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Analysis of adenolymphangitis-causing microbes in podoconiosis lymphedema patients in Cameroon

Submission date
04/07/2025

Recruitment status
Recruiting

Registration date
31/07/2025

Overall study status
Ongoing

Last Edited
30/07/2025

Condition category
Injury, Occupational Diseases, Poisoning

[_] 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
Podoconiosis is a non-filarial form of elephantiasis, characterized by massive swelling of the lower limbs (lymphedema; LE), occurring in individuals who have been exposed to red clay soil derived from alkaline volcanic rock. This disease is associated with individuals living in low-income countries, especially in the tropics with high altitude and high seasonal rainfall. Podoconiosis patients experience painful intermittent inflammatory episodes of acute adenolymphangitis (ADL) attacks. These episodes of ADL are characterized by malaise, fever, chills, diffuse inflammation, swelling of the limbs, lymphangitis, adenitis and, eventually, skin peeling. They occur frequently and contribute substantially to the disability and social effects associated with podoconiosis. Episodes of ADL attacks are generally believed to be caused by bacteria and fungi that penetrate dry and cracked skin on the feet. Additionally, the presence of skin lesions on affected LE legs is thought to allow exogenous bacteria to enter the body. Different studies have pointed to several bacteria. From our podoconiosis cohorts, several bacterial species were reported on the legs of people suffering from podoconiosis. Using next-generation sequencing (NGS) to analyze for pathogens in blood samples collected from patients during an ADL attack, 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) to identify differences in the pathogen composition before and during an acute attack. If wounds are present, samples will be collected and analysed, comparison will be made to non-LE samples from chronic wounds of other origins, e.g. diabetes. Antimicrobial sensitivity will be done on isolates of medical importance.

Who can participate?
LE patients willing to join the study in the study regions, control group with and without chronic wounds and non-communicable diseases (NCDs)

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 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, 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 identification and antimicrobial sensitivity of bacteria and fungi. For the control patients, only baseline sampling involving the collection of skin swabs and blood will be done. At study start, all participants will be checked for NCDs, mainly diabetes and hypertension.

What are the possible benefits and risks of participating?
Participants with LE will benefit from hygiene and morbidity management training to reduce the frequency of acute attacks and to improve their condition. Additionally, each affected participant will receive a LE hygiene kit. Medically relevant findings (including incidental findings) from the examinations and sample analysis can be obtained if desired. 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?
University of Buea (Cameroon), Faculty of Science, Department of Microbiology and Parasitology

When is the study starting and how long is it expected to run for?
July 2025 to December 2028

Who is funding the study?
1. German Federal Ministry of Research, Technology and Space (BMFTR)
2. Research Networks for Health Innovations in Sub-Saharan Africa

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
Nil known

Study information

Scientific Title
TAKeOFF – Microbiome: analysis of ADL attack causing microbes in podoconiosis lymphedema patients in Cameroon.

Acronym
TAKeOFF – Microbiome Cameroon

Study objectives
This study aims to identify pathogens associated with adenolymphangitis 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 02/05/2025, Comite Ethique de la Recherche pour la Sante Humaine (CNERSH) (P.O Box 1937, Yaounde, 00000, Cameroon; +237-222-234-579; minsanterecherche@yahoo.fr), ref: 2025/04/1801/CE/CNERSH/SP

2. submitted 23/06/2025, Ethikkommission an der Medizinischen Fakultät der Rheinischen Friedrich-Wilhelms-Universität Bonn (Venusberg-Campus 1, Bonn, 53127, Germany; +49 228 287 51931; ethik@ukbonn.de), ref: 2025-224-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
Podoconiosis (non-filarial lymphedema)

Interventions
Blood samples and skin swabs will be collected from lymphedema (LE) patients during baseline and at the onset of an adenolymphangitis (ADL) attack, to identify organisms associated with episodes of ADL attacks. In addition to the skin swabs, swabs will also be taken from wounds if present. Wound swabs will be taken from participants with LE and also from those with chronic wounds of other origins. Analysis of the collected samples will be done using next-generation sequencing (NGS) and culture methods. Antimicrobial patterns will also be performed. At baseline, all participants will be checked for non-communicable diseases (NCDs), mainly diabetes and hypertension.

Intervention Type
Other

Primary outcome(s)
Detection of pathogens of medical significance associated with the onset of adenolymphangitis (ADL) attacks, measured in blood, skin swabs and wounds using next-generation sequencing (NGS) during an ADL attack in comparison to baseline

Key secondary outcome(s))
1. Skin-microbiome composition will be analysed in podoconiosis lymphedema (LE) participants at baseline and during adenolymphangitis (ADL) attacks, and compared with baseline samples from participants in the control group using next-generation sequencing (16S/18S) and microbial culture analysis (API biochemical tests, MALDI-TOF, or Vitek 2 Compact).
2. Antimicrobial sensitivity in ADL causative bacteria and/or fungi are measured at baseline and during ADL attack using culture and sensitivity testing (disc-diffusion and/or Vitek AST cards).
3. Wound assessment in LE patients and their AMR profile are measured at baseline and during ADL attacks using NGS, culture and sensitivity testing (disk-diffusion and/or Vitek AST cards). Results will be compared with wounds of other origins (e.g., diabetic wounds/ulcers) examined at the same time points using the same methods.
4. Compare skin-microbiome profiles across LE stages using baseline and ADL samples analysed by NGS (16S/18S) and cultures.
5. Effects of non-communicable diseases (e.g., diabetes and hypertension) on LE changes will be examined at baseline and during ADL attack using the 5-point scale staging according to Tekola et al, 2008. Effects of NCDs on skin microbiome of LE patients at baseline and during ADL will be measured using NGS and cultures
6. Immune responses during ADL attack will be analysed from whole blood samples collected at baseline and ADL. Peripheral Blood Mononuclear Cells (PBMCs) and plasma will be prepared. In PBMCs, the immune cell populations (e.g., T cells and granulocytes) will be analysed using flow cytometry. Plasma will be used to analyse 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) with or without chronic wounds of other origin (e. g. diabetes, injury)
3. Must have lived in an endemic area (West and North West Regions) for at least two (2) years
4. 15 years and above
5. Able and willing to give informed consent/ to provide assent to participate in the study

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
15 years

Sex
All

Key exclusion criteria
Any significant condition (including medical and psychological/ psychiatric disorder) which in the opinion of the study clinician might interfere with the conduct of the study.

Date of first enrolment
07/07/2025

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
Cameroon

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Sponsor information

Organisation
University of Buea

ROR
https://ror.org/041kdhz15

Funder(s)

Funder type
Government

Funder Name
German Federal Ministry of Research, Technology and Space

Funder Name
Research Networks for Health Innovations in Sub-Saharan Africa

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