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Microbiome analysis of adenolymphangitis-causing bacteria in filarial lymphedema patients

Submission date
29/12/2024

Recruitment status
Recruiting

Registration date
15/01/2025

Overall study status
Ongoing

Last Edited
14/03/2025

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
Filarial lymphedema is a symptom of lymphatic filariasis, a disease caused by microscopic parasitic worms that are transmitted to humans by mosquitoes. Patients with filarial lymphedema suffer from episodes of adenolymphangitis (ADL) attacks. ADL attacks are painful inflammatory episodes, presenting with fever, inflammation of the affected limbs, malaise and other symptoms that result in the patients being unable to perform normal duties for days. Basic hygiene interventions have been shown to reduce episodes of ADL attacks. In addition to ADL contributing to loss of income due to the patients being unable to perform normal duties, it has also been shown to lead to lymphedema progression.
The exact cause of ADL attacks still remains unknown, although secondary bacterial infections that get access through cracks in the skin have been thought to trigger the attacks.
Using next-generation sequencing (NGS) to analyze pathogens (bacteria) in blood samples collected from lymphedema patients, this study aims to identify organisms associated with the inflammatory episode. In addition to the assessment of blood, NGS will be performed on swabs collected from the affected and unaffected limbs as well as sentinel sites (belly bottom and groin) and wounds to identify differences in pathogen composition before and during an acute attack. Additionally, follow-up samples will be collected after the identification of medically interesting pathogens, to test for antimicrobial sensitivity.

Who can participate?
Lymphedema participants aged 18 years or older willing to join the study in the study region and non-lymphedema patients as controls

What does the study involve?
Blood samples and swab sets (always three pairs of swabs: two from each leg, two pooled from the belly button and from the groin crease) will be collected at the study start (baseline) and during an ADL attack. In addition, swabs might also be taken from wounds (e.g., parts of the legs where there are skin cracks, secretion of tissue fluid and skin lesions).
Blood and swabs will be collected for performing NGS, culture and antimicrobial sensitivity (AST), and immunology. If pathogens of medical importance are found in the blood through

either blood cultures or NGS during ADL attacks, NGS will be performed on the set of swabs. For controls (without LE), only baseline sampling involving the collection of skin swabs and blood will be done.

What are the possible benefits and risks of participating?
The benefits for participants are training and supplies for local care of lymphedema. In addition, medication needed to alleviate an ADL attack will be provided. Medically relevant findings (including incidental findings) from the examinations and sample analysis can be obtained if desired.
There is no risk for the participant from swab sampling of the healthy skin. The equipment for taking skin swabs will be sterile and only handled by trained staff. Swabbing the wounds may cause local pain and irritations. In some cases, there might be an increased risk of infection. If this occurs, appropriate treatment will be provided.
The potential risks of the needle stick for blood drawing include pain, fainting, infection and bruising, or a small hematoma. The bruising may last up to 72 hours. Rarely, a swelling (hematoma) may appear which is easily treated with local pressure. Infections from the needle puncture are rare, but if this does occur, appropriate treatment will be given. In very rare cases, blood sampling can lead to nerve lesions, which could be permanent.

Where is the study run from?
National Institute for Medical Research (NIMR) and Sokoinne Referral Hospital, Lindi, Tanzania

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

Who is funding the study?
German Federal Ministry of Education and Research (BMBF) Research Networks for Health Innovations in Sub-Saharan Africa

Who is the main contact?
Dr Abdallah Ngenya, abdallah.ngenya@nimr.or.tz

Contact information

Type(s)
Public, Scientific, Principal investigator

Contact name
Dr Abdallah Ngenya

Contact details
3 Barack Obama Drive
Dar es Salaam
Tanzania
11101
+255 (0)719223937
abdallah.ngenya@nimr.or.tz

Type(s)
Scientific

Contact name
Prof Achim Hoerauf

ORCID ID
https://orcid.org/0000-0002-8671-3831

Contact details
Venusberg-Campus 1
Bonn
Germany
53127
+49 (0)228 28715673
achim.hoerauf@ukbonn.de

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
Nil known

Study information

Scientific Title
TAKeOFF – microbiome analysis of adenolymphangitis-causing bacteria in filarial lymphedema patients: a study in the Lindi region

Acronym
TAKeOFF-Microbiome-TZ

Study objectives
The aim of this study is to identify pathogens associated with adenolymphangitis (ADL) attacks using next-generation sequencing, and testing antimicrobial sensitivity, with the aim of providing better treatment options in morbidity management

Ethics approval required
Ethics approval required

Ethics approval(s)
1. approved 31/10/2024, Medical Research Coordination Committee (MRCC) (3 Barack Obama Drive, Dar es Salaam, 11101, Tanzania; +255 22 2121400; ethics@nimr.or.tz), ref: NIMR/HQ/R.8a /Vol.IX/4742

2. approved 10/12/2024, Ethics Committee at the Medical Faculty of the University Bonn (Venusberg-Campus 1, Bonn, 53127, Germany; +49-228-287-51931; ethik@ukbonn.de), ref: 2024-34-BO

Study design
Prospective cohort study

Primary study design
Observational

Study type(s)
Diagnostic, Quality of life, Screening

Health condition(s) or problem(s) studied
Filarial lymphedema

Interventions
Blood samples and skin swabs will be collected from LE patients during baseline and at the onset of an ADL attack, to identify organisms associated with episodes of adenolymphangitis (ADL) attacks in LE patients. Analysis will be done using next-generation sequencing (NGS) and culture methods. Follow-up samples will be collected after the identification of medically interesting pathogens, to test for antimicrobial sensitivity.

Intervention Type
Other

Primary outcome(s)
1. Identification of bacteria and fungi in blood collected during ADL attacks (V2 or/and V3) up to species level with NGS (mainly 16/18s) and blood culture (identification with MALDI-TOF or Vitek 2 Compact System) before and during attacks
2. Identification of bacteria and fungi from skin swabs of the same participant taken at ADL and baseline (V1), using NGS and cultures from cryopreserved microbial isolates (for methods of identification see above), and NGS from blood samples taken at V1
3. Identification of changes or similarities in bacteria and fungi from blood and skin swabs in ADL and baseline samples (for identification methods see above)
4. Assessment of antimicrobial sensitivity of bacteria and/or fungi of medical interest, identified in outcomes 1-2, primarily using Vitek AST

Key secondary outcome(s))
1. Similarities or changes in the microbiome of LE participants at baseline and during ADL, compared to that of participants in the control group at baseline, measured with NGS (mainly 16 /18s) and blood culture (identification with MALDI-TOF or Vitek 2 Compact System)
2. Similarities or changes between the microbiome of participants grouped by lymphedema stage measured using collected study data at baseline and during ADL with NGS (mainly 16/18s) and blood culture (identification with MALDI-TOF or Vitek 2 Compact System)
3. Immune response during ADL attacks is analyzed from whole blood samples collected at baseline and ADL. Peripheral Blood Mononuclear Cells (PBMCs) and plasma are prepared. In PBMCs, the immune cell populations (e.g., T cells and granulocytes) are analyzed using flow cytometry. Plasma is used to analyze pro-inflammatory and Th1/Th2/Th17 immune responses and chemokines using Luminex and ELISA techniques.

Completion date
31/03/2028

Eligibility

Key inclusion criteria
1. Lymphedema of at least one leg (cases)
2. Participants without lymphedema (controls)
3. Aged 18 years and above
4. Able and willing to provide informed consent (or assent, where applicable) to participate in the study

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Any significant condition (including medical and psychological/psychiatric disorders) that, in the opinion of the study clinician, might interfere with the conduct of the study
2. Lymphedema of non-filarial origin

Date of first enrolment
12/03/2025

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
Tanzania

Study participating centre
National Institute for Medical Research (NIMR)
3 Barack Obama Drive
Dar es Salaam
Tanzania
11101

Study participating centre
Sokoine regional refferal hospital laboratory
P.o.box 1011
Lindi
Tanzania
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Sponsor information

Organisation
National Institute for Medical Research

ROR
https://ror.org/05fjs7w98

Funder(s)

Funder type
Government

Funder Name
Research Networks for Health Innovations in Sub-Saharan Africa sponsored by the Federal Ministry of Education and Research (BMBF)

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

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
Study website	Study website	11/11/2025	11/11/2025	No	Yes