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Analysis of acute adenolymphangitis attack causing bacteria in filarial lymphoedema patients

Submission date
03/12/2024

Recruitment status
No longer recruiting

Registration date
17/12/2024

Overall study status
Ongoing

Last Edited
17/12/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] 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 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 in blood samples collected from 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 the 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 to perform NGS, culture and antimicrobial sensitivity testing (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 swabs. Swabs will be processed for later identification and AST of bacteria and fungi. For the control patients, only baseline sampling involving the collection of skin swabs and blood will be done.

What are the possible benefits and risks of participating?
Participants with filarial lymphedema will benefit from hygiene and morbidity management training in order to reduce the frequency of acute attacks to improve their condition. Additionally, each affected participant will receive a lymphedema hygiene kit.
The equipment for taking skin swabs will be sterile and only handled by trained staff. Therefore, no risks arise from this procedure.
The potential risks of the needle stick for blood drawing include pain, 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?
1. Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR) (Ghana)
2. Kwame Nkrumah University of Science and Technology (KNUST) (Ghana)

When is the study starting and how long is it expected to run for?
September 2021 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?
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Contact information

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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 acute adenolymphangitis attack causing bacteria in filarial lymphedema patients

Acronym
TAKeOFF – Microbiome – GH

Study objectives
The aim of this study is to identify pathogens associated with acute adenolymphangitis (ADL) attack 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 20/11/2024, The Committee for Human Research, Publication and Ethics (CHRPE) of the Kwame Nkrumah University of Science and Technology (KNUST) (South-end, Asuogya Road, Kumasi, 0000, Ghana; +233 (0)205453785; chrpe@knust.edu.gh), ref: CHRPE/AP/1230/24

2. approved 12/09/2024, Ethics Committee at the Medical Faculty of the University Bonn (Venusberg-Campus 1, Bonn, 53127, Germany; +49 (0)228 287 51931; ethik@ukbonn.de), ref: 2024-328-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 lymphedema (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 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. Identifying 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
2. Identifying similarities or changes between the microbiome of participants grouped by lymphedema stage measured using collected study data at baseline and during ADL
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 proinflammatory and Th1/Th2/Th17 immune responses and chemokines using Luminex and ELISA techniques.

Completion date

31/03/2028

Eligibility

Key inclusion criteria
Male and female participants 18 years of age and above with/without LE (cases/controls)

(LEDoxy clinical trial cohorts, previously screened but excluded LEDoxy LE participants, LE participants in the community willing to join the study + controls with a similar working/housing environment)

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Male and female participants below 18 years of age
2. LE of non-filarial origin
3. Any other condition or severe comorbidities (except for features of the filarial disease) that, in the opinion of the study team, would risk the safety or rights of a participant or would render the participant unable to comply with the protocol
4. Inability or unwillingness of study participant to give informed consent to participate in the study

Date of first enrolment
04/12/2024

Date of final enrolment
30/06/2025

Locations

Countries of recruitment
Ghana

Study participating centre

Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR) Kwame Nkrumah University of Science and Technology (KNUST)
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Sponsor information

Organisation
Kumasi Centre for Collaborative Research in Tropical Medicine

ROR
https://ror.org/032d9sg77

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