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RESEARCH LETTER

A Protocol for the Nigerian Neonatal Acute Kidney Injury Continuum Prospective Study

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INTRODUCTION

Neonatal acute kidney injury (AKI) is characterized by a sudden decline in renal function, or a failure of physiologic rise in glomerular filtrate rate, leading to the kidneys' inability to maintain fluid and electrolyte homeostasis.[1,2] Despite the significant attention given to the epidemiology of AKI in adult and older pediatric populations, there is a paucity of data on neonatal AKI. There has been a notable lack of focus on the neonatal AKI continuum consisting of acute kidney disease, as well as its progression to chronic kidney disease.[1–3] This is particularly important given the limited evidence from high-income countries on the long-term complications associated with neonatal AKI extending beyond childhood into adulthood, as well as its potential contribution to the rising burden of non-communicable disease, which has recently gained prominence in public health.[4–8] In addition, the observation that risk factors associated with poor renal outcomes in high-income countries, such as sepsis, liver failure, and smaller weight for age, are more prevalent in low-income and middle-income countries gives credence to an AKI continuum study.[9,S1,S2]

Currently, there is insufficient data to provide evidence and contextualized data on the impact of the neonatal AKI continuum, especially on infant health, in low-middle-income-countries. The current understanding of the diagnostic and prognostic implications of the neonatal AKI continuum is inadequate for informing practical preventive measures. This lack of knowledge translation and evidence-based clinical guidelines hinders the effective management of the neonatal AKI continuum. The implications are that, there is a dearth or lack of local information to guide follow-up schedules in the sub-population; and that evidence-based, effective preventive interventions are not being used.[S3]

This study, therefore, has the potential to improve our understanding of the etiology and risk factors for the AKI continuum, provide evidence to support early detection and diagnosis, provide background information on the natural progression and outcomes of this continuum, and provide information on optimal management strategies. In addition, a better understanding of the risk factors and underlying mechanisms may inform evidence-based, population-specific preventive strategies.

We hypothesize that neonatal AKI is highly prevalent in Nigeria and that a significant proportion would progress to acute kidney disease and chronic kidney disease.

This study seeks answers to the following questions:

1. What are the incidences of neonatal AKI, neonatal acute kidney disease, and progression to chronic kidney disease in Nigeria?
2. What are the risk factors associated with neonatal AKI in Nigeria?

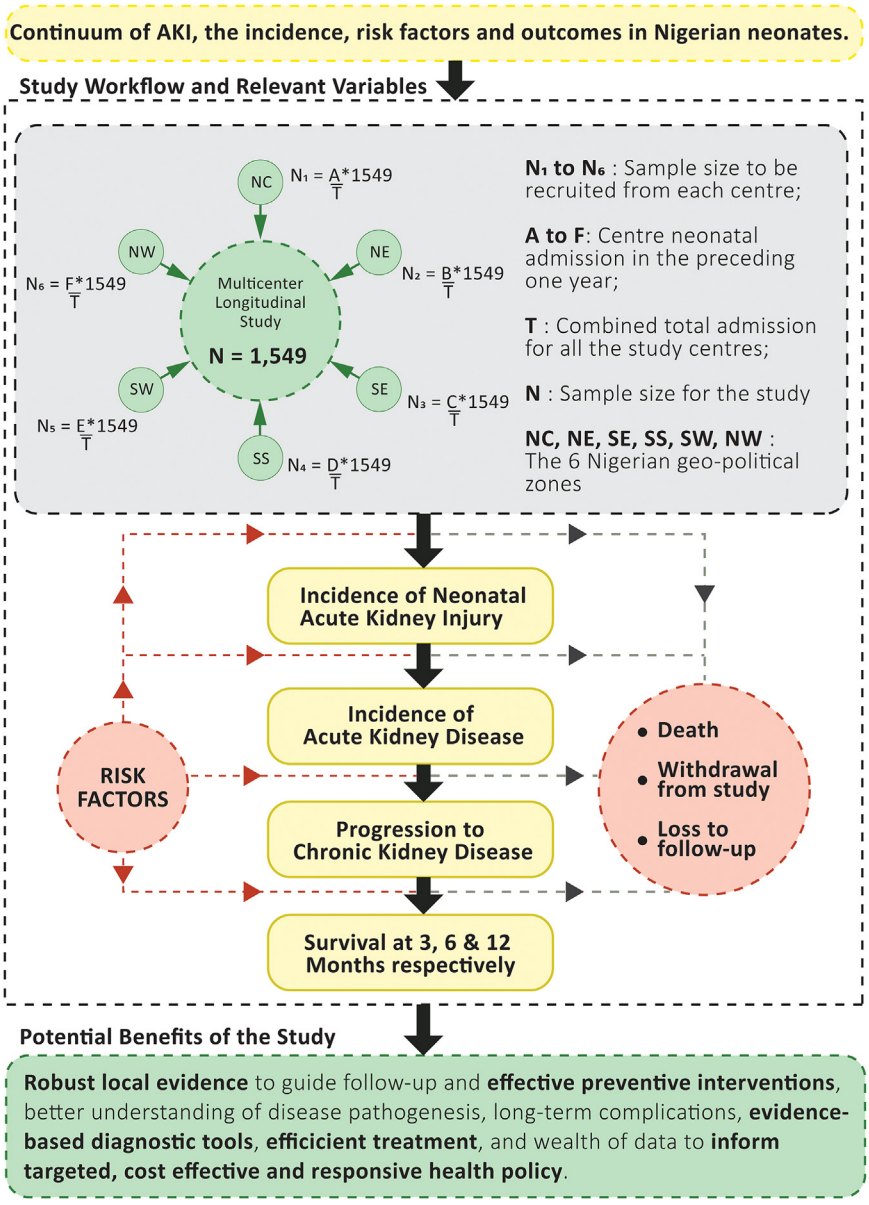

Figure 1. Flow diagram of the NEOAKINUM conceptual framework.

3. What renal supportive care is available for infants with the AKI continuum?
4. What are the outcomes of the neonatal AKI continuum (hospitalization outcomes-death/survival; survival at 6 months, at 12 months, and progression to chronic kidney disease)?

The Nigerian Neonatal Acute Kidney Injury Continuum (NEOAKINUM: Neo-Neonatal AKINUM-Acute Kidney Injury Continuum) study hopes to answer the above questions by providing basic epidemiological data on the AKI continuum, including incidences of AKI, acute kidney disease, and chronic kidney disease, as well as risk factors and outcomes through a multicenter, multiregional prospective cohort study in Nigeria's six geopolitical zones (Supplementary Table S1, Figure 1). Data from this study will be compared to reports from high-income countries to determine the variability of neonatal kidney disease epidemiology. The findings of this study may stimulate further neonatal nephrology research and provide data for historical control for interventional studies in the future with the ultimate goal of improving neonatal AKI outcomes.

General Objectives

To assess the continuum of AKI, the incidence, risk factors and outcomes in Nigerian neonates.

Specific Objectives

1. Determine the incidences of neonatal AKI, neonatal acute kidney disease, and chronic kidney disease in Nigeria.
2. Determine the risk factors associated with neonatal AKI in Nigeria.

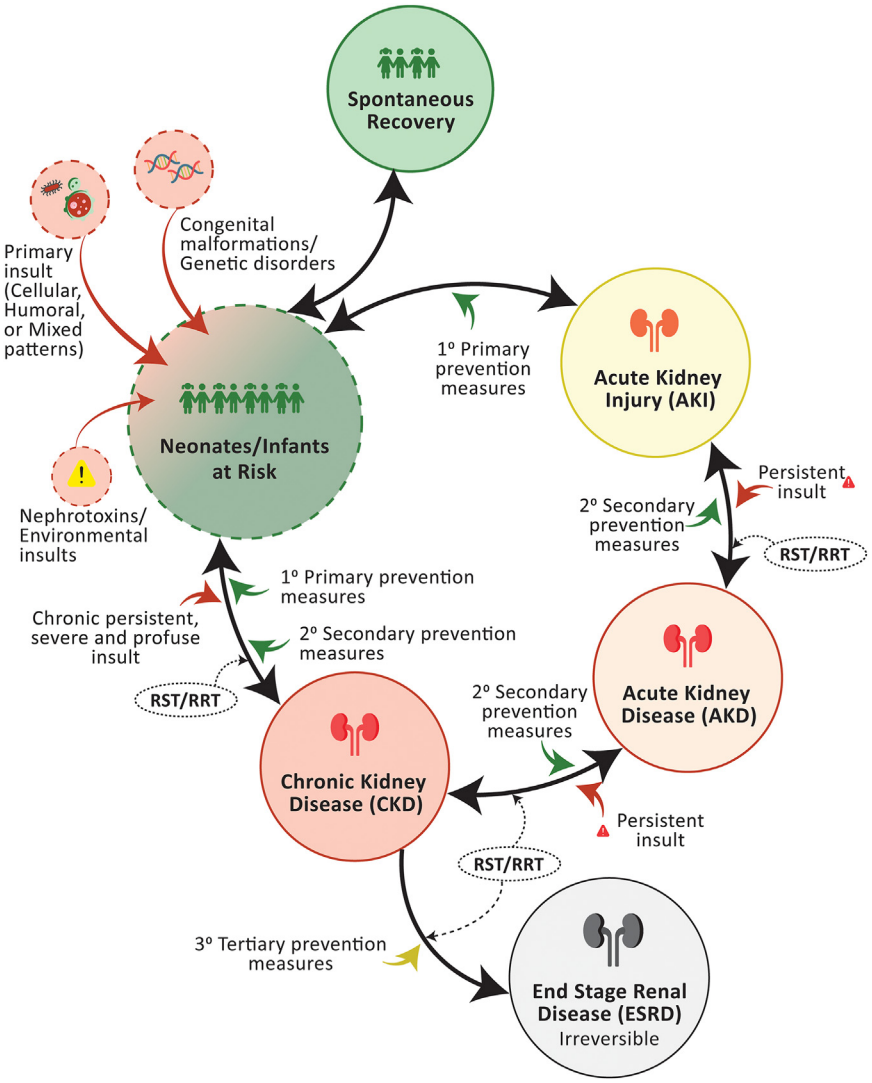

Figure 2. Neonatal AKI-risk factors, pathogenesis, preventative measures, and progression. AKI, acute kidney injury; RRT, renal replacement therapy; RST, renal supportive therapy.

3. Determine available renal supportive interventions are available for infants with AKI continuum.
4. Determine the outcomes (hospitalization outcomes-death/survival; survival at 6 months, 12 months, progression to CKD) of neonatal AKI continuum

Eligibility Criteria

Inclusion Criteria

1. Neonates (less than 28 days old) admitted to neonatal units in Nigerian hospitals.
2. Admitted infants who have received intravenous fluids for at least 48 hours.

Exclusion Criteria

1. Refusal of caregivers to give consent.
2. Neonates who died within 48 hours of admission.
3. Presence of severe congenital malformation, including severe congenital anomalies of the kidney and urinary tract.
4. Failure to determine AKI status.
5. Infants that require specialized care and must be transferred or relocated with limited follow-up opportunities.

The methods' details including the study proforma (Supplementary Table S2) are provided as Supplementary Material.

DISCUSSION

This study aims to determine the prevalence of neonatal AKI, neonatal acute kidney disease, and the likelihood of developing chronic kidney disease in a group of infants from Nigeria.

It is anticipated that this study will also provide information on the risk factors associated with neonatal AKI and the outcomes of the neonatal AKI continuum in the form of in-hospital survival or mortality,

longitudinal survival rates at 6 and 12 months, and the probability of progression to CKD.

Neonatal AKI is a significant public health concern, especially in low-income and middle-income-countries like Nigeria. The actual narrative in low-middle-income countries is largely unknown, with no data to support policy or effective resource distribution. Furthermore, the role of environmental exposure in disease causation and progression is of current interest. This expanded on the idea that each region is required to identify local exposure and develop personalized interventions based on locally available resources. Given the unique genetic composition and significant Black population of Nigeria, it is desirable to collect indigenous data on the neonatal AKI continuum in order to establish tailored preventative measures and document the accessibility of renal support care (Figure 2).

To maximize the utilization of limited resources, it is essential to implement targeted renal protection measures. This is feasible through the implementation of primary, secondary, and tertiary preventive measures at various stages of the disease process, as illustrated in Figure 2.

This goal requires a comprehensive understanding of the pathogenetic mechanism of the AKI continuum, and the risk factors involved in its development to inform the implementation of evidence-based interventions. By addressing the knowledge gap with regard to the continuum of AKI in neonates, researchers can discern prospects for timely intervention and enhanced management approaches.

This proposed longitudinal study is one of the few to examine AKI progression, including acute kidney disease and chronic kidney disease, in a low-resource setting. The multicenter study, which includes large sample size and research experts, will ensure external validity.

Conclusion

The incidence of neonatal AKI, acute kidney disease, and progression to CKD from this study will be compared with reports from high-income countries to describe the variability in the epidemiology of neonatal AKI continuum. This will lay the groundwork for advocacy and intervention to improve neonatal AKI outcomes in Nigeria. Future interventional studies on neonatal AKI in the specified population may use this study's findings as historical controls.

DISCLOSURE

All the authors declared no competing interests.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

Supplementary References.

Table S1. List of participating centers in six geopolitical zones in Nigeria.

Table S2. Study proforma.

REFERENCES

1. Jetton JG, Boohaker LJ, Sethi SK, et al. Incidence and outcomes of neonatal acute kidney injury (AWAKEN): a multicentre, multinational, observational cohort study. *Lancet Child Adolesc Health*. 2017;1:184–194. https://doi.org/10.1016/S2352-4642(17)30069-X
2. Askenazi DJ. AWAKEN-Ing a new frontier in neonatal nephrology. *Front Pediatr*. 2020;8:21. https://doi.org/10.3389/fped.2020.00021
3. Basu RK, Kaddourah A, Terrell T, et al. Assessment of Worldwide Acute Kidney Injury, Renal Angina and Epidemiology in critically ill children (AWARE): study protocol for a prospective observational study. *BMC Nephrol*. 2015;16:1–8. https://doi.org/10.1186/s12882-015-0016-6
4. Akkoc G, Duzova A, Korkmaz A, Oguz B, Yigit S, Yurdakok M. Long-term follow-up of patients after acute kidney injury in the neonatal period: abnormal ambulatory blood pressure findings. *BMC Nephrol*. 2022;23:116. https://doi.org/10.1186/s12882-022-02735-5
5. Coca SG, Singanamala S, Parikh CR. Chronic kidney disease after acute kidney injury: a systematic review and meta-analysis. *Kidney Int*. 2012;81:442–448. https://doi.org/10.1038/ki.2011.379
6. Chawla LS, Kimmel PL. Acute kidney injury and chronic kidney disease: an integrated clinical syndrome. *Kidney Int*. 2012;82:516–524. https://doi.org/10.1038/ki.2012.208
7. Alao MA, Ibrahim OR, Ademola AD, Asinobi AO. Factors associated with mortality and long-term outcomes of pediatric acute kidney injury in a resource limited setting. *Nephron*. 2023;147:1–11. https://doi.org/10.1159/000528079
8. Alao MA, Ibrahim OR, Asinobi AO, Akinsola A. Long-term survival of children following acute peritoneal dialysis in a resource-limited setting. *Kidney Res Clin Pract*. 2020;39:469–478. https://doi.org/10.23876/j.krcp.20.055
9. Li J, Shen L, Qian K. Global, regional, and national incidence and mortality of neonatal sepsis and other neonatal infections, 1990–2019. *Front Public Health*. 2023;11:1139832. https://doi.org/10.3389/fpubh.2023.1139832