ISRCTN10699064 https://doi.org/10.1186/ISRCTN10699064

Cardiac disease in adolescents with perinatal HIV infection and receiving antiretroviral therapy

Submission date	**Recruitment status**	[X] Prospectively registered
13/05/2022	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
06/06/2022	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
01/08/2023	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims

Many children with perinatal HIV are now surviving to adolescence because of increased access to antiretroviral therapy (ART). Despite effective ART, non-AIDS-defining illnesses including cardiac (heart) disease have been described in both adults and children. Many children with perinatal HIV in Sub-Saharan Africa (SSA) start ART much later than children with HIV in high-income countries (aged 7.9 years vs 0.9 years, respectively) and are likely to have more HIV-related cardiac damage. Researchers have previously reported a high prevalence of cardiac abnormalities based on echocardiography examination and commonly left heart abnormalities. The causes of cardiac disease in HIV remain poorly understood but chronic inflammation due to HIV and/or other co-infections that may occur is believed to be one of the main drivers. Cardiac magnetic resonance (CMR) is unique in identifying tissue characteristics including scarring and inflammation, helping to understand underlying disease processes. In addition it enables more accurate structural and functional assessment of the heart. The aims of this study are to assess the structure, function and tissue characteristics of the heart using CMR. Biomarkers of scarring and inflammation will also be measured to help understand the causes of cardiac disease in children with perinatal HIV.

Who can participate?

Adolescents aged between 10 to 19 years with perinatal HIV and those without HIV

What does the study involve?

Two groups of adolescents will be enrolled (with and without HIV). Clinical and other medical history will be collected using questionnaires. Assessments including height, weight, blood pressure and blood tests will be performed (HIV group: CD4 count, HIV viral load, full blood count and serum creatinine). For adolescents without HIV, only full blood count and serum creatinine tests will be performed. All participants will be examined using CMR and blood samples will be collected to test for biomarkers of inflammation and scarring.

What are the possible benefits and risks of participating?

Adolescents without HIV will benefit from screening for HIV and those who test HIV-positive will

be referred to the HIV clinic for onward care. All test results will be made available to the participant's physician to assist with care. Participants diagnosed with cardiac disease will be referred for cardiac services for further management. All participants will benefit by finding out how well their heart is working.
Risks to participants may include CMR contrast negative reactions. During CMR, participants will receive a contrast agent as part of the examination. The contrast may cause a mild headache, rash and very rarely a more severe allergic reaction. These severe reactions generally respond very well to standard emergency drug treatment. Participants may experience anxiety while awaiting the results of tests done. To reduce the anxiety, they will be assured of referral for continued care should the results be abnormal.

Where is the study run from?
Sally Mugabe Central Hospital (Zimbabwe)

When is the study starting and how long is it expected to run for?
June 2021 to June 2024

Who is funding the study?
European and Developing Countries Clinical Trials Partnership (EDCTP)

Who is the main contact?
Dr Edith Majonga
edithmajonga@gmail.com

Contact information

Type(s)
Principal investigator

Contact name
Dr Edith Majonga

Contact details
Biomedical Research and Training Institute
10 Seagrave Road
Harare
Zimbabwe
00263
+263 (0)776296357
edithmajonga@gmail.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
Version 2/ 17/10/2021

Study information

Scientific Title
Characterisation Of caRdiac Disease in adolescents with perinatally-acquired HIV infection in the antiretroviral therapy era

Acronym
CORD

Study objectives
The main aims of this study are to assess myocardial disease using cardiac magnetic resonance imaging in adolescents with perinatal HIV and established on antiretroviral therapy (ART). Secondly, this study seeks to understand the role of inflammation and fibrosis in the pathophysiological process of HIV-associated cardiac dysfunction.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 04/08/2021, Sally Mugabe Hospital Ethics Committee (PO Box ST14, Southerton, Harare, Zimbabwe; +263 (0)242 621100/19; info@hararehospital.gov.zw), ref: HCHEC 220721/57
2. Approved 14/08/2021, Biomedical Research and Training Institute (IRB) (10 Seagrave Road, Avondale, Harare, Zimbabwe; +263 (0)242 336691; mutenherwaf@gmail.com), ref: AP165/2021
3. Approved 28/10/2021, Medical Research Council of Zimbabwe (Cnr Josiah Tongogara and Mazowe Street, Harare, Zimbabwe, +263 (0)242 791193; mrcz@mrcz.org.zw), ref: MRCZ/A/2788

Study design
Observational cross-sectional study

Primary study design
Observational

Study type(s)
Screening

Health condition(s) or problem(s) studied
Myocardial disease in adolescents with perinatal HIV and receiving antiretroviral therapy (ART)

Interventions
Electronic clinic data and patient-held records will be used to confirm clinical and ART history. A clinical questionnaire will be administered by the research nurse to record demographic, prior medical history (previous illnesses and treatment history other than ART) and other exposures to risk factors for cardiac disease (tobacco smoking and drug history). Participants will undergo clinical assessment including anthropometry, heart rate, blood pressure, respiratory rate, pulse oximetry and New York Heart Association (NYHA) functional score. Participants without HIV will be screened for HIV prior to enrolment using an oral mucosal test.

CD4 count will be measured using a point of care Alere PIMA analyser. Blood samples will be collected from all participants for HIV viral load, Full blood count, serum creatinine, cytomegalovirus DNA and biomarkers tests. Biomarkers for myocardial stress and injury, fibrosis and systemic inflammation will be measured using bead multi-analyte assays (Luminex).

A standardized 12-lead electrocardiogram (ECG) and transthoracic echocardiography will be performed. Criteria for cardiac measurements will be based on the American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI). A cardiac magnetic resonance imaging scan will be performed using a standard protocol including cine imaging using steady-state free precession with breath-hold for quantification of cardiac volumes and mass. Gadolinium-based contrast will be injected into the participants to assess late gadolinium-enhancement (LGE) for the presence, location and extent of focal fibrosis and parametric mapping (T1 and T2) for diffuse disease. All measured parameters will be adjusted to body surface area. Extracellular volume will be estimated from pre- and post-contrast T1 mapping and haematocrit.

Intervention Type
Other

Primary outcome(s)
1. Cardiac structural abnormalities measured by left ventricular (LV) mass and LV mass index; LV and right ventricular (RV) volumes, LV wall thickness on cardiac magnetic resonance imaging (CMR) at a single timepoint
2. Cardiac functional abnormalities measured by RV and LV ejection fractions, systolic and diastolic strain rate on CMR at a single timepoint
3. Myocardial fibrosis measured by presence and extent (%) of late-gadolinium enhancement at a single timepoint

Key secondary outcome(s))
1. Biomarkers of cardiac disease, fibrosis and inflammation (GDF-15, Troponin-I, NT-proBNP, ST2, CRP, IL-6, TNF-alpha, soluble CD14, Galectin-3, TIMP-1) measured by Luminex technology in plasma at a single timepoint
2. CMV DNAemia measured by quantitative polymerase chain reaction at a single timepoint
3. Risk factors for cardiac abnormalities measured by CMR at a single timepoint
4. Association between biomarkers, CMV DNAemia and cardiac abnormalities measured by multivariable statistical analysis at a single timepoint

Completion date
30/06/2024

Eligibility

Key inclusion criteria
1. Aged 10-19 years
2. Adolescents with HIV taking ART for at least 6 months
3. Adolescents without HIV for the comparison group

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
10 years

Upper age limit
19 years

Sex
All

Key exclusion criteria
1. Contra-indications to CMR (implantable cardiac devices, pacemakers, and claustrophobia)
2. Severe renal impairment (defined as an estimated glomerular filtration rate (eGFR) <30 ml /min)

Date of first enrolment
01/09/2022

Date of final enrolment
30/12/2023

Locations

Countries of recruitment
Zimbabwe

Study participating centre
Sally Mugabe Central Hospital
Harare
Zimbabwe
00263

Sponsor information

Organisation
Biomedical Research and Training Institute

ROR
https://ror.org/0130vhy65

Funder(s)

Funder type
Research organisation

Funder Name
European and Developing Countries Clinical Trials Partnership

Alternative Name(s)
Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, The European & Developing Countries Clinical Trials Partnership (EDCTP), The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan
Data will primarily be shared with scientific collaborators, but the researchers will facilitate data sharing with any group requesting access to individual patient records, using anonymised data. The datasets generated during and/or analysed during the current study are/will be available upon request from Edith Majonga (edithmajonga@gmail.com).

IPD sharing plan summary
Available on request