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The effect of malnutrition and diabetes on outcomes for drug-resistant and drug sensitive patients starting anti-tuberculosis treatment

Submission date
11/12/2019

Recruitment status
No longer recruiting

Registration date
03/01/2020

Overall study status
Completed

Last Edited
28/02/2024

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Undernutrition (malnutrition) is both a risk factor for and consequence of active tuberculosis (TB) disease. Malnutrition is a common clinical finding in patients with active TB disease and is associated with mortality, but the mechanism/s of effect are not well understood and there is a lack of high-quality evidence to determine the efficacy of interventions to prevent or treat malnutrition in TB patients, in the Philippines or globally. Diabetes mellitus is another known risk factor for active TB disease and has been associated with risk of death and poor treatment outcomes whilst TB may also negatively affect blood sugar control. Under-diagnosis or poor management of diabetes may increase risk of poor TB treatment outcomes. Diabetes and increased nutritional needs may also contribute to an increased financial burden during TB treatment and potentially catastrophic levels of costs to the household.
This study aims to study the effects of malnutrition and diabetes in both drug-resistant TB (DR-TB) and drug sensitive (DS-TB) patients attending public facility TB directly observed treatment, short-course (DOTS) programmes in the Philippines.

Who can participate?
Aged 18 or more (adults) who are initiating a new TB treatment regimen, participating in NTP DOTS and iDOTS centres.

What does the study involve?
Participants initiating a new TB treatment regimen are invited to join the study, and are followed up every month until treatment completion. This is observational research, and no intervention is involved. During treatment, participants are asked to complete questionnaires on health and social factors including TB diagnosis, treatment, compliance to medications, side effects of medications, quality of life, food security, appetite, depression, stigma and self-esteem. Participants are also measured for their weight, height, handgrip strength, mid upper arm circumference and waist/hip circumference. Participants also provide blood samples from finger pricks to measure haemoglobin for anaemia and HbA1c as a marker of glucose dysregulation and probable diabetes.

What are the possible benefits and risks of participating?
Participants will benefit from increased opportunities for being screened for diabetes and anaemia, with point of care tests. Results will be made immediately available and forwarded to the appropriate health staff for referral or treatment as deemed appropriate by the local physician. There are no notable risks with participating however participants may experience discomfort when they provide blood samples.

Where is the study run from?
This study is being run from three public health centres in Manila, and five health centres in Cebu and five health centres in Negros Occidental (Philippines).

When is the study starting and how long is it expected to run for?
August 2018 until December 2022

Who is funding the study?
Nagasaki University, Japan

Who is the main contact?
Prof. Sharon Cox (scientific)
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Contact information

Type(s)
Scientific

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Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
St-ATT V2.0 3rd May 2019

Study information

Scientific Title
Effects of malnutrition and diabetes on treatment outcome and total patient costs in Filipino drug resistant and drug sensitive patients starting anti-TB treatment: A cohort study

Acronym
St-ATT

Study objectives
The aim of this study is to measure the effects of malnutrition and diabetes in patients with tuberculosis and investigate associations with treatment outcome through potential effects on treatment compliance, drug side effects, glycemic control, weight gain and nutrition during treatment and cell-mediated immune responses.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 01/03/2018, Nagasaki University: School of Tropical Medicine and Global Health (1-12-4 Sakamoto, Nagasaki, 852-8523, Japan; +81(0)95-819-7583; tmgh_jimu@ml.nagasaki-u.ac.jp), ref: n/a, (minor amendment approved 20/11/2018, amendment approved 05/06/2019)
2. Approved 14/05/2018, Asian Eye Institute (St. Cabrini Medical Center, 8th Floor Phinma Plaza, Rockwell Center, Makati City, 1200, Philippines; +63-(0)2 898-2020; scmcaeierc@gmail.com), ref: ERC # 2018-008, (minor amendment approved 01/10/2018, amendment approved 24/05/2019)
3. Approved 10/05/2018, London School of Hygiene and Tropical Medicine (Keppel Street, London WC1E 7HT, UK; +44-(0)20-7636-8636; ethics@lshtm.ac.uk), ref: 14894, (minor amendment approved 14/12/2018, amendment approved 04/06/2019)

4. Approved 02/10/2018, San Lazaro Hospital – RERU (Quiricada St., Sta. Cruz, Manila, 1003, Philippines; +63-(0)920-310-3211; slh.iso.reru@gmail.com), ref: SLH-RERU-2018-004-E
5. Approved 05/10/2018, Dr. Pablo O. Torre Memorial Hospital [Riverside] (BS Aquino Dr, Bacolod, 6100, Negros, Philippines; +63-(0)34-433-7333; ethics_dpotmh@yahoo.com), ref: DPOTMH-REC, (amendment approved 02/08/2019)

Study design
Observational prospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Tuberculosis, malnutrition, diabetes

Interventions
Participants initiating a new TB treatment regimen are invited to join the study, and are followed up every month until treatment completion. At the time of enrolment, participants are asked if they will also participate in the patient cost assessment, which will involve home-based interviews about household expenditure associated with seeking diagnosis and treatment for their TB, and additional costs from diabetes and costs on different foods or supplements being taken due to their health condition.

At the end of TB treatment, if participants provide additional consent, they will be followed up for a further two years at six-monthly intervals for assessment of lung function and recurrent TB.

During treatment, participants complete questionnaires conducted by research nurses on health and social factors including TB diagnosis, treatment, compliance to medications, side effects of medications, quality of life, food security, appetite, depression, stigma and self-esteem. Participants are also measured for their weight, height, handgrip strength, mid-upper arm circumference and waist/hip circumference. Participants also provide blood samples from finger pricks to measure haemoglobin for anaemia and HbA1c as a marker of glucose dysregulation and probable diabetes.

At baseline, if additional consent is given, a subset of participants will have a venous blood sample collected to assess immune responses to TB. At the end of treatment, participants will be asked a questionnaire to assess their lung function. For those that provide additional consent, lung function will also be assessed during post-treatment follow-up at 6 monthly

intervals using spirometry (participants are asked to blow into a small digitial machine that measures the volume of air exhaled as a measure of lung capacity and function) and in some cases a six minute walk test. Participants will be followed up at six monthly intervals for two years for TB symptoms and health seeking behavior, plus nutritional status (weight, handgrip strength, mid-upper arm circumference and waist/hip circumference. Finger-prick blood samples will be collected to monitor anaemia and glucose dysregulation/diabetes status.

Intervention Type
Mixed

Primary outcome measure
Adverse TB treatment outcome at end of study defined as death, loss to follow-up, default (two or more consecutive months of interrupted treatment) or treatment failure.

Secondary outcome measures
1. Adverse treatment outcome in the secondary outcome also includes relapse/ recurrent active TB diagnosed clinically or bacteriologically confirmed within 2 years of completing treatment.
2. Catastrophic household expenditure assessed by measuring total patient costs (direct medical costs, direct on-medical costs, indirect costs and coping strategies) using an adapted version of the WHO costing tool, with data collected at the start of treatment, end of intensive treatment phase, mid continuation phase and end of treatment
3. Reduced lung function assessed using the St Georges Respiratory Questionnaire and FEV1 measured by spirometry at the start of treatment, end of intensive treatment phase, mid continuation phase and end of treatment
4. Development/evolution of hyperglycaemia and diabetes. For participants with newly diagnosed diabetes during TB treatment, we will assess the proportion who remain diabetic during post-treatment follow-up. Conversely, we will assess the proportion who were non-diabetic during TB treatment who become diabetic during post-treatment follow-up (HbA1c >=6. 5% or diagnosed externally and placed on treatment)

Exposures outcomes:
1. Diabetes – primary exposure will be diabetes present at any one time point during treatment (HbA1c >= 6.5% or on recognized drug treatment for diabetes), secondary will be HbA1C >= 7% at 2 or more time points or on recognized drug treatment for diabetes. Exploratory analysis will assess the effect of degree of hyperglycaemia during treatment on TB treatment outcomes
2. Malnutrition - primary exposure will be moderate/severe malnutrition at the start of treatment defined as BMI< 17kg/m². Secondary analyses will explore the effect of changes in nutritional status during treatment using repeated measures analysis. Risk of recurrent TB will be explored by BMI status (moderate/severe malnutrition) at the end of TB treatment as the primary analysis

Co-factors outcomes:
Measured during treatment:
1. Demographic factors; age, sex, DOTS center, education level, social service category, occupation, cigarette smoking, alcohol and etc
2. Clinical management; TB diagnosis, symptom history, treatment regimen, treatment history, co-morbidities, chest x-ray, drug related adverse events
3. Nutrition status; height (cm), weight (kg) using SECA digital scale, handgrip strength using Jamar Hand Dynamometer, mid-upper arm circumference and waist/hip circumferences (cm) using SECA measuring tape, weight loss, appetite and body composition by bio-impedance analysis

4. Clinical investigations: blood pressure (mmHg) using Tanita, and haemoglobin using Hemocue 301+, random plasma glucose and HbA1c. Oral glucose tolerance test is conducted for participants whose HbA1c is 5.7 - 6.5%. HIV rapid diagnostic test is conducted if consent is given
5. Household food security is adapted from U.S. Household Food Security Survey Module (US HFSSM)
6. Quality of life is measured using the WHO Quality of Life BREF survey
7. Risk factors related to adherence; depression using Hospital Anxiety Depression Scale (HADS), Social & family support by using Multidimensional scale of perceived social support (MSPSS), stigma using Berger scale of stigma, self-esteem using Rosenberg Self-esteem Scale (RSES) and TB treatment adherence last 7 days
Measured at end of treatment and post-treatment
1. Chest x-ray
2. Anthropometry, household food security, quality of life and the risk factors related to adherence as described in during treatment.
3. Clinical investigations: blood pressure, and haemoglobin, random plasma glucose and HbA1c.
4. Active TB screening is adapted from WHO symptom screening
5. Lung health; lung spirometry using ndd EasyOne, 6-minute walk test, modified Medical Research Council Dyspnea score, St George Respiratory Questionnaire
6. Functional impairment on work/school, social life and family life using Sheehan Disability scale
7. Health-related behaviors; smoking, alcohol and substance abuse
8. Symptom history and health seeking behavior

Overall study start date
01/04/2018

Completion date
31/12/2022

Eligibility

Key inclusion criteria
Aged 18 or more (adults) who are initiating a new TB treatment regimen

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
800

Key exclusion criteria

1. Pregnant woman
2. Plan to move away from the study site or do not give consent to participate
3. Started the current ATT regimen more than 5 days before enrolment
4. Currently imprisoned
5. Severe medical or psychiatric disorder which in the opinion of the local investigators might interfere with the ability to give true informed consent or to adhere to the study requirements
6. Taking part in any investigational product trials related to TB and/or lung disease or diabetes.

Date of first enrolment
01/08/2018

Date of final enrolment
21/02/2020

Locations

Countries of recruitment
Philippines

Study participating centre
San Lazaro Hospital
Quiricada St
Santa Cruz
Manila
Philippines
1004

Study participating centre
San Nicolas Health Center
521 Asuncion St.
Binondo
Manila
Philippines
1002

Study participating centre
Pedro Gil Health Center
1423 A. Francisco St.
Bgy 803
San Andres Bukid
Manila
Philippines
1008

Study participating centre
Bago City Health Center
Bago City Hall, 6101
Bago City
Philippines
6101

Study participating centre
Valladolid Municipal Health Office
Sarandin St. Brgy. Poblacion
Valladolid
Negros Occidental
Philippines
6103

Study participating centre
Bacolod City Health Office
BBB St
Bacolod
Negros Occidental
Philippines
6100

Study participating centre
La Carlota City Health Office
Jereza St. Brgy. 1 Poblacion
La Carlota City
Negros Occidental
Philippines
6130

Study participating centre
Pablo O. Torres Memorial Hospital
BS Aquino Dr
Bacolod
Negros Occidental
Philippines
6100

Study participating centre
Compostela Rural Health Unit
Poblacion
Compostela
Cebu
Philippines
6003

Study participating centre
Consolacion Rural Health Unit / Consolacion Municipal Health Office
Poblacion Occidental
Consolacion
Cebu
Philippines
6001

Study participating centre
Eversley Childs Sanitarium and General Hospital
Upper Jagobiao Rd
Mandaue City
Cebu
Philippines
6014

Study participating centre
Lapu - Lapu City Health Office
Lapu City
Cebu
Philippines
6015

Study participating centre
Carmen Health Center
Poblacion Carmen
Cebu
Philippines
6005

Sponsor information

Organisation
Nagasaki University

Sponsor details
Nagasaki University
Graduate School of Tropical Medicine and Global Health
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tmgh_jimu@ml.nagasaki-u.ac.jp

Sponsor type
University/education

Website
http://www.tmgh.nagasaki-u.ac.jp/

ROR
https://ror.org/058h74p94

Funder(s)

Funder type
University/education

Funder Name
Nagasaki University

Results and Publications

Publication and dissemination plan
Results to be shared with the Department of Health. Planned publications in international peer reviewed journals.

Intention to publish date
30/06/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository London School of Hygiene and Tropical Medicine server at https://maltbdots.odk.lshtm.ac.uk with only investigators having access to the data. Anonymized

data will be stored in a recognized data repository after study completion. Upon publication of the main results this data will be made publicly available. Participant consent was obtained to store anonymized data in repository for period of 10 years after study completion.

IPD sharing plan summary

Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		25/09/2023	28/02/2024	Yes	No
Results article	cross-sectional analysis of data collected at enrolment	17/11/2021	28/02/2024	Yes	No