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Testing a treatment called isoniazid monotherapy to prevent the progression of chronic kidney disease in latent (without any symptoms) tuberculosis in Bangladesh

Submission date
06/12/2023

Recruitment status
Recruiting

Registration date
13/12/2023

Overall study status
Ongoing

Last Edited
10/04/2026

Condition category
Urological and Genital Diseases

[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
We aim to conduct a clinical study to investigate the potential benefits of treating latent tuberculosis infection (LTBI) in individuals residing in developing countries with a high incidence of both tuberculosis (TB) and LTBI. Specifically, we are interested in understanding whether treating LTBI can have positive effects on the health of patients with chronic kidney disease (CKD). Our study will explore various health aspects, including assessing whether LTBI treatment reduces the risk of developing active TB, enhances muscle strength (indicative of nutritional status), improves the body's response to insulin, and regulates inflammation levels in the body.

Who can participate?
Patients with Latent Tuberculosis Infection (LTBI), and Chronic Kidney Disease (CKD)

What does the study involve?
Patients will be randomly assigned to one of two groups, similar to flipping a coin. One group will receive daily anti-TB drugs (Isoniazid 5mg/kg and Pyridoxine 20mg) for six months, while the other group will receive no treatment.

The study will span three years, with patients seen by study staff every three months during their usual Kidney Foundation clinic visits. Routine blood tests recommended by their clinic doctor will continue, and any special study-related tests will be provided at no cost to the patients.

What are the possible benefits and risks of participating?
As a participant in this research study, patients may not benefit directly; information from this study will help other people with CKD in the future, whether we should treat LTBI. We already know in many developed countries, in accordance with WHO (World Health Organization) guidelines, LTBI is treated with anti-TB drugs.
The Isoniazid and Pyridoxine given in this study rarely cause any serious adverse effects.

Uncommon side effects that you might encounter include anorexia, nausea, vomiting, abdominal discomfort, persistent fatigue, or weakness, dark-coloured urine, pale stools, or jaundice. If side effects are severe, especially if there is evidence that the liver function is affected, they will be asked to stop treatment. We will be monitoring their liver and other tests every 3 months. If they become symptomatic while on treatment they will be asked to contact a member of the research study group immediately (details listed below).

Where is the study run from?
Kidney Foundation (Bangladesh)

When is the study starting and how long is it expected to run for?
March 2023 to February 2028

Who is funding the study?
1. Kidney Foundation (Bangladesh)
2. Barts Health NHS Trust (UK)
3. Queen Mary University London (UK)

Who is the main contact?
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Study information

Scientific Title
A single centre, open-label, randomised clinical trial evaluating Isoniazid Monotherapy treatment to Prevent Accelerated Chronic kidney disease in latent Tuberculosis in a High Incidence Country.

Acronym
IMPACT-HIC

Study objectives
Whether treatment with 6 months' isoniazid plus pyridoxine have any effect on the rate of change in eGFR of CKD patients (eGFR 20-60) with Latent Tuberculosis Infection (LTBI)

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 21/03/2023, Institutional Ethical Committee, Kidney Foundation Hospital and Research Institute (Plot5/2, Road-1, Mirpur-2, Dhaka, 1216, Bangladesh; +880 2-9024074; rashid@bol-online.com), ref: KFHRI/ECC-002/2023

Primary study design
Interventional

Study design
Single-site open-label randomized clinical trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic kidney disease with latent tuberculosis infection

Interventions
Intervention - IMP with 6 months isoniazid 5mg/kg/day maximum daily dose 300 mg (plus pyridoxine 20 mg)

Comparison group – The alternative group will receive no treatment compared with the intervention group as per current practice in Bangladesh.

Patients will then be randomized into one of two groups. One group will receive IMP daily, for 6 months while the second group will receive standard care (no specific treatment for LTBI) for 6 months.

The randomization envelopes will be grouped into 20 Blocks (10 envelopes within each group).
Each group will contain 5 envelopes specifying IMP and 5 no treatment in random order.
Each envelope will be identified by the Block number and kit number
The study will comprise of four stratified groups of patients:
A. Diabetic and No Glomerulonephritis
B. Diabetic and Glomerulonephritis
C. Non-Diabetic and Glomerulonephritis
D. Non-Diabetic and No Glomerulonephritis

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Isoniazid/pyridoxine

Primary outcome(s)
Rate of change in renal function assessed by eGFR [ml/min/1.73m^2] over 2 years (1.5 years after administration of 6 months of isoniazid therapy 5mg/kg (maximum 300mg) plus pyridoxine 20mg or no treatment.
The eGFR will be calculated using the CKD EPI equation using age, sex, and creatinine. This will be evaluated every 3 months as part of standard care at 0, 3, 6, 9, 12, 15,18,21 and 24 months.

Key secondary outcome(s)
1. Reactivation of TB monthly during the 2 years follow-up period from initiation of trial.
If positive: patient will be withdrawn from trial to initiate TB treatment as deemed clinically appropriate (but will continue follow up for endpoints).
2. Survival benefits-mortality measured using Kaplan-Meier estimate at the end of the study.
3. Effect on other parameters of kidney function performed at CKD clinic as standard practice including but exclusively: urinary microalbumin (ACR), 0, 3, 6 and 12 months.

4. The effect of IMP in the inflammatory status assessed by serum CRP and optical density of IGRA at screening then 9 months and 12 months from initiation of therapy
5. Safety endpoints: SAEs, AEs and liver enzymes (SGPT, ALP, Bilirubin) at 0, 3, 6 and 12 months

Completion date
01/02/2028

Eligibility

Key inclusion criteria
1. Patients (male or female) eGFR 20-60 [ml/min/1.73m^2] attending Kidney Foundation Hospital, Bangladesh.
2. Aged 19 to 75 years inclusive
3. Willing to comply with study schedule
4. Interferon-gamma release assay (IGRA) positive

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
19 Years

Upper age limit
75 Years

Sex
All

Total final enrolment
134

Key exclusion criteria
1. Active TB or previous known treatment of active TB or LTBI
2. Clinically significant history of abnormal physical and/or mental health as judged by the investigator other than conditions related to chronic kidney disease such as history of liver disease, including viral hepatitis, chronic liver disease, harmful alcohol intake.
3. Participation in an investigational drug trial in the 3 months prior to administration of the initial dose of study drug
4. Subject with a known hypersensitivity or contraindication to Isoniazid and Pyridoxine
5. Female participant who is pregnant or lactating during the trial.
6. History of functional kidney transplant 6 months before study entry

Date of first enrolment
01/01/2024

Date of final enrolment
01/01/2027

Locations

Countries of recruitment
Bangladesh

Study participating centre
Kidney Foundation Hospital and Research Institute, Bangladesh
Plot 5/2, Road-1, Mirpur-2
Dhaka
Bangladesh
1216

Sponsor information

Organisation
Kidney Foundation Hospital and Research Institute, Bangladesh

ROR
https://ror.org/03fnc0m43

Organisation
Bart's Health NHS Trust

Organisation
Queen Mary University of London

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Research organisation

Funder Name
Kidney Foundation Hospital and Research Institute, Bangladesh

Funder Name
Barts Health NHS Trust

Alternative Name(s)
Barts Health

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
United Kingdom

Funder Name
Queen Mary University of London

Alternative Name(s)
Queen Mary Uni of London, Queen Mary, Queen Mary and Westfield College, The London Hospital Medical College, St Bartholomew's Hospital Medical College, Westfield College, East London College/Queen Mary College, QMUL, QM

Funding Body Type
Government organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and /or analysed during the current study will be stored in a non-publicly available repository (Kidney Foundation Hospital and Research Institute, Bangladesh's research lab) and are available from the corresponding author on reasonable request tasnuva.kashem@gmail.com

IPD sharing plan summary

Available on request, Stored in non-publicly available repository