

Deranged Kidney Function in Neonates in Kano: A Cause for Concern

Abstract

Background: In neonates, derangement in kidney function on admission is often overlooked, especially in resource-constrained settings, and is associated with increased risk of morbidity and mortality. This study aimed to describe the burden of acute kidney injury (AKI) in neonates admitted to a tertiary hospital in northern Nigeria.

Methods: The laboratory results of serum electrolytes, urea and creatinine of all neonates aged 5 days and over admitted into the newborn unit over a period of six months were retrospectively reviewed and values compared with neonatal reference ranges. The age and sex of each neonate were recorded. Results of repeat samples and those without age and/or sex indicated were excluded. Kidney function was classified based

on the degree of rise in serum creatinine relative to normal values.

Results: The results of the first serum chemistry samples of 131 admitted neonates (58.8% male); median (IQR) age 10 (7, 14) days were analyzed. Electrolyte abnormalities, most commonly sodium and chloride, were present in 74.8% of the samples. Fifty-six neonates (42.7%) had AKI, 5 of them (8.9%) being in the severe category. More male neonates had AKI than females (62.5% vs 37.5%). There was a positive correlation between the degree of AKI and the numbers of deranged electrolytes ($\rho = 0.200, p = 0.022$).

Conclusion: The burden of AKI is high in this cohort.

Keywords: Acute kidney injury, deranged electrolytes, neonates, Nigeria.

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Introduction

There are few reports on different aspects of deranged kidney function in neonates in the developing world including Nigeria. In admitted neonates, this is probably because kidney dysfunction is usually asymptomatic and only suspected when a newborn fails to pass urine over several hours and/or serum creatinine is noticed to be elevated. These may even not be apparent for several days particularly in resource-constrained settings where staff responsible for newborn care are very few and facilities for evaluation and diagnosis of kidney dysfunction are limited. While there are studies highlighting the burden, progression and outcome of acute kidney injury (AKI) in neonates in

the developed world, the developing world which has the highest burdens of neonatal mortality has not placed enough emphasis on AKI which is known to be associated with some of the most common neonatal disease conditions such as sepsis, prematurity and perinatal asphyxia, and is an independent predictor of mortality.

According to the United Nations, the neonatal mortality rate (NMR) in Nigeria is 35/1000 live births, one of the highest in the world. In northern Nigeria, an observational study put the NMR in a primary hospital at 46/1000 live births. Kano state, north-western Nigeria, has some of the worst health indices in the country. It is the second most populous state in the country but has only one facility which

offers specialized neonatal care - the Special Care Baby Unit (SCBU) of Aminu Kano Teaching Hospital (AKTH). This unit receives and manages critically ill neonates from Kano state, as well as from neighbouring states. This retrospective review of results takes a snapshot of the burden of AKI among neonates admitted to the unit who had serum electrolytes, urea and creatinine done on admission.

Methods

This was a retrospective review of records of electrolytes, urea and creatinine in neonates aged 5 days and over who were admitted to the SCBU of AKTH, a tertiary health center in north-western Nigeria, between January 1 and June 30, 2019. Admission age and sex of the patients as well as these results were extracted from the records. Excluded were results which were from repeat samples on same patients and those with missing data. Approval for the study was obtained from the Research Ethics Committee of AKTH. Being a retrospective review of laboratory results, the need for informed consent was waived. The upper limits of normal (ULN) for age were used for categorization of derangements in serum urea and creatinine, as there were no baseline serum creatinine results to use as reference. Kidney dysfunction was then classified based on degree of derangement in serum creatinine into mild (1.5 to 1.9 times ULN), moderate (2.0 to 2.9 times ULN) and severe (≥ 3 times ULN) AKI. For the purposes of this study, reference ranges for serum electrolyte values used were sodium (Na) = 135 – 145mmol/L, potassium (K) = 3.5 to 6.0mmol/L, chloride (Cl) = 95 – 108mmol/L, and bicarbonate (HCO_3^-) = 16 – 24mmol/L.

Data were entered into an Excel spreadsheet (Microsoft Excel, version 2007) and exported to SPSS version 20.0 for statistical analysis. Categorical variables were expressed as proportions and associations determined using the Pearson Chi square test. Continuous variables were not normally distributed as determined visually using the histogram and the Q-Q plots and statistically using the Kolmogorov-Smirnov Z test. They were thus reported as medians with interquartile ranges (IQR). Spearman's rank correlation was computed to assess the relationship between serum creatinine and the

electrolytes. A p-value of <0.05 was considered to be statistically significant.

Results

Four hundred and sixty eight neonates were admitted during the study period, and results of 131 neonates (77 male, 58.8%) who met the study criteria were analyzed. Median (IQR) age at admission was 10 (7, 14) days. Over three-quarters ($n = 101$, 77.1%) of the neonates were 14 days of age or less, those 7 days of age or less accounting for almost half of the number ($n = 48$, 47.5%). The demographic characteristics of the neonates and the median (IQR) values of the biochemical variables are represented in Table 1.

Serum electrolytes were deranged in 98 (74.8%) of the neonates, a quarter of them ($n = 25$, 25.5%) having more than 2 derangements. Table 2 shows the various biochemical abnormalities seen in the studied neonates. Sodium abnormalities were seen in 54.2% of results, chloride abnormalities in 42.8%, bicarbonate abnormalities in 28.2% and potassium abnormalities in 23.7%. Serum urea was elevated in the results of 35 (26.7%) neonates and serum creatinine was elevated above the upper limit of normal for age in 86 (65.6%) neonates. Fifty-six neonates (42.7%) were determined to have AKI (with serum creatinine levels at least 1.5 times higher than the upper limit of normal for age) and this was categorized as mild in 34 neonates (26.0%), moderate in 17 (13.0%) and severe in 5 (3.8%) neonates.

The proportion of neonates with AKI increased with increase in numbers of deranged electrolytes but this association was not significant (34.4% in neonates with one deranged electrolyte vs 83.3% in those with four deranged electrolytes; $\chi^2 = 8.971$, $p = 0.062$). With regards to degree of kidney dysfunction, higher proportions of deranged electrolytes were seen in successively higher severities of AKI as seen in Table 3. There was a positive correlation between the severity of AKI and the numbers of deranged electrolytes ($r = 0.200$, $p = 0.022$).

Male neonates had higher proportions of AKI at all stages than the female neonates as shown in Table 4. Furthermore, a higher proportion of neonates 14 days

of age or less on admission had deranged serum electrolytes and AKI compared to those who were admitted at over 14 days of age. However, none of these achieved statistical significance.

There was a positive correlation between serum potassium and creatinine ($r = 0.226$, $p = 0.009$) while that between serum bicarbonate and creatinine was negative ($r = -0.191$, $p = 0.029$). For sodium and chloride, the correlation with creatinine was not significant.

Table 1: Demographic characteristics and median (IQR) values of biochemical parameters of the studied neonates

Demographic variables	
Age, median (IQR)	10 (7, 14)
Age category, n (%)	
•	48 (36.6)
• 8 – 14 days	53 (40.5)
• 15 – 21 days	22 (16.8)
• >21 days	8 (6.1)
Sex, female, n (%)	54 (41.2)
Biochemical parameters	
• Serum urea, mmol/L, median (IQR)	4.3 (3.2, 8.0)
• Serum creatinine, μ mol/L, median (IQR)	72.0 (42.0, 101.0)
• Serum sodium, mmol/L, median (IQR)	138 (133, 143)
• Serum potassium, mmol/L, median (IQR)	4.7 (4.1, 5.5)
• Serum chloride, mmol/L, median (IQR)	100 (94, 104)
• Serum bicarbonate, mmol/L, median (IQR)	19 (17, 22)

IQR – interquartile range

Table 2: Biochemical abnormalities in the studied neonates

Biochemical parameter	Category n(%)			Total
	Low	Normal	High	
Sodium	48 (36.6)	60 (45.8)	23 (17.6)	131
Potassium	11 (8.4)	100 (76.3)	20 (15.3)	131
Chloride	34 (26.0)	75 (57.3)	22 (16.8)	131
Bicarbonate	21 (16.0)	94 (71.8)	16 (12.2)	131
Urea	-	96 (73.3)	35 (26.7)	131
Creatinine	-	45 (34.4)	86 (65.6)	131

Table 3: Presence and severity of AKI in neonates with deranged electrolytes

Number of deranged electrolytes	Severity of AKI n(%)				Total
	None	Mild	Moderate	Severe	
None	21 (28.0)	7 (20.6)	4 (23.5)	1 (20.0)	33 (25.2)
One	21 (28.0)	7 (20.6)	3 (17.6)	1 (20.0)	32 (24.4)
Two	25 (33.3)	11 (32.4)	5 (29.4)	0 (0.0)	41 (31.3)
Three	7 (9.3)	7 (20.6)	4 (23.5)	1 (20.0)	19 (14.5)
Four	1 (1.3)	2 (5.9)	1 (5.9)	2 (40.0)	6 (4.6)
Total	75	34	17	5	131

$\chi^2 = 22.166$, $p = 0.036$

Table 4: Association between sex and severity of AKI

Sex	Severity of AKI n (%)			Total
	Mild	Moderate	Severe	
Female	13 (38.2)	8 (47.1)	0 (0.0)	21 (37.5)
Male	21 (61.8)	9 (52.9)	5 (100.0)	35 (62.5)
Total	34	17	5	56

$\chi^2 = 3.671$, $p = 0.160$

Discussion

In this study, 42.7% of the neonates studied had AKI. This is slightly lower than the 44.8% reported by Duzova et al¹⁰ in Turkey and 46.1% reported by Emmanuel et al in Uyo south-southern Nigeria. However, the study by Emmanuel et al was only done on neonates with birth asphyxia in whom it is known that AKI occurs to a higher degree. More than half of the neonates in the Turkish study were on mechanical ventilation as at the time of diagnosis. Higher prevalence values (56%) were obtained in studies from India and Taiwan in neonates with perinatal asphyxia and extreme low birth weight respectively. In this study, the serum chemistry results of babies admitted at less than 5 days of age were not included as maternal serum creatinine is known to have influence on the neonatal serum creatinine level in the first few days of life. It is thus possible that the true burden of AKI may have been underestimated as a large proportion of the results of babies with perinatal asphyxia and premature babies would have been excluded, conditions which are among the most common in the center, and which would have presented within the first 24 hours of life. Other African countries have reported varying prevalence figures such as 31.5% in Tanzania, 33.3% in Zimbabwe, 27.1% in Sudan, 11.7% in Kenya, and 10.8% in Egypt, with differences due to

methodology applied and the definition of AKI used. It is however clear that the burden of AKI in neonates remains high as they are a heterogeneous population with unique risk factors for AKI related to gestational age, birth weight and other maternal, congenital, and perinatal conditions.

The presence of electrolyte derangement in three-quarters of the results was alarming. However, although they were all admitted neonates, details of their clinical conditions were not available. A similar figure was obtained in Pakistan in a retrospective study done on neonates with probable and culture-proven sepsis. However, Islam et al in Bangladesh obtained a lower prevalence of 40% in a prospective study done on healthy preterm low birth weight babies, none of whom was said to have had mixed electrolyte abnormalities. Various types of electrolyte derangements in neonates under different clinical situations have been reported by different authors. However, studies on electrolyte derangements and their possible association with kidney dysfunction are rare, and none has been published from this region.

In this study, almost one in every ten neonates with AKI had the severe form of AKI. Although lower than what was the case in other studies, this is worrisome because it implies the failure of earlier identification of kidney disease in the neonates. It could also be due to the severity of the underlying clinical condition causing AKI in the neonates, or late presentation to the facility. Management of severe AKI in neonates is particularly challenging especially where the materials and technology for its management are lacking. While peritoneal dialysis (PD) is currently the only available option for dialytic management of severe AKI in neonates in Nigeria, the improvised method is the only available form of PD in Kano. Severe forms of AKI are associated with increased morbidity and mortality including higher risks of developing chronic kidney disease, a condition fraught with management challenges in many parts of the world.

The higher proportion of male neonates with AKI is not surprising. It is possible that some of these neonates have unidentified congenital anomalies of

the kidneys and urinary tract which are known to be about three times commoner in boys, and associated with poor kidney function. However, as this study did not review diagnostic considerations or imaging results, the author is unable to comment on this.

Being a review of laboratory results, it was not possible to determine the gestational ages or clinical status and outcomes of the studied neonates as these were not captured in the laboratory records. This study may have underestimated the true burden of AKI as, being the only tertiary referral center in the region with large proportions of critically ill neonates admitted within hours of birth, the exclusion of results of babies under 5 days of age and the use of the upper limits of normal ranges of creatinine for determining the degree of kidney dysfunction could have led to the reporting of lower prevalence values. This study however brings to the fore the need for a prospective study to accurately determine the burden of kidney disease and the associated clinical features and outcomes in this population in a bid to reduce the associated morbidity and mortality.

Conclusion

The burden of AKI is high in neonates in Kano, and calls for further investigation.

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Statements and Declarations

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Conflict of interest - The author declares no conflict of interest.

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