

Original Research Article

AN AUDIT OF THE USE OF RENAL FUNCTION TESTS AMONG PAEDIATRIC MORTALITIES

ABSTRACT

Background

Acute kidney injury is a frequent and serious complication in critically ill children and it is an independent risk factor for mortality. The reported 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. It is not known what proportion of such children had renal function tests. 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 and to identify any cases of missing diagnosis.

Methods:

This was a descriptive analytical study of the mortalities in the Department of Paediatrics, University College Hospital, Ibadan and those that died of kidney failure between August 2004 and May 2006. Data from the departmental mortality database collected on a weekly basis were analyzed.

Results:

Out of 4,941 admissions, there were 542 mortalities (age range of 1day -13 years) giving a mortality rate of 11%. Over 80% of the mortalities were under-fives. Overall, low birth weight, malaria, severe perinatal asphyxia, meningitis and neonatal tetanus were the leading five diagnoses. 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 failures. There is an urgent need to improve the monitoring of renal function in at-risk and critically ill patients in order to institute appropriate treatment if in failure. Failure to apply these measures will continue to adversely affect the under-five mortality rate in Nigeria. 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.

38 INTRODUCTION

39 Acute kidney injury (AKI) previously known as acute renal failure is a syndrome
 40 characterized by a rapid loss of the kidney's excretory function and is typically diagnosed by
 41 the accumulation of end products of nitrogen metabolism (urea and creatinine) or
 42 decreased urine output, or both [1]. AKI is a frequent and serious complication in critically ill
 43 children and has been shown to be an independent risk factor for mortality, prolonged
 44 length of intensive care unit (ICU) stay, prolonged mechanical ventilation and progression to
 45 chronic kidney disease [2-6]. The reported incidence rate of AKI in children admitted to
 46 pediatric intensive care units (PICUs) ranges from 8% to 89% [5, 7-11]. A global increase in
 47 the incidence of AKI is being reported but in the developing countries where a higher
 48 prevalence is expected, as a result of poor socioeconomic and environmental factors,
 49 reliable data is sparse on the incidence, prevalence, causes and recovery from the disease
 50 [12].

51 Previously published reports on morbidity and mortality from Emergency Pediatric Units
 52 and Special Care Baby Units where critically ill children are managed across our country [13-
 53 20], did not show AKI to be an important cause of death. The reported major causes of
 54 childhood morbidity and mortality in our environment, namely, diarrhoeal diseases, malaria,
 55 septicaemia, severe birth asphyxia and malignancies, are conditions frequently complicated
 56 by kidney failure, yet kidney failure is conspicuously absent in many of these reports. It is
 57 not known what proportion of these dying children had their renal functions evaluated and
 58 monitored. It seems therefore that the primary diseases are usually highlighted but the
 59 significant contributors to morbidity and mortality are not investigated.

60 Additionally, it has been noted by Nephrologists working in our setting that most of the
 61 patients with kidney failure present late to hospital [21-23] and these unfortunately are the
 62 tip of the iceberg. There are many from the outer parts of our cities and rural areas that do
 63 not have access to the few paediatric nephrology units available in the country. One
 64 therefore wonders at the fate of those who suffer from severe malaria, sepsis,
 65 gastroenteritis, pneumonia, severe birth asphyxia complicated by AKI. Those deaths are not
 66 reported.

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

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

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

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

86

87 Aim

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

92

93 Methodology

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

97 A regular weekly mortality review meeting chaired by the Head of Department of
98 Paediatrics was started at the University College Hospital, Ibadan in 1965 and still holds till
99 date. The meetings are attended by all medical personnel and senior Nursing Staff of the
100 Department and on a weekly basis all admissions and mortalities of the previous week are
101 documented and discussed. The data documented in the departmental mortality cards
102 include patients' demography, presenting complaints, clinical features, investigations and
103 their results, duration of illness, the course of the illness and cause(s) of death. Additional
104 laboratory results and clinical information obtained at the mortality meetings are used to
105 review the primary diagnoses and final diagnoses are arrived at.

106 In this study, the clinical and laboratory data of the mortalities were reviewed in order to
107 confirm the causes of death and the results of renal function tests were extracted and
108 analyzed. The diagnoses of these conditions were made based on their standard definitions,
109 predicated on the typical clinical features and the confirmatory laboratory and radiologic
110 results. Data obtained were analyzed using the SPSS 16 for Windows software. Simple
111 statistics of proportions and percentages were used for analysis.

112

113 Results

114 Out of 4,941 admissions into the paediatric wards over the period of 21 months, there were
115 542 mortalities, giving a mortality rate of 11%. The ages of the mortalities ranged from 1 day
116 – 13 years and 57.4% (n= 311) were males. The age distribution among the mortalities
117 indicated that the proportionate mortality decreased with increasing age with 232 (42.8%)
118 being neonates, 20.1% aged 1- 5 years while 6.5% were aged more than 10 years. (Table 1)
119 Table 1

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

120 Age distribution of Mortalities

With regards to the duration of hospital stay, over 60% were on admission for over 24hours. 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)

Table 2

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

Duration of Hospital stay

The distribution of primary diagnoses indicated that among the neonates, low birth weight was the predominant cause of mortality and this was followed by perinatal asphyxia, neonatal tetanus and neonatal sepsis (Table 3).

Table 3

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-circumscision bleeding	1	0.4
Failure to thrive	1	0.4
Birth injury	1	0.4
Total	232	100

Principal Diagnosis in Neonates (Aged 0-28 days)

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 4)

144

145 Table 4

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 renal failure	6	1.1
Tetanus	6	1.1
HIV	5	0.9
Acute renal failure	4	0.7

146 Primary diagnosis in all age groups

147

148 Review of renal function tests obtained ante- and post-mortem showed that serum urea
 149 and serum creatinine levels were documented in 217 (40%) and 49 (9%) of the mortalities
 150 respectively. Among patients in whom serum urea was documented, 26 (12%) had serum
 151 creatinine $\geq 150\text{mg/dl}$ while 13 (6.0%) had levels $\geq 200\text{mg/dl}$ (Table 5).

152 Table 5

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

153 Categorization of Serum Urea levels among patients with results of renal function tests:
 154 217/542 (40%)

155

156 Among the 49 patients with available serum creatinine results, 10 (20.4%) had serum
 157 creatinine $\geq 3\text{mg/dl}$ (Table 6).

Table 6

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

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

The number of the mortalities in whom serum potassium had been estimated was 229 with 15 (6.6%) having levels greater than 6.5mmol/dl. Using the 6% that had serum urea of ≥200mg/dl and 6.6% that had serum potassium >6.5mmol/dl, 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 as serum urea ≥ 150mg/dl. If renal failure is defined by serum urea ≥200mg/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 that had serum urea estimation died of kidney-related disorders. Excluding these 3, kidney failure occurred in between 6% and 12% of cases compared with the documented 1.8%.

Discussion:

This study has demonstrated the under-utilization of renal function tests in the management of critically ill children seen at a tertiary hospital, which is a reflection of the practice in our setting generally. About 60% of children did not have renal function tests done either at the referral hospital or at the tertiary centre. This practice is not due to lack of knowledge by the healthcare givers, but rather because of prioritization in the face of limited financial resources to settle costs of management. A typical example will be a 4-year old boy who presents with features of severe malaria manifesting with severe anaemia (haematocrit of 12%), impairment of consciousness and Plasmodium falciparum hyper-parasitaemia. The managing team, because of limited resources would likely focus on grouping and cross-matching, blood sugar and cerebrospinal fluid (CSF) analysis, blood transfusion, and parenteral antimalarials. Since these parents pay out of pocket at the point of care, investigations considered to be of utmost importance are usually carried out. The patient might well have AKI as a co-morbidity, which would not have been given attention until either the child becomes anuric or moribund. The same practice occurs in the setting of sepsis and intravascular haemolysis with haemoglobinuria.

This study has also highlighted the missed diagnoses which 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 3mg/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 Ibadan. 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.

Table 7

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 Haemoglobinopathies	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

PRINCIPAL CAUSES OF DEATH AT DIFFERENT CENTRES AND TIMES IN THE COUNTRY.

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

Even in present times, similar patterns are being recorded from different parts of Nigeria; however, HIV infection is assuming greater prominence [25-31]. Unfortunately, these 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 [27]. 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 [32] which showed that 181(11%) of 1626 school-aged children studied between 1961 and 1990 died of kidney disease.

AKI, undoubtedly, complicates the common causes of mortality in our setting but is apparently not investigated for nor monitored for. A critically ill child may have a normal renal function at presentation but may not 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 other reasons. 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 but at a cost. If appropriate premium is placed on these tests by medical practitioners and policy makers, provision of equipped laboratories for these basic tests 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 most of these patients.

Some of the newer Paediatric Nephrology Units in Nigeria have in recent times recorded low average annual prevalence of kidney failure among their renal admissions [33, 34]. 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 [35]. We are of the opinion that medical practitioners are not diagnosing these cases of kidney failure because we do not investigate for them for various reasons. 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 [36,37]. Since then the AKIN criteria, paediatric RIFLE and KDIGO criteria for staging AKI have been proposed and utilized. A new consensus definition merging the RIFLE criteria and the Acute Kidney Injury Network definition has emerged from the Kidney Disease: Improving Global Outcomes (K-DIGO) group [24]. It is pertinent to mention that based on the peculiarities of the newborn infants a neonatal-RIFLE is now being propagated [38]. In essence simultaneous monitoring of the serum creatinine and urinary output should detect the early and late stages of AKI. Chertow and his colleagues [39] have shown that a rise in serum creatinine by $\geq 0.3\text{mg/dl}$ can contribute significantly to mortality. The importance of a relative 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 detecting AKI early enough and are projecting newer biomarkers that will improve its early detection [39]. While awaiting availability and acceptability of the newer biomarkers for earlier detection of AKI such as Neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule1 (KIM1), Cystatin C [40-43], medical practitioners should ensure that serum creatinine and urinary output are monitored and nephrotoxic agents 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 made to rule it out in these 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 negatively 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.

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. As lumbar puncture with 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.

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

Ethics Statement

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.