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Effectiveness of C-reactive protein testing for optimising antibiotic treatment in neonates and children in Zanzibar

Submission date
15/01/2024

Recruitment status
No longer recruiting

Registration date
22/01/2024

Overall study status
Completed

Last Edited
13/05/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
The global increase in bacterial resistance to antibiotics is particularly impacting children due to the overuse and misuse of these medications. Insufficient diagnostic tools for timely identification of bacterial infections in children contribute to the problem by leading to the unnecessary prescription of antibiotics. C-reactive protein (CRP), a biomarker produced in response to inflammation, once measured, can aid clinicians in assessing the presence and severity of conditions like bacterial infections. Traditionally, diagnosing sepsis in this population involves time-consuming laboratory tests. The introduction of CRP Point-of-Care Testing (POCT) offers a potential solution for a quick and cost-effective diagnosis that can guide immediate treatment decisions. This trial aims to explore the effectiveness of CRP POCT in optimizing antibiotic treatment for neonates and children with suspected sepsis. By assessing CRP levels at the point of care, the trial aims to enhance diagnostic accuracy, tailor treatment strategies, and potentially improve children's outcomes. The trial intends to recruit participants in Zanzibar and assess the impact of CRP POCT on diagnostic practices, contributing to the global understanding of antibiotic use practices in the pediatric population. Ultimately, the findings of this trial have the potential to improve healthcare practices, particularly in resource-limited settings like Tanzania, and optimize antibiotic usage in neonatal and pediatric care.

Who can participate?
Neonates at risk of/with early onset sepsis admitted neonates (0-28 days) with suspected sepsis and admitted children (6 months to 12 years) with febrile illness or diarrhea in selected hospitals in Zanzibar

What does the study involve:
Neonates between 0 and 28 days with the risk of early-onset sepsis according to the WHO criteria or admitted with suspected sepsis and children between 6 months and 12 years admitted with either febrile illness or/and diarrheal disease will be screened for eligibility at the participating hospitals by a research assistant (RA) before routine examination by a clinician. Parents/caregivers of eligible children will be requested for informed consent to participation, after having received oral and written information regarding the trial followed by subsequent

randomization. Participants will be randomized to the intervention group (CRP POCT) or control group (usual care) by a responsible RA through the Sealed EnvelopTM programme. Case report forms (CRFs) will be filled out by RA for all participants at the first consultation. Participants assigned to the intervention group will have a CRP POCT during the consultation with their clinician where whereas children in the control group will not have the CRP POCT test taken. Participants will be randomized by a responsible RA through the Sealed Envelop™ programme. All participants will be contacted on the 7th and 28th day after randomization, by telephone calls from the RA who is blinded to the group allocation. If not reached by telephone the assistant will visit the child at the home address. Both interventional and control groups will receive standard care based on the Zanzibar/Hospital treatment guidelines.

What are the possible benefits and risks of participating?
Participants will benefit from a more accurate diagnosis of bacterial infection improved accuracy in diagnosing sepsis, better treatment decisions based on diagnostic information, and contributing to medical knowledge for potential future improvements in patient care. Potential risks include discomfort during blood sample collection and any inconvenience from additional testing (if it may be required).

Where is the study run from?
The Zan_CRP-POCT trial is being run by Zanzibar Health Research Institute and takes place at Mnazi Mmoja Hospital in Unguja and Chake Chake Hospital, Vitongoji Hospital and Adbullah Mzee (Mkoani) Hospital in Pemba.

When is the study starting and how long is it expected to run for:
February 2024 to May 2025

Who is funding the study?
International Centre for Antimicrobial Resistance Solutions (ICARS)

Who is the main contact:
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil Known

ClinicalTrials.gov (NCT)
Nil Known

Protocol serial number
Zan_CRP-POCT 001

Study information

Scientific Title
Effectiveness of the C-reactive protein point-of-care testing in optimizing antibiotic treatment in neonates and children: an open-label, individual randomized controlled trial

Acronym
Zan_CRP-POCT

Study objectives
The hypothesis is that using CRP POCT to support the clinical decision-making on the antibiotic treatment of neonatal and pediatric patients in selected hospitals in Zanzibar will safely help to 1) reduce the use of prophylactic antibiotics in neonates with WHO risk factor of early-onset sepsis and 2) ensure adequate and appropriate antibiotic treatment for neonates with sepsis. Furthermore, for children 6 months to 12 years, the hypothesis is that 3) the use of CRP POCT will help to identify the majority of children who suffer from non-bacterial infections and assist in withholding or discontinuing antibiotic treatment when no benefit can be expected thus lowering unnecessary use of antibiotics or shortening the duration of use.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 28/12/2023, Zanzibar Health Research Ethics Committee (ZAHREC) (Zanzibar Health Research Institute (ZAHRI), P.O. Box 236, Zanzibar, 72208, Tanzania; +255(0) 776 264 880; zahrec@zahri.go.tz), ref: ZAHREC/04/AMEND/DEC/2023/11

Study design
Multicenter open-label individually randomized controlled trial

Primary study design
Interventional

Study type(s)
Efficacy

Health condition(s) or problem(s) studied
Neonates at risk of early onset sepsis, admitted neonates (0-28 days) with clinical signs of sepsis and admitted children (6 months to 12 years) with febrile illness or diarrhea

Interventions
In the proposed trial, CRP POCT equipment is scheduled to be supplied to the selected hospitals, accompanied by training sessions on its use and interpretation to support the clinical evaluation of neonates and children. The protocol outlines the procedures for CRP POCT measurement for neonates with risk factors for early onset sepsis, where levels below 30mg/L indicate no need for antibiotic treatment, 30-50mg/L warrant caution and clinical assessment, and levels above 50mg/L indicate the necessity for antibiotic treatment. For neonates admitted with suspected sepsis in the CRP group, regardless of CRP levels, antibiotic treatment will be initiated, and CRP reassessed after 18-24 hours. In the case of children aged 6 months to 12 years with fever, history of fever (in the last 72 hours), or diarrhea in the intervention group, CRP will be assessed

at admission and after 18-24 hours. Communication will emphasize that CRP levels below 10mg /L suggest non-severe disease, between 10-50mg/L may require antibiotics based on trend, and levels above 50mg/L likely necessitate antibiotic continuation. Healthcare workers will be trained to consider both clinical symptoms and CRP values in diagnosis and treatment decisions, utilizing the Aidian QuickRead go CRP POCT machine for rapid results. The study will employ individual randomization through the Sealed Envelope™ program, with follow-up remaining blinded, and stratification by gender within the three study groups.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
QuikRead go CRP POCT

Primary outcome(s)
1. Duration of antibiotic treatment (number of 24-hour periods between the start and end of antibiotic treatment) measured using g patient medical records and clinical data registry filled by research assistants daily within 14 days of the admittance of included neonates and children in each study arm (superiority analysis)
2. Days to relapse of infection measured using patient medical records and follow-up forms within 72 hours after completion of the initial course of antibiotics and at the 7th and 28th day after randomization

Key secondary outcome(s))
1. Antibiotic consumption measured using records quantifying prescribed daily doses and daily defined dosage throughout the entire duration of antibiotic treatment at the end of the study
2. Antibiotics prescribed at birth or admittance measured using records of the type and dosage of antibiotics prescribed at the time of birth or admittance to the hospital at the end of the study
3. The number of days admitted in the hospital measured using records of the total days from admission to discharge until the patient was discharged at the end of the study
4. The number of days until the resolution of symptoms measured using records tracking the time from initial symptoms to complete resolution until symptoms are completely resolved at the end of the study
5. The number of days until discharge measured using records counting the days from admission to hospital discharge until the patient is discharged at the end of the study
6. Development of clinical signs of sepsis measured using records of the clinical assessment for the presence of sepsis indicators throughout the entire study duration
7. The number of days in antibiotic treatment (Drugs, Doses Administered) measured using records of the duration and dosage of antibiotic treatment throughout the entire duration of antibiotic therapy
8. The number of blood cultures before antibiotic treatment measured using records counting the instances of blood cultures taken before antibiotic initiation before the initiation of antibiotic treatment
9. Choice of antibiotic treatment according to local guidelines measured using records of the prescribed antibiotics in alignment with local guidelines at the time of antibiotic prescription at the end of the study
10. Re-admittance within 14 days measured using records tracking instances of re-admittance within 14 days following the initial discharge

11. Mortality measured using records documenting instances of patient mortality throughout the entire study duration

Completion date
31/05/2025

Eligibility

Key inclusion criteria
1. Between 0-28 days (inclusive) and fulfilling one of two inclusion criteria
1.1. Newborns at risk of early onset sepsis according to the WHO criteria and therefore eligible for prophylactic antibiotic treatment example:
1.1.1. Membranes ruptured over 18 hours before delivery or
1.1.2. Maternal fever (over 38 °C) during labour or
1.1.3. Amniotic fluid is foul smelling or purulent
1.2. All children from day 0 to day 28 admitted with suspected sepsis (clinical signs subjectively judged by the clinician)
2. Children between 6 months and 12 years with need of admission with either:
2.1. Febrile illness with a temperature above 38 degrees or below 36 degrees at admission, or a history of febrile illness within the last 72 hours
2.2. Diarrhea disease (defined as the passage of 3 or more loose or liquid stools per day) with or without fever
3. Parents/caregivers of admitted children are able and willing to comply with all study requirements
4. Parents/caregivers of admitted children are able and willing to give voluntary Informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
0 days

Upper age limit
12 years

Sex
All

Total final enrolment
1800

Key exclusion criteria

1. Age >28 days until 6 months
2. Severely ill where measurement of CRP POCT would delay the treatment process
3. Neonates who need surgery or have major congenital malformations that will require hospital admission
4. Children with known immunosuppression or severe chronic disease (HIV, hepatic disease, history of neoplastic disease, long-term systemic steroid use or similar conditions as assessed by the health care worker)
5. Parents/caregivers who are not able to participate in follow-up procedures
6. Positive rapid diagnostic test for malaria
7. Have taken antibiotics within 24 hours before admittance

Date of first enrolment
01/02/2024

Date of final enrolment
30/09/2024

Locations

Countries of recruitment
Tanzania

Study participating centre
Mnazi Mmoja Hospital
Stone Town-Vuga Street
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Study participating centre
Chake Chake Hospital
Kichungwani, Chake Chake
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74201

Study participating centre
Vitongoji District Hospital
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Pemba
Tanzania
74212

Study participating centre
Abdullah Mzee (Mkoani) Hospital
Mkoani, Pemba, Zanzibar, Tanzania
Pemba
Tanzania
74101

Study participating centre
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North Unguja
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Sponsor information

Organisation
International Centre for Antimicrobial Resistance Solutions (ICARS)

Funder(s)

Funder type
Research organisation

Funder Name
International Centre for Antimicrobial Resistance Solutions (ICARS)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study are currently stored in a non-publicly available REDCap database. These data will become available in the foreseeable future after undergoing proper cleaning and anonymisation to remove any patient-identifiable information. As a research team, we have not yet finalized the duration for which the data will be stored or the criteria for access. These details will be shared once we have discussed and agreed on them internally.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes