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Acute kidney injury progression to chronic kidney disease in children hospitalized with severe malaria

Submission date
15/05/2025

Recruitment status
No longer recruiting

Registration date
21/05/2025

Overall study status
Ongoing

Last Edited
16/07/2025

Condition category
Urological and Genital Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Acute kidney injury (AKI) is an abrupt loss of kidney function that occurs in 25-59% of children hospitalized with severe malaria. AKI is one of the strongest risk factors for death in children with severe malaria and is associated with long-term cognitive and kidney problems. Following injury, the kidney undergoes a repair process to restore normal kidney function. If the repair process goes awry and is 'maladaptive', it can lead to persistent kidney injury and chronic kidney disease (CKD). Our previous studies showed an increased risk of CKD in severe malaria survivors. These results led to our central hypothesis that persistent activation of pathways associated with severe malaria-associated AKI contributes to maladaptive repair following AKI and increases CKD risk.

Who can participate?
Children 3 months of age to 16 years hospitalized with severe malaria and healthy volunteer community children (as controls), to understand the baseline prevalence of kidney disease in the population.

What does the study involve?
Children with severe malaria will have their kidney function assessed during hospitalization and will return for five scheduled follow-up visits to evaluate their kidney function and health-related quality of life. Community children will have a baseline and follow-up assessment of kidney function and health-related quality of life.

What are the possible benefits and risks of participating?
There are no direct benefits to study participation. Risks are minimal as the study only involves blood draws and non-invasive imaging of kidney size and function.

Where is the study run from?
The study will be conducted at three referral hospitals across Uganda.

When is the study starting and how long is it expected to run for?
January 2022 to July 2027

Who is funding the study?
1. The National Institutes of Health (NIH) through the National Institute of Allergy and Infectious Diseases (NIAID) (USA)
2. The Fogarty International Center of the NIH (USA)

Who is the main contact?
Dr Andrea L. Conroy, conroya@iu.edu

Contact information

Type(s)
Public, Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
R01 AI165946-01, K43TW012586

Study information

Scientific Title
Malaria Associated Pathogenesis of Chronic Kidney Disease (MAP-CKD): a prospective study of acute kidney injury and chronic kidney disease in children hospitalized with severe malaria

Acronym

MAP-CKD

Study objectives
The objective of this study is to prospectively define the impact of severe malaria in childhood on kidney injury and recovery and to define pathways of maladaptive repair that may represent modifiable targets to improve long-term outcomes following AKI. This study is also aimed at delineating the kidney-brain axis among children with severe malaria by assessing how these pathways impact neurological and behavioral outcomes.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 09/06/2022, Makerere University School of Biomedical Sciences Research Ethics Committee (SBSREC) (College of Health Sciences, PO Box 7072, Kampala, -, Uganda; +256 779340363/+256701940363; biomedicalresearch62@gmail.com), ref: SBS-REC, protocol number: SBS-2022-173

Study design
Multicenter prospective observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Prevention, Quality of life, Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Chronic kidney disease progression following severe malaria-associated acute kidney injury

Interventions
This is a prospective observational cohort study that will recruit children with severe malaria through the emergency room of participating clinical sites (Mulago National Referral Hospital, Lira Regional Referral Hospital, Jinja Regional Referral Hospital). Malaria will be defined based on the presence of a positive blood smear or rapid diagnostic test for Plasmodium falciparum HRP-2 or pan lactate dehydrogenase (LDH). Children will be eligible if they have diagnostic evidence of malaria, require inpatient hospitalization, will be treated with parenteral antimalarial therapy, and there is no alternative diagnosis considered more likely. Community children from the same household or household compound area of children with severe malaria will be enrolled. On enrollment, all children will have a detailed medical history, baseline health assessment, physical exam, laboratory tests (blood, urine) and abdominal ultrasound to assess the kidney and urinary bladder. During hospitalization kidney health will be assessed using serial

creatinine measures and urine output monitoring. Children with severe malaria will return at 1, 2, and 4 months follow-up to assess clinical and renal recovery. At 4 months a diagnosis of chronic kidney disease is possible for children with sustained evidence of kidney disease over follow-up. An abdominal ultrasound will be repeated at 4 months. All children will return at 12 and 24 months follow-up to assess kidney function. At all visits health-related quality of life will be assessed. Cognition and behavior will be assessed in severe malaria survivors from Mulago and Jinja at 12- and 24-month follow-up who are greater than 3 years of age at the time of testing. A final abdominal ultrasound will be conducted at 24 months.

Intervention Type
Other

Primary outcome measure
Chronic kidney disease (CKD), defined as an eGFR <90 ml/min/1.73 m2 using the U25 eGFR formula or age-specific albuminuria sustained over 3 months, measured at at 1, 2, 4, 12, 24 months

Secondary outcome measures
1. Hypertension (stage 2) (systolic or diastolic blood pressure of 99% or >140/90 mmHg) at scheduled follow-up visits at 1, 2, 4, 12 and 24 months
2. Acute kidney disease (AKD), defined as AKI present for more than 7 days or the presence of low eGFR at scheduled follow-up visits at 1, 2, 4, 12 and 24 months
3. Cognitive deficits measured using the Kaufman Assessment Battery for Children, Second Edition (KABC-II) at 12 and 24 months follow-up
4. Behavioral problems measured using the Child Behavior Checklist (CBCL) at 12 and 24 months follow-up
5. Cerebral edema, defined using apparent diffusion coefficient maps of Magnetic Resonance Images during hospitalization
6. Health-related quality of life measured using the Pediatric Quality of Life Inventory (PedsQL) over scheduled follow-up visits at 1, 2, 4, 12 and 24 months
7. Post-discharge mortality based on parental report over the 24-month follow-up period.
8. Hyperfiltration, defined as sustained eGFR >180 ml/min per 1.73m2, using serum creatinine over follow-up

Overall study start date
01/01/2022

Completion date
01/07/2027

Eligibility

Key inclusion criteria
Severe malaria:
1. Aged between 90 days and <16 years of age
2. Require inpatient hospitalization
3. Have a clinical diagnosis of severe malaria supported by a positive rapid diagnostic test for Plasmodium falciparum HRP-2 antigen, or direct visualization of asexual parasites by microscopy.

Community children:
1. Aged between 90 days and <16 years of age
2. Live in the same or neighboring household as a child with severe malaria

Participant type(s)
Healthy volunteer, Patient

Age group
Child

Lower age limit
3 Months

Upper age limit
16 Years

Sex
Both

Target number of participants
1125

Key exclusion criteria
Severe malaria:
1. Children on maintenance dialysis or known to have chronic kidney disease
2. The presence of congenital heart disease, pre-existing neurological disease or cerebral palsy
3. Enrollment in another study that may affect participation

Community children:
1. The same as those for children with severe malaria, but also include a previous hospitalization
1. A history of illness requiring medical treatment or medication use in the previous four weeks
3. Evidence of fever or active illness on physical examination

Date of first enrolment
14/08/2023

Date of final enrolment
01/08/2025

Locations

Countries of recruitment
Uganda

Study participating centre
Jinja Regional Referral Hospital
Nalufenya Rd
Jinja

Uganda
00000

Study participating centre
Lira Regional Referral Hospital
21-41 Ngetta Road Police Rd
Lira
Uganda
00000

Study participating centre
Mulago National Referral Hospital
Mulago Hill Rd.
Kampala
Uganda
00000

Sponsor information

Organisation
Indiana University Indianapolis

Sponsor details
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Sponsor type
University/education

Website
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ROR
https://ror.org/03eftgw80

Funder(s)

Funder type
Government

Funder Name
National Institutes of Health

Alternative Name(s)
Institutos Nacionales de la Salud, US National Institutes of Health, NIH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Results and Publications

Publication and dissemination plan
Planned publication in an open-access journal

Intention to publish date
01/08/2028

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Andrea L. Conroy (conroya@iu.edu). Once the data are published, they will be stored in a publicly available repository.

IPD sharing plan summary
Stored in publicly available repository, Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		15/07/2025	16/07/2025	Yes	No