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Understanding and managing fevers from infections spread by animals

Submission date
13/06/2024

Registration date
27/06/2024

Last Edited
17/06/2024

Recruitment status
Recruiting

Overall study status
Ongoing

Condition category
Infections and Infestations

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

Plain English summary of protocol
Background and study aims
Acute fevers are a major health problem in sub-Saharan Africa, where they cause nearly 40% of children's deaths. When children have a fever, they are often assumed to have malaria or a bacterial infection and are treated for these conditions. This may lead to wrong treatment, causing preventable deaths, and unnecessary use of antibiotics, which adds to the problem of rising antimicrobial resistance. Many of these fevers might actually be caused by diseases passed from animals to people, known as zoonotic infections. These diseases are not studied as much as other causes of fever, and diagnosing them is tough because doctors do not have much training in them and testing is limited in Africa. This study aims to understand how common these zoonotic infections are and to find better ways to diagnose and manage the fevers they cause.

Who can participate?
Children aged 2 months to under 18 years, of both sexes, who come to participating health facilities with an acute fever.

What does the study involve?
The children will have a series of health checks and tests. The researchers will take a small amount of blood and urine to test for different infections that might be causing their fever. They will use both well-established and cutting-edge tests to see if they can enhance how they diagnose these illnesses. The researchers will also talk with the children and their caregivers about their symptoms, recent animal contacts, and other potential sources of infection they have been exposed to.

What are the possible benefits and risks of participating?
Children participating in this study may benefit from extra tests that could identify a treatable infection that might otherwise go undiagnosed. By joining this study, they will also help increase our understanding of how often these zoonotic infections occur, which could improve how doctors treat similar cases in the future. There may be some minor risks, such as short-term pain, bruising, or infection where the blood is taken, but there are no other significant risks involved in participating in the study.

Where is the study run from?
This study is a collaboration among researchers from:
1. University of Liverpool (lead) and Liverpool School of Tropical Medicine (UK)
2. Kabale University (joint lead) and Makerere University (Uganda)
3. University of Nairobi and International Livestock Research Institute (ILRI) (Kenya)
4. Addis Ababa University and ILRI (Ethiopia)

When is the study starting and how long is it expected to run for?
November 2022 to June 2028

Who is funding the study?
National Institute for Health and Care Research (UK)

Who is the main contact?
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Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
NIHR156365

Study information

Scientific Title
NIHR Global Health Research Group on zoonotic causes of acute febrile illness

Acronym
ZAFI

Study objectives
Acute fevers are a leading cause of child deaths in sub-Saharan Africa. Many of these fevers are due to diseases spread from animals to humans, known as 'zoonoses'. Diagnosing these infections is often overlooked in low-resource areas, leading to poor awareness and delayed treatment. Improving the recognition and diagnosis of zoonoses can enhance early detection and treatment, ultimately saving lives and reducing illness from these infections.

Ethics approval required
Ethics approval required

Ethics approval(s)
notYetSubmitted

Study design
Multicenter facility-based cross-sectional study

Primary study design
Observational

Study type(s)
Diagnostic, Other

Health condition(s) or problem(s) studied
Zoonotic causes of acute febrile illness in children

Interventions
Following consent/assent, a detailed questionnaire on symptoms/signs, socio-economic status, dietary preferences/practices and other household exposures (human, animal, environment) will be completed by the study nurse. All enrolled patients will receive a malaria rapid diagnostic test (RDT). Patients with a positive test will generally exit the study at this stage and will be treated with antimalarials according to clinical guidelines at each facility.

Subsequently, blood (5 ml by venepuncture) and voided urine will be collected and submitted for bacterial culture and Gram staining. Markers of inflammation (white blood cell counts and c-reactive protein) will be assessed in all patients. In patients with positive blood culture, suspect Salmonella colonies will be subjected to multiplex PCR to detect S. typhi (typhoid) and pan-Salmonellae.

In patients with a negative culture, blood will be further subjected to comprehensive pathogen testing using reference standard diagnostics, qPCR and novel diagnostic platforms for bacterial zoonotic pathogens (Brucella, Leptospira, Coxiella, Rickettsia spp.) and arboviral infections (Crimean-Congo Hemorrhagic Fever [CCHF], Rift Valley Fever [RVF], Dengue Virus [DENV], Chikungunya Virus [CHIKV], Zika Virus [ZIKV], West Nile Virus [WNV], Yellow Fever [YF]). PCR fragments from confirmed Leptospira cases will also be subjected to serotyping. Patients that receive a positive diagnosis for a bacterial infection will be treated with appropriate antibiotics and all patients will receive supportive treatment as indicated according to clinical guidelines at each facility.

Intervention Type
Other

Primary outcome(s)
The presence of one or more bacterial zoonotic pathogens or arboviruses measured using reference standard diagnostics, qPCR and novel diagnostic platforms at presentation to the health centre

Key secondary outcome(s))
1. Clinical characteristics measured using clinical history, physical examination and laboratory testing at presentation to the health centre
2. Socio-economic status, dietary preferences/practices and other household exposures measured using questionnaire designed for the study at presentation to the health centre
3. Diagnostic accuracy, time to result, and potential impact on treatment measured using clinical and laboratory records after application of novel diagnostic platforms

Completion date
30/06/2028

Eligibility

Key inclusion criteria
1. Male and female children aged ≥2 months and <18 years
2. Presents to healthcare facility with a history of fever in the past 48 h, OR an axillary temperature >37.5°C, OR a rectal temperature of ≥38.0°C
3. Caregiver provides full and free informed consent
4. Children aged 8-17 years provide full and free assent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
2 months

Upper age limit
17 years

Sex
All

Key exclusion criteria
1. Unknown age
2. Known malignancy, renal failure, hepatic failure, bone marrow aplasia
3. Trauma, surgery

Date of first enrolment
01/07/2025

Date of final enrolment
30/09/2027

Locations

Countries of recruitment
Ethiopia

Kenya

Uganda

Study participating centre
Kabale Regional Referral Hospital
Kabale
Uganda
-

Study participating centre
Mulago National Referral Hospital
Kampala
Uganda
-

Study participating centre
Mbagathi County Hospital
Nairobi
Kenya
-

Study participating centre
Loitoktok Sub-County Hospital
Oloitoktok
Kenya
-

Study participating centre

Ziway Health Centre
Ziway
Ethiopia
-

Study participating centre
Butajira General Hospital
Butajira
Ethiopia
-

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date