the primary records of 10 cases of renal failure, the diagnosis of renal failure was not documented initially in 16/26 (61.5%) cases if renal failure is defined by serum urea ≥ 150 mg/dl. If renal failure is defined by serum urea ≥200 mg/dl, 13 patients had renal failure and this means that 3/13 (23.1%) were missed ante-mortem.

Including the 2 cases of nephrotic syndrome and 1 case of polycystic kidney disease primarily reported among the mortalities and depending on the chosen cut-off levels of serum urea, between 16 (7.4%) and 29 (13.4%) patients who had serum urea estimation died of kidney-related disorders. Excluding the 3 aforementioned cases, kidney failure occurred in between 6% and 12% of cases compared with the documented 1.8% (Table 3).

4. DISCUSSION

This study has demonstrated the under-utilization of renal function tests in the management of critically ill children seen at this tertiary hospital, which is a reflection of the practice in our setting generally. About 60% of children did not have renal function tests performed, either at the referral hospital or at the tertiary centre. This failure is not due to lack of knowledge by the healthcare givers, but likely due to prioritization in the face of limited financial resources to settle costs of management. A typical example would be a 4-year old boy with severe malaria presenting with severe anaemia (haematocrit of 12%), impairment of consciousness and Plasmodium falciparum hyper-parasitaemia. The managing team, because of limited resources and since parents pay out of pocket at the point of care, would most likely focus on grouping and cross-matching, blood sugar and cerebrospinal fluid (CSF) analysis, blood transfusion, and parenteral antimalarial therapy. The patient might well have AKI as a co-morbidity, which would not have been considered until either the child becomes anuric or moribund. The same scenario occurs in the setting of sepsis and intravascular haemolysis with haemoglobinuria. Late presentation of patients and lack of facilities are other possible explanations.

This study has also highlighted the missed diagnoses that would have led to under-reporting of the true contribution of kidney failures. Knowing that up to 50% of children with AKI may have the non-oliguric form, it would be mis-leading to depend only on the presence of oliguria to make a diagnosis of AKI. The primary analysis of the data showed that 1.8% had kidney failure, which is about the same as rates documented in our environment if detected at all [17]. Repeat analysis of the ante- and post-mortem results showed that kidney failure occurred in at least 6% of the 217 patients that had serum urea analysis. If the 3 cases of nephrotic syndrome and polycystic kidney disease are included, renal disorders contributed to at least 16 (7.4%) deaths among the 217 mortalities. This is comparable to deaths from neonatal tetanus and pneumonias.

The number of the mortalities that had serum creatinine estimated in this study was too small for reasonable conclusions to be drawn from the result. It is however notable that 20.4% of the 49 that did the test had serum creatinine equal to or greater than 3 mg/dl, which should equate to tripling of serum creatinine in a toddler.

With regards to the mortality pattern, this study has re-affirmed that the common causes of death in our children did not change significantly [13-21]. Table 7 shows a comparison of some of the old reports from Ilorin, Lagos and Ibadan with the more recent reports from the latter. Pneumonia and gastroenteritis were the major causes of mortality in the 1960s, 1970s and 1980s in Ilorin and Ibadan while in recent times, low birth weight/pre-maturity, severe birth asphyxia and malaria are the major causes seen in Ibadan.

Even in present times, similar patterns are being recorded from different parts of Nigeria; however, HIV infection is assuming greater prominence [26-32]. Unfortunately, the recent reviews of paediatric mortalities fail to pick up a significant number of patients with kidney failure. The only review which was post-neonatal and highlighted kidney disease was from Port-Harcourt, South-south Nigeria, where there is a functioning Paediatric Nephrology Unit. The authors found 6 cases of kidney disease (11.5%) out of 52 under-fives that died on their paediatric wards [28]. A pointer to the under-reporting of renal disease in relation to paediatric mortalities in many centres in Nigeria is the autopsy study by Akang et al. [33] which showed that 181(11%) of 1626 school-aged children studied between 1961 and 1990 died of kidney disease.

Table 7. Principal causes of death at different centres and times in the country

Diagnosis	% of total deaths UITH (1983- 1984). A 2-Year review	% of total deaths LUTH (Ransome-Kuti 1972)	% of total deaths UCH (1969-1973). A 5-year review	% of total deaths UCH (1996-2000). A 5-year review	% of total deaths UCH (2004-2006). A 21-month review
Pneumonia	12.5	5	14.4	4.7	4.2
Gastroenteritis	12	9	16.3	2.6	2.4
Measles with complications	10	0.5	4.0	3.5	4.1
Preterm with complications	9.1	-	13.6	11.5 (Preterm/LBW)	14.9 (LBW)
Malnutrition	9.5	2.0	9.3	4.4	2.0
Febrile convulsions	6.2	11.0	-	-	-
Septicaemia	5.7	-	3.7	4.6	3.5
Birth Asphyxia	5.7	-	-	10.5	10.5
Severe anaemia minus Haemoglo-binopathies	4.5	3.5	4.6	5.2	0.7
Meningitis	3.2	3.0	5.4	4.7	6.5
Severe malaria	-	?	1.3	6.2	13.7

UITH-University of Ilorin Teaching Hospital; LUTH-Lagos University Teaching Hospital; UCH-University College Hospital, Ibadan

AKI, undoubtedly, complicates the common causes of mortality in our setting but its presence is apparently neither assessed nor monitored. A critically ill child might have normal renal function at presentation, but may be unable to sustain it with clinical deterioration, hence the need for repeated tests. Many reasons could be advanced for not assessing/monitoring renal function in these cases, notably financial constraints, late arrival, non-functioning laboratories among others. Although these challenges may be real, more effort should be made to find solutions to them if we are to reduce the under-five mortality rates in our environment. In our hospital presently, a new and much better equipped laboratory has been established through the Public-Private Partnership Initiative. It ensures that the results of investigations are obtained promptly, though at a cost. If medical practitioners and policy makers would place appropriate premium on these basic tests, provision of equipped laboratories should be a priority. It is pertinent to point out that over 60% of the patients in the present study stayed on admission for more than three days. There should be no justifiable reason for not monitoring the renal function in any of such patients.

Some of the newer Paediatric Nephrolgy Units in Nigeria have in recent times recorded low average annual prevalence of kidney failure among their renal admissions [34,35]. This is surprising and probably a reflection of the referral pattern. An older report on mortalities from some centres in Africa showed a similar pattern to the reports from Nigeria [36]. We are of the opinion that medical practitioners are missing the diagnosis of kidney failure, because we do not investigate for them. Provisions should be made for such key, treatment-guiding, life-saving investigations to be routine in managing critically ill individuals in our setting.

The lack of a systematic definition of acute renal failure (ARF) in the past led to significant confusion in the comparison of epidemiologic data and outcome measures globally.

In 2004, the Acute Dialysis Quality Initiative (ADQI) group published the RIFLE classification of ARF, based on changes from the patient's baseline either in serum creatinine level or glomerular filtration rate (GFR), urine output (UO), or both. This consensus definition was aimed at standardizing the reporting of AKI and enhancing the understanding of its prevention and treatment [37,38]. Since then the AKIN (Acute Kidney Injury Network) criteria, paediatric RIFLE and KDIGO criteria for staging AKI have been proposed and utilized. The new consensus definition evolved from merging the RIFLE and AKIN criteria by the Kidney Disease: Improving

Global Outcomes (K-DIGO) group [24]. It is pertinent to mention that based on the peculiarities of newborn infants, a neonatal-RIFLE is now being propagated [39]. In essence simultaneous monitoring of the serum creatinine and urinary output should detect the early and late stages of AKI. Chertow et al. [40] have shown that a rise in serum creatinine by ≥0.3 mg/dl can contribute significantly to mortality. The importance of a relatively small but acute rise in serum creatinine as a risk factor for mortality in critically ill patients, has been demonstrated both in children and adults. Serum creatinine estimation is therefore mandatory in all critically ill children as an early detection and intervention with renal replacement therapy (RRT) will save such lives.

During the period of the present study, in our general paediatric practice, more requests were made for serum urea than creatinine, probably because serum urea was more easily accessible and regarded as a good guide. Even though serum creatinine has its limitations in estimating renal function, it is considered a better biomarker for AKI than serum urea [33].

The international nephrology community has recognized the limitations of the currently used biomarkers in early detection of AKI. Newer biomarkers, such as Neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule1 (KIM1), Cystatin C [41-44], are being projected to address this issue [40]. While awaiting availability and acceptability of these newer biomarkers, medical practitioners should ensure that serum creatinine and urinary output are monitored, and that nephrotoxic agents are avoided in high-risk patients.

The findings from this study and the review of data from our environment have demonstrated that kidney failure is frequently under-diagnosed in children in our environment. Consequently, its contribution to morbidity and mortality in critically ill children is not appreciated. This under-reporting might have contributed to the non-establishment of effective and functional units for renal replacement therapy in Nigeria. Healthcare workers should therefore have a high index of suspicion for AKI and ensure that appropriate monitoring is done, to rule it out in such children. Failure to highlight the importance of AKI, which has been shown to be an independent risk factor for mortality [3-5], will continue to adversely affect the mortality rate in our patients, the health-care policies and the priority placed on establishing facilities for its management. The contribution of AKI to the persistence of the high under-five mortality in our setting needs to be holistically evaluated.

5. CONCLUSION

This study has highlighted the low rate of utilization of renal function tests in the management of critically ill patients in our setting. There is an urgent need to improve the monitoring of renal function in these patients. It should always be borne in mind that going by the present KDIGO AKI guideline, a diagnosis of AKI cannot be confidently made without serum creatinine estimation and quantifying of the urine output. There is need to identify the at-risk patients and institute appropriate measures, failure of which will adversely affect local childhood mortality rates. Just as cerebrospinal fluid analysis is important in ruling out meningitis in Paediatrics practice, so is serum creatinine monitoring for ruling out AKI at the present, and should be ensured.

6. LIMITATIONS

The chances of having a few un-retrieved results may still be possible.

ETHICAL APPROVAL

Ethical clearance was obtained from the University of Ibadan/University College Hospital, Ibadan Joint Ethical Committee to study the trends of renal disorders in our Unit. Since secondary data were used, individual patient consent was not obtained. The patients' individual data were however anonymized and not traceable to them in this study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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