The TB-HEART Study: prevalence of cardiac pathology among newly diagnosed patients with tuberculosis with and without HIV in Zambia

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BACKGROUND AND PURPOSE

Cardiovascular diseases (CVD) burden is rapidly increasing in sub-Saharan Africa (SSA) where tuberculosis and HIV prevalence remain high.[1-3] Recent data suggest pulmonary tuberculosis (PTB) is associated with increased CVD morbidity[4] However, the mechanisms of cardiac injury remain poorly understood.

The TB-HEART study is a cross-sectional and natural history study consecutively recruiting participants with newly-diagnosed PTB, living with and without HIV in Zambia. The primary outcome is the burden of cardiac pathology in PTB patients with and without HIV.

METHODS

Participants with bacteriologically-proven PTB, consecutively recruited from an outpatient settings in Lusaka, Zambia, undergo detailed clinical and functional assessments including point-of-care and standard two-dimensional (2D) echocardiography.

Participants are reviewed at completion of TB treatment when all assessments are repeated. The target sample size is 250 participants with PTB, with and without HIV, matched 2: 1 to participants without PTB, stratified by HIV – see **Figure 1**.

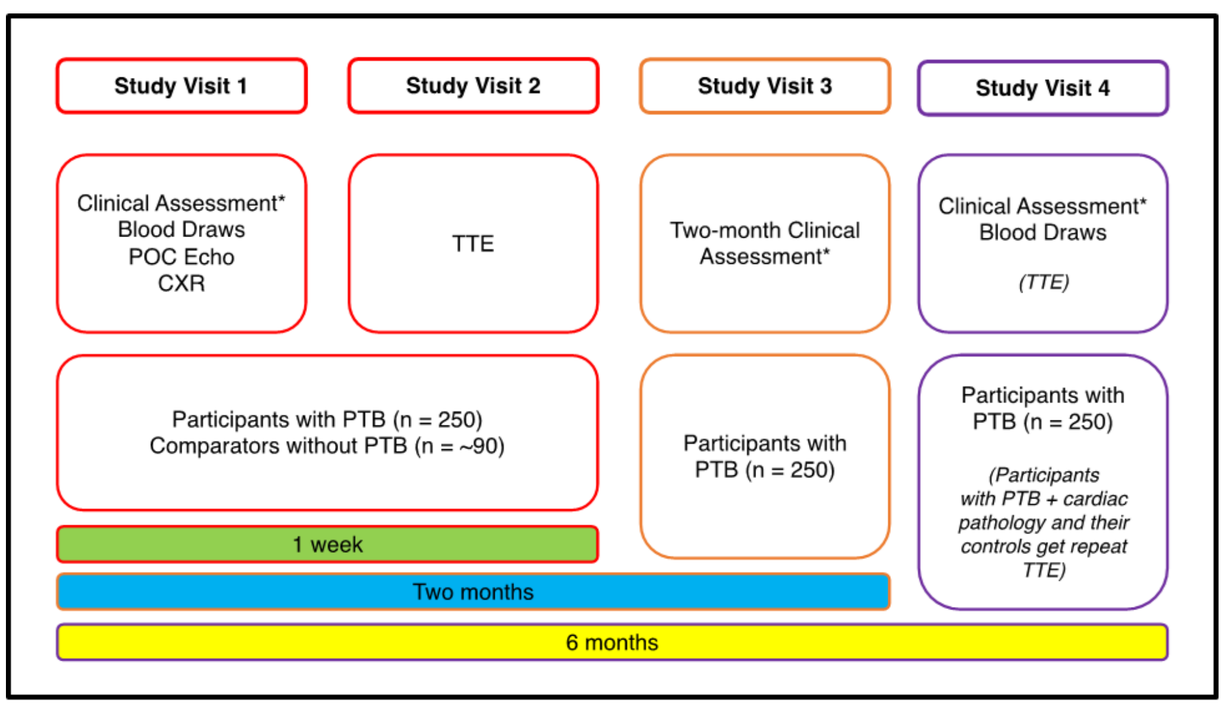


Figure 1 – Study Flow Diagram. Describes the study visits that participants attend over the course of six months. *Clinical Assessment is history and examination, functional assessment (Bandim TB, WHO Performance Status, and six-minute walk test). Blood draws are cardiac and inflammation biomarkers. CXR = Chest X-ray; POC Echo = point of care echocardiography; TTE = transthoracic echocardiogram; PTB = pulmonary TB.

RESULTS

Since 1 November 2023, we have recruited 73 participants with a mean age of 35.3±10.9 years of whom 51/73 (69.9%) are male and 19/73 (23.5%) are living with HIV. Baseline characteristics stratified by HIV status are summarised in **Table 1**.

We detected significant cardiac pathology (defined as left ventricular ejection fraction (LVEF) <51% and/or pericardial effusion >2cm in depth) in 8/65 (12.3%) participants for whom 2D-echocardiography had been completed.

Median LVEF was 61.2% (IQR 57.7-67.8). LVEF was normal in 59/65 (91%); mildly abnormal in 5/65 (7.7%); and moderately abnormal in 1/65 (1.5%) participants, respectively.

Pericardial effusion >0.5cm was detected in 16/65 (24.6%) participants and maximum effusion depth was >2cm in 2/16 (3.1%), 1-2cm in 12/16 (75%) and <1cm in 2/16 (12.5%).

2D-echocardiography findings, stratified by HIV-status, are described in **Table 2** alongside two echocardiography stills of typical pericardial effusion findings in one participant in **Figure 2**.

1. WHO. Global Tuberculosis Report 2021.. **2.** Yuyun MF et al. *Glob Heart*. 2020;15(1):15. **3.** WHO. WHO global lists of high burden countries for tuberculosis (TB). **4.** Basham Ca et al. *PLOS ONE*. 2020;15(7):e0235821. **5.** Bates M et al. Lancet Infect Dis. 2015;15(5):544-51. **6.** Mucheleng'Anga LA et al. International Journal of Infectious Diseases. 2022;124:S75-S81. **7.** Lopez-Lopez JP et al. JAMA. 2021;10(7):e019435.

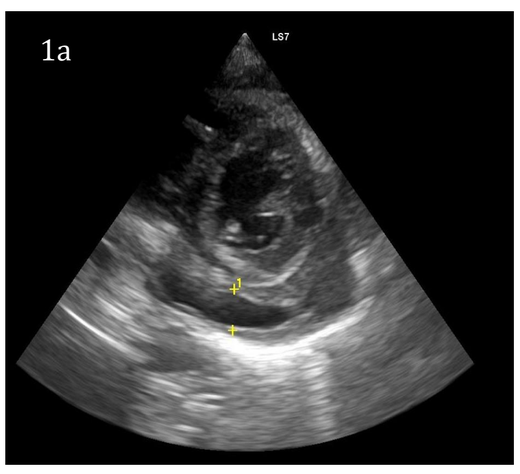
BASELINE CHARACTERISTICS

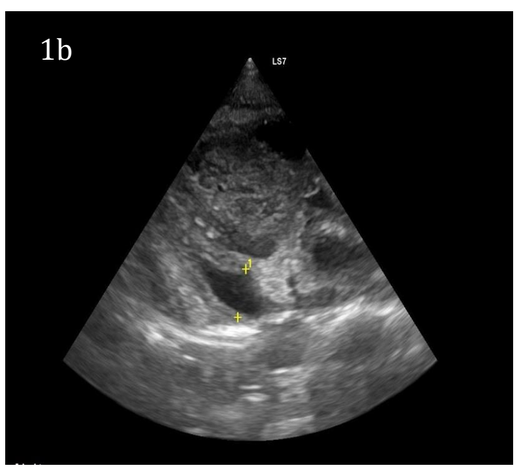
	All participants	HIV-positive	HIV-negative
N, %	73 (100)	19 (23.5)	54 (76.5)
Age, in years (± SD)	35.3 (±10.9)	37.5 (±8.1)	34.5 (±11.8)
Sex			
Male	51 (69.9)	12 (63.2)	39 (72.2)
Female	22 (30.1)	7 (36.8)	15 (27.8)
HH income, USD (median, IQR)	55.9 (30.1–107.7)	55.9 (30.1–129.2)	49.5 (34.4–107.7)
CVD risk factors, N (%)			
History of smoking	39 (53.4)	8 (42)	31 (57.4)
Hypertension	3 (4.1)	2 (10.5)	1 (1.8)
TB symptoms at presentation			
Cough >28 days	42 (63.6)	12 (70.6)	30 (61.2)
Chest pain >28 days	14 (30.4)	2 (18.2)	12 (34.3)
Anthropometrics			
BMI (mean, SD)	19 (±3.7)	20.1 (±4.9)	18.7 (±3.2)
Clinical observations			
Heart rate, in b/min (mean ±SD)	109 (±17.4)	104 (±18.5)	111 (±16.8)
Abnormal CVD exam, N (%)	31 (42.5)	8 (42.1)	23 (42.5)
WHO performance score, N (%)			
0	17 (23.3)	4 (21)	13 (24.1)
1	20 (27.4)	5 (26.3)	15 (27.8)
2	23 (31.5)	6 (31.6)	17 (31.5)
3	10 (13.7)	2 (10.5)	8 (14.8)
4	3 (4.1)	2 (10.5)	1 (1.8)

Table 1 - Baseline characteristics of participants recruited to the TB-HEART study, stratified by HIV status.

IMAGING FEATURES

Figure 1a and 1b – Pericardial effusion with maximal depth of 2cm in parasternal short axis view (1a) and in parasternal long axis view (1b) in a 49-year-old HIV-negative participant with pulmonary TB for whom adjuvant steroids (prednisolone 1mg/kg for 6 weeks) was added to standard anti-tuberculous therapy.





2D-ECHOCARDIOGRAPHY RESULTS

N, %	All participants	HIV-positive	HIV-negative
LVEF %, median (IQR)	**61.2 (57.7-67.8)**	**63.5 (59.7-68.1)**	**61 (56.8-66.4)**
Normal (LVEF >49%), N (%)	59 (91)	15 (88.2)	44 (91.6)
Midly reduced (LVEF 41-48%), N (%)	5 (7.7)	1 (5.9)	4 (8.4)
Reduced (LVEF <40%), N (%)	1 (1.5)	1 (5.9)	-
Pericardial effusion, max depth in cm, N (%)			
Any	16 (24.6)	3 (17.6)	13 (27)
0.5 – 1 cm	2 (3.1)	-	2 (4.2)
1 – 2 cm	12 (18.4)	3 (17.6)	9 (18.7)
>2cm	2 (3.1)	-	2 (4.2)
Absent	49 (75.4)	14 (82.3)	35 (72.9)

Table 2 – Cardiac pathology detected on 2D-echocardiography in 65/73 participants of the TB-HEART study for whom results are available. LVEF is defined by Simpson's Biplane Method, where LVEF >51% is normal; LVEF 41-50% is mildly abnormal; LVEF <40% is moderately abnormal in accordance with European Society of Cardiology Guidelines

CONCLUSIONS

Our preliminary results demonstrate a higher-than-expected prevalence of cardiac pathology among participants with PTB with and without HIV, which ranges from 1-7% in autopsy studies and case series.(5-7) The most common cardiac pathology was pericardial effusion.

Further analyses will include cardiac biomarkers; repeat clinical and echocardiographic assessments at TB treatment completion; and comparator data, to determine associations between prevalent cardiac pathology and PTB controlling for HIV and TB status, respectively.
This may have important implications for clinical practice to prevent complications such as constrictive pericarditis; and policy design to better integrate TB and HIV patient services with preventative care to reduce future CVD risk.