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The prevalence of concurrent pulmonary and extrapulmonary tuberculosis in Uganda: a retrospective study

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Abstract

Background: Concurrent pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB) is associated with poor treatment outcomes yet its epidemiology in Uganda is unknown. The purpose of this study was to determine the prevalence, associated factors, and treatment outcomes of concurrent PTB and EPTB among patients at a national tuberculosis (TB) treatment center located at Mulago National Referral Hospital in Kampala, Uganda.

Methods: We conducted a retrospective review of charts for people with TB who were enrolled in care between January 2015 and December 2019. Eligible charts were for people with pulmonary bacteriologically confirmed TB enrolled into care in the period under study. Concurrent PTB and EPTB was defined as PTB and bacteriological, histopathological, and/or radiological features of TB at another noncontiguous sites.

Results: Overall, 400 patient charts were eligible, of whom 240 (60.0%) were aged 15–34 years and 205 (51.3%) were female. The prevalence of concurrent PTB and EPTB was 8.5% (34/400) [95% confidence interval (CI): 6.0–11.7%]. People with concurrent PTB and EPTB were more likely to have at least one comorbidity (82.4% *versus* 37.2%, $p < 0.001$), of which HIV was the most frequent. Furthermore, people with concurrent PTB and EPTB were more likely to have empyema (15% *versus* 2.6%, $p = 0.028$) but less likely to have bronchopneumonic opacification (0.0% *versus* 15.3%, $p = 0.043$) on chest x-ray imaging. People with concurrent PTB and EPTB had higher mortality (26.5% *versus* 6.37%) and a lower cure rate (41.2% *versus* 64.8%), $p = 0.002$.

Conclusion: Our findings highlight the need for early detection of TB before dissemination particularly among people who use alcohol and people with HIV.

Keywords: disseminated, EPTB, HIV, outcomes, PTB, tuberculosis, Uganda

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Introduction

Tuberculosis (TB), which is caused by the bacterium *Mycobacterium tuberculosis*, is a major public health problem.[1] It remains a major threat to humanity despite improvements in health care systems and the widespread implementation of TB control programs. According to World Health Organization (WHO), TB is one of the top 10 causes of death worldwide with an estimated 10 million new cases in 2020, of which majority were in South-East Asia and sub-Saharan Africa.[2] At least 1.5 million people were estimated to have died from TB in 2020 up from the 1.4 million estimated deaths in 2019.[2] In Uganda alone, there is an estimated 87,000 new TB cases annually and a prevalence of 253 per 100,000 persons.[3] WHO has recently reclassified Uganda as high-burdened country for both TB and TB/HIV co-infection.[4] There is need to further characterize the epidemiology of TB in the country to inform interventions to reduce the TB burden and improve TB outcomes.

TB typically affects the lung parenchyma [pulmonary tuberculosis (PTB)] but can also affect other sites [extrapulmonary tuberculosis (EPTB)].[5] Concurrent PTB and EPTB is also widely reported in literature but are not well characterized in sub-Saharan Africa. In the United States, the prevalence of concurrent PTB and EPTB was low (2.2%) but did not show a significant decline over a 15-year period and was associated with longer hospital stay.[6] At least 70% of inpatients with EPTB had concurrent PTB in China.[7] In South Korea, 50% of people with EPTB and fever of unknown origin had concurrent PTB and EPTB, although only 23.4% of them showed typical findings of PTB on chest x-ray imaging.[8] A study among people with TB/HIV co-infection in Romania found that 30% of them had concurrent PTB and EPTB, suggesting that people with HIV may have a higher prevalence of concurrent PTB and EPTB.[9]

There is still scarcity of data on the characteristics and treatment outcomes of people with concurrent PTB and EPTB particularly in sub-Saharan Africa where the prevalence of HIV among TB cases is high (32%).[10] The purpose of this study, therefore, was to determine the prevalence, associated factors, and treatment outcomes of concurrent PTB and EPTB among people with TB at a national TB treatment center in Uganda.

Methods

Study setting

This study took place at the TB unit of Mulago National Referral Hospital from December 2019 to September 2020. This is the largest TB Treatment Center in Uganda and manages more than 200 patients per quarter. The facility is in Kampala, the capital city of Uganda. It is a center of excellence for drug-sensitive and drug-resistant TB, offering both outpatient and inpatient services. The facility offers care to both referral (about 40%) and nonreferral cases. All patients underwent standard TB treatment as recommended by the Uganda National TB guidelines. The recommended treatment regimen for drug-susceptible TB in Uganda is Rifampicin (R), Isoniazid (H), Ethambutol (E), and Pyrazinamide (Z) which is divided into two phases, that is, a 2-month initial phase where all the four drugs are used and followed by a 4-month continuation phase involving only two drugs, that is, R and H.[11] The duration of treatment for TB Bone and TB Meningitis is a 1-year period constituting a 2-month initial phase of RHZE and 10 months of RH while a 6-month regimen for all others forms of TB as explained above.

Study design and sample size estimation

We used a retrospective study design and retrospectively reviewed charts of TB cases managed at this unit from January 2015 to December 2019. Using OpenEpi,[12] we estimated the sample size to be 406, assuming a prevalence of 50%, a 10% incomplete data rate, a confidence level of 95%, and a known population of TB cases (7460) in the period under study.

Study participants

We included patients' charts for whom PTB was bacteriologically confirmed using sputum Ziehl–Neelsen (ZN) stain, Xpert MTB/RIF, and/or mycobacterium culture as evidenced by laboratory results from the patients' charts. Among these bacteriologically confirmed PTB case files, we further sought for those with concurrent EPTB. Patient files were selected by systematic sampling of every 19th patient file in the unit TB register and those with missing files were replaced by the next file. We excluded charts with missing information on age and sex.

Data collection and study measurements

Using a data abstraction form, data on HIV status, occupation, history of alcohol use, cigarette smoking, other substance abuse, and other potential risk factors for concurrent PTB and EPTB such as comorbidities (diabetes mellitus, HIV/AIDS, and cancer) and history of TB treatment were extracted from the charts by health workers. The treatment outcome data were extracted from the unit TB register for each patient. Baseline chest x-ray films were evaluated by a radiologist for hilar/mediastinal lymphadenopathy, bronchopneumonic opacification, segmental/lobar consolidation, cavities, miliary opacification, pleural effusion, empyema, bronchiectasis, atelectasis, fibrotic bands, pneumothorax, and bullae. The location of the lesion was described by side and zone of the lung. EPTB was diagnosed by abdominal ultrasound scan (abdominal TB), echocardiogram (TB pericarditis), ascitic/cerebral spinal fluid Xpert MTB/RIF, and spinal magnetic resonance imaging (MRI). We considered the following as features of abdominal TB on abdominal ultrasound scan: ascites

with fibrous stranding, splenic hypoechoic lesions, organomegaly of spleen and liver, and abdominal lymphadenopathy. Features of spine TB on spine imagining were intraosseous and para spinal abscess, vertebral body destruction and collapse, and loss of trabecular pattern. There were no other forms of EPTB observed in this cohort.

Study outcomes

Concurrent PTB and EPTB was defined as having PTB (all patients had bacteriologically confirmed TB on sputum samples) and features of TB at any another site. The prevalence of concurrent PTB and EPTB was computed as the proportion of patients with concurrent PTB and EPTB to the entire study population. Treatment outcomes were cure, death, treatment failure, or loss to follow-up as defined by the WHO[13] and Uganda National TB and Leprosy Program guidelines[11] as follows:

Cure – a PTB patient with bacteriologically confirmed TB at the beginning of treatment who was smear- or culture-negative in the last month of treatment and on at least one previous occasion.
Death – death during TB treatment from any cause.
Treatment failure – a TB patient whose sputum smear or culture is positive at month 5 or later during treatment, or was negative at beginning and is smear-positive at 2 months.
Loss to follow-up: a TB patient who did not start treatment or who completed more than 1 month of treatment and was interrupted for 2 consecutive months or more.
Completed treatment – a TB patient who completed treatment without evidence of failure BUT with no record to show that sputum smear or culture results in the last month of treatment and on at least one previous occasion were negative, either because tests were not done or because results are unavailable. Factors associated with TB were those variables for which the frequencies were significantly different among people with, and without, concurrent PTB and EPTB.

Statistical analysis

Raw data were entered in EpiData 3.0. Normality was assessed using the Shapiro-Wilk test. Means were compared using the Student t test, whereas percentages for categorical data were compared using χ^2 test and Fisher's exact test. The statistical significance was determined using a p value of 0.05 and a 95% confidence interval (CI) is presented for point estimates. The data were analyzed using SAS Version 9.4.[14] Data sets used in this analysis are available from the corresponding author upon reasonable request.

Results

Sociodemographic and clinical characteristics of patients with and without concurrent PTB and EPTB

A total of 476 TB cases were reviewed, of which 400 met the eligibility criteria (Figure 1). Of all cases, 240 (60.0%) were aged 15–34 years and 205 (51.3%) were female. Furthermore, 170 (42.82%) belonged to the Bantu ethnic group, 93 (23.25%) were casual laborers and comorbidities were found in 164 (41%) of cases. HIV co-infection was observed among 159 (39.8%) cases. Table 1 summarizes sociodemographic characteristics, while Table 2 shows clinical characteristics of the study participants with and without concurrent PTB and EPTB.

Prevalence of concurrent PTB and EPTB

Of the 400 PTB cases reviewed, 34 (8.5%) (95% CI: 5.96–11.68%) had concurrent PTB and EPTB. The most common sites of EPTB were the abdomen ($n = 18$), larynx ($n = 1$), and other sites (pericardium, brain, spine) ($n = 7$). Miliary TB was present in eight cases with concurrent PTB and EPTB. An ultrasound was used to confirm abdominal TB, Xpert MTB/RIF assay was done on cerebral spinal fluid for TB brain, MRI was done for TB spine, echocardiogram was performed in TB pericardium, and histology was performed for the one case with laryngeal TB.

Treatment outcomes of people with concurrent PTB and EPTB

Overall, treatment success (cure and treatment completion) was observed among 317 (80.25%). Patients with concurrent PTB and EPTB ($n = 34$) had higher mortality (26.5% *versus* 6.37%) and a lower cure rate (41.2% *versus* 64.8%), $p = 0.002$, than patients with PTB only as shown in Table 2.

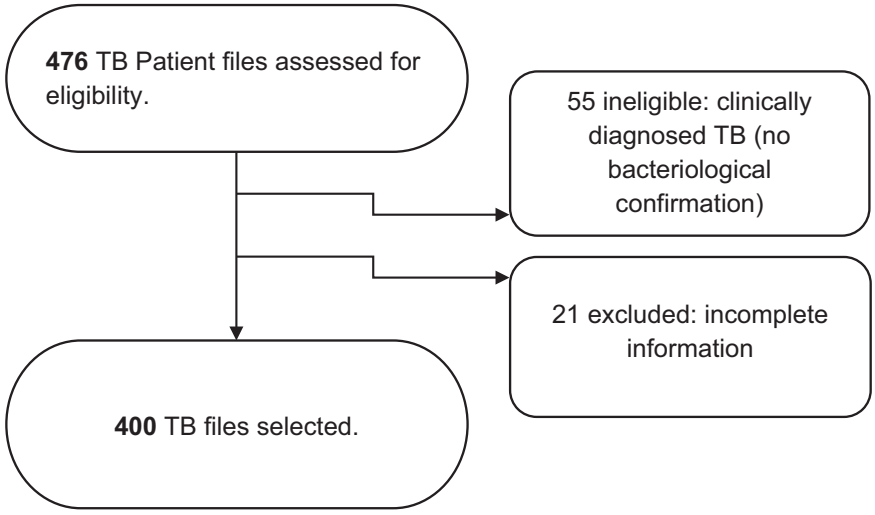

Figure 1. Study flow diagram.

Factors associated with concurrent PTB and EPTB

As shown in Tables 1 and 2, people with concurrent PTB and EPTB were more likely to report alcohol use (30.0% *versus* 13.2%, $p=0.005$) and had at least one comorbidity (82.4% *versus* 37.2%, $p<0.001$). Notably, 34 (100%) cases with concurrent PTB and EPTB had HIV co-infection as compared with only 131 (35.8%) cases with PTB alone. Also, there were fewer people from the Bantu ethnic group with concurrent PTB and EPTB than PTB alone (85.2% *versus* 87.0%, $p=0.048$).

Chest x-ray findings among people with concurrent PTB and EPTB

Of all cases, 156 (39.0%) had normal chest x-rays. Patients with concurrent PTB and EPTB were more likely to have empyema (15.0% *versus* 2.6%, $p=0.028$) but less likely to have bilateral bronchopneumonic opacification (0.0% *versus* 15.3%, $p=0.043$) on chest x-ray imaging as shown in Table 2.

Discussion

Concurrent PTB and EPTB is a potentially lethal form of TB that affects other organs, alongside the lung parenchyma, through lymphohematogenous spread to lymph nodes, pleura, genitourinary tract, bones and joints, meninges, peritoneum, and pericardium. Concurrent PTB and EPTB has been increasingly observed in immunocompromised hosts, especially in developing countries, due to higher rates of TB-HIV co-infection.[15] However, little is known about the burden, risk factors, and treatment outcome of this condition in Africa.

In our study, the modal age was 15–34 years, which is consistent with the most frequent age group affected by TB.[16] The prevalence of concurrent PTB and EPTB was found to be 9%, which is similar to that reported in Oman (10%)[17] but higher than the estimate in the United States (2.2%).[6] This difference is likely to be due to the high prevalence of comorbidities in our study and the study from Oman. Differences in estimating the burden of concurrent PTB and EPTB are affected by variations in the study populations and definition of concurrent PTB and TB, which is sometimes conflated with disseminated tuberculosis (DTB). In Portugal, for example, the prevalence of DTB was 20% but DTB was defined as involvement of more than two noncontiguous organs or identification of *M. tuberculosis* in blood or bone marrow in a population of people with PTB.[18] There is therefore a need to standardize these definitions such that there is consistency in determining and reporting the prevalence of DTB and concurrent PTB and EPTB.

It is often difficult to establish the diagnosis of concurrent PTB and EPTB because the clinical

Table 1. Sociodemographic characteristics of people with TB stratified by having concurrent PTB and EPTB.

Characteristic	Total *n* (%)	With concurrent PTB and EPTB *n* (%)	Without concurrent PTB and EPTB *n* (%)	*p* value
Age (years)	**(*N* = 400)**	**(*n* = 34)**	**(*n* = 366)**	0.6773
<15	7 (1.75)	1 (2.94)	6 (1.64)	
15–34	240 (60.0)	23 (67.65)	217 (59.29)	
35–60	142 (35.5)	9 (26.47)	133 (36.34)	
>60	11 (2.75)	1 (2.94)	10 (2.73)	
Sex	**(*N* = 400)**	**(*n* = 34)**	**(*n* = 366)**	0.6093
Male	195 (48.75)	18 (52.94)	177 (48.36)	
Female	205 (51.25)	16 (47.06)	189 (51.64)	
Occupation	**(*N* = 138)**	**(*n* = 19)**	**(*n* = 109)**	0.0501
Formal work	10 (7.25)	1 (5.26)	9 (7.56)	
Causal work	93 (67.39)	15 (65.55)	78 (78.95)	
Unemployed	35 (25.36)	3 (15.79)	32 (26.89)	
Marital status	**(*N* = 67)**	**(*n* = 9)**	**(*n* = 58)**	0.1589
Married	48 (71.64)	8 (88.89)	40 (68.97)	
Divorced	1 (1.49)	0 (0)	1 (1.27)	
Single	18 (26.87)	1 (11.11)	17 (29.31)	
Education status	**(*N* = 19)**	**(*n* = 2)**	**(*n* = 17)**	0.0585
Tertiary	6 (31.58)	0 (0)	6 (35.29)	
Secondary	8 (42.11)	0 (0)	8 (47.06)	
Primary	5 (26.32)	2 (100)	3 (17.65)	

EPTB, extrapulmonary tuberculosis; PTB, pulmonary tuberculosis.

presentation is often nonspecific, with symptoms varying according to the affected organs.[19] In our study, the commonest site of dissemination was the abdomen. In contrast, Leeds *et al.*[20] in their retrospective review of EPTB cases in the United States found the most common site of dissemination to be lymphatic spread, while pleural TB was the commonest in Ghana.[21] Ultrasound scan services are more readily available in Uganda than other advanced diagnostic methods such as pleural and lymph node biopsy and histology. This may have influenced the frequency of abdominal TB that we observed due to higher diagnostic capability for abdominal TB than other sites. It is possible that some sites of TB dissemination were not encountered due to lack of readily available diagnostic resources.

Similar to previous reports by Meira *et al.*[22] and Wang *et al.*,[15] we found concurrent PTB and EPTB to be associated with comorbidities of which HIV was the most predominant (100% of patients with concurrent PTB and EPTB had HIV co-infection). This should be expected

Table 2. Clinical characteristics of people with TB stratified by concurrent PTB and EPTB.

Characteristic	Total (*N* = 400) *n* (%)	With concurrent PTB and EPTB (n = 34) *n*(%)	Without concurrent PTB and EPTB (n = 366) *n*(%)	*p* value
Year of treatment initiation				0.6239
Missing	5 (1.5)	0 (0)	5 (1.37)	
2015	120 (30.25)	14 (41.18)	106 (28.96)	
2016	101 (25.5)	7 (20.59)	94 (25.68)	
2017	89 (20.75)	5 (14.71)	84 (22.95)	
2018	44 (12)	5 (14.71)	39 (10.66)	
2019	41 (10)	3 (8.82)	38 (10.38)	
Type of TB				0.4863
New case	355 (88.75)	32 (94.12)	323 (88.25)	
Relapse	34 (8.5)	2 (5.88)	32 (8.74)	
Return after loss to follow-up	11 (2.75)	0 (0)	11 (3.01)	
Tool used in diagnosis of PTB				0.5006
Xpert MTB/RIF	51 (12.75)	2 (5.88)	49 (13.39)	
ZN staining	29 (7.25)	3 (8.82)	26 (7.1)	
Both Xpert MTB/RIF and chest x-ray	260 (65)	25 (73.53)	235 (64.21)	
Both Xpert MTB/RIF and ZN staining	12 (3)	0 (0)	12 (3.28)	
Both ZN staining and chest x-ray	35 (8.75)	3 (8.82)	8 (8.74)	
ZN staining, chest x-ray, and Xpert MTB/RIF Xpert	7 (1.75)	0 (0)	7 (1.91)	
Mycobacterium culture	3 (0.75)	0 (0)	3 (0.82)	
Others	3 (0.75)	1 (2.94)	2 (0.55)	
Unknown	1 (2.94)	1 (2.94)	0	
Patients with comorbidities				<**0.0001***
No	236 (59.0)	6 (17.65)	230 (62.84)	
Yes	164 (41.0)	28 (82.35)	136 (37.16)	
Comorbidities present				1.0000
HIV/AIDS	159 (96.95)	28 (100.00)	131 (96.32)	
Cancer	1 (0.61)	0 (0.00)	1 (0.74)	
Diabetes mellitus	4 (2.44)	0 (0.00)	4 (2.94)	

(Continued)

Table 2. (Continued)

Characteristic	Total (*N* = 400) *n* (%)	With concurrent PTB and EPTB (n = 34) *n*(%)	Without concurrent PTB and EPTB (n = 366) *n*(%)	*p* value
Treatment outcome				**0.0024***
Cured	248 (62.78)	14 (41.18)	234 (64.82)	
Treatment failure	6 (1.52)	1 (2.94)	5 (1.39)	
Lost to follow-up	16 (4.05)	1 (2.94)	15 (4.16)	
Completed Treatment	69 (17.47)	8 (23.53)	61 (16.9)	
Transferred	4 (1.01)	0 (0)	4 (1.11)	
Died	32 (8.1)	9 (26.47)	23 (6.37)	
Unknown	20 (5.06)	1 (2.94)	19 (5.26)	
Substances abused	**(*N* = 78)**	**(*n* = 10)**	**(*n* = 68)**	**0.0052***
Tobacco	7 (8.97)	0 (0)	7 (10.29)	
Alcohol	12 (15.38)	3 (30.00)	9 (13.24)	
Marijuana	1 (1.28)	0 (0)	1 (1.47)	
Others	7 (8.97)	1 (10.00)	6 (8.82)	
None	33 (42.31)	5 (50.00)	28 (41.18)	
Both alcohol and tobacco	18 (23.08)	1 (10.00)	17 (25.00)	
CHEST X-RAY FINDINGS				
Normal x-ray findings				0.7856
Yes	156 (39.00)	14 (41.18)	142 (38.80)	
No	244 (61.00)	20 (58.82)	224 (61.20)	
Bilateral bronchopneumonic opacification				**0.0432***
Yes	30 (13.89)	0 (0)	30 (15.31)	
No	186 (86.11)	20 (100)	166 (84.69)	
Consolidation				0.7992
Yes	54 (24.88)	6 (30.00)	48 (24.37)	
No	163 (75.12)	14 (70.00)	149 (75.63)	
Cavitations				0.1611
Yes	18 (8.33)	0 (0)	18 (9.18)	
No	198 (91.67)	20 (100)	178 (90.82)	
Atelectasis				0.9024

(Continued)

Table 2. (Continued)

Characteristic	Total (*N* = 400) *n* (%)	With concurrent PTB and EPTB (n = 34) *n*(%)	Without concurrent PTB and EPTB (n = 366) *n*(%)	*p* value
Yes	6 (2.78)	1 (5)	5 (2.55)	
No	210 (97.22)	19 (95)	191 (97.45)	
Fibrotic bands				0.2952
Yes	49 (22.58)	3 (15.00)	46 (23.35)	
No	168 (77.42)	17 (85.00)	195 (76.65)	
Bullae				0.9074
Yes	1 (0.46)	0 (0)	1 (0.51)	
No	215 (99.54)	20 (100)	195 (99.49)	
Lymphadenopathy				0.0480
Yes	97 (44.91)	5 (25)	92 (46.94)	
No	119 (55.09)	15 (75)	104 (53.06)	
Pleural effusion				0.8682
Yes	72 (33.33)	7 (35)	65 (33.16)	
No	144 (66.67)	13 (65)	131 (66.84)	
Empyema				**0.0283***
Yes	8 (3.7)	3 (15)	5 (2.55)	
No	208 (96.3)	17 (85)	191 (97.45)	

EPTB, extrapulmonary tuberculosis; MTB, *Mycobacterium tuberculosis*; PTB, pulmonary tuberculosis.
*Statistically significant result.

because HIV globally impairs immune responses against *M tuberculosis* resulting in TB dissemination.[23] The findings therefore re-emphasize the need to scale up uptake of TB prevention therapies among people with HIV. However, people with HIV in our study might have preferentially undergone workup for EPTB. This might explain why no HIV-negative individual had concurrent PTB and EPTB.

Our findings about the treatment outcomes are consistent with other studies that found DTB to be highly fatal.[24] We found that people with concurrent PTB and EPTB had a fourfold mortality rate as compared with those with PTB. In Portugal, Meira *et al.*[22] found a mortality rate of 36% among patients with DTB but was not significantly higher than that among patients without DTB (21%). However, many patients in their study had other comorbidities and HIV was prevalent in only 47% (cf. 100% in our study) of patients with DTB. The rate of cure was lower in the people with concurrent PTB in our study. This is expected since patients with predominantly extrapulmonary forms of TB may be unable to produce sputum during treatment follow-up to enable confirmation of TB cure.[25] From our results, it is evident that patients with concurrent PTB and EPTB were more likely to be assigned 'treatment completion' as opposed to cure.

Typical chest radiographic findings in concurrent PTB and EPTB are not well established. In our study, only 35% of concurrent PTB and EPTB

cases had miliary pattern. In contrast, Khan[19] estimates that the classic miliary pattern occurs in 85–90% cases of DTB. It is unclear whether this is among patients with any form of concurrent PTB and EPTB per se or among patients with TB bacteremia (miliary TB). Interestingly, we found that people with concurrent PTB and EPTB were more likely to have empyema but less likely to have bronchopneumonic opacities. More studies are needed to characterize chest x-ray findings among patients with concurrent PTB and EPTB.

Although we found alcohol use to be common among people with concurrent PTB and EPTB in our study, the numbers were too few to make meaningful interpretation of these data. Nonetheless, alcohol consumption blunts qualitative and quantitative CD4+ and CD8+ T-lymphocyte cell immune responses against TB resulting in poor formation of granulomas and a high bacillary load burden.[26]

Our study had limitations. We had a small number of cases with concurrent PTB and EPTB which limited our ability to construct a robust model for predictors of concurrent PTB and EPTB. We also did not evaluate some biomedical differences such as anemia, organ dysfunction, and clinical symptoms. These were not consistently documented in the charts. Finally, our study was at a national referral center and our estimate of the prevalence may be an overestimate due to referral bias. Notwithstanding, we provide the first description of the epidemiology and treatment outcomes of concurrent PTB and EPTB in Uganda.

Conclusion

Concurrent PTB and EPTB is prevalent in Uganda especially among TB/HIV co-infected individuals and there seems to be an underestimation of the threat it poses. All concurrent PTB and EPTB cases were found in people with HIV. A higher mortality was observed in concurrent PTB and EPTB than in those with PTB only. Our findings highlight the need for early detection of TB before dissemination in individuals with HIV. More studies are needed to determine the diagnostic accuracy of chest imaging in investigating concurrent PTB and EPTB and the role of ethnicity as a risk factor for concurrent PTB and EPTB.

Ethics approval and consent to participate

The study was approved by the Mulago Hospital Research and Ethics Committee (reference number: MHREC#1808). The study was conducted after a consent waiver was obtained from the ethics committee.

Consent for publication

Not applicable.

Author contributions

Eddy Kyagulanyi: Conceptualization; Data curation; Formal analysis; Investigation; Resources; Software; Supervision; Visualization; Writing – original draft; Writing – review & editing.

Joy Mirembe: Conceptualization; Data curation; Formal analysis; Funding acquisition; Project administration; Resources; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

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Jaffar Tamale: Formal analysis; Methodology; Resources; Software; Writing – original draft; Writing – review & editing.

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Availability of data and materials
Datasets used in this analysis are available from the corresponding author upon reasonable request.

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