Treatment success and mortality among adults with tuberculosis in rural eastern Uganda: a retrospective cohort study

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Abstract

Background

Successful treatment of tuberculosis leads to clinical and public health benefits such as reduction in transmission, complications, and mortality among patients. However, data are limited on treatment outcomes and the associated factors among persons with bacteriologically confirmed pulmonary (BC-PTB) in rural areas of high tuberculosis and Human Immunodeficiency Virus (HIV) burden countries such as Uganda. We investigated factors associated with successful treatment of tuberculosis and mortality among adult persons with BC-PTB in rural eastern Uganda.

Methods

We constructed a retrospective cohort of patients with BC-PTB from a routine tuberculosis clinic database in eastern Uganda. We performed bivariate and multivariate analysis. Using a 5% level of significance, we used the modified Poisson regression analysis to determine factors independently associated with treatment success and mortality.

Results

We retrieved 1,123 patient records. Of these, 477(42.5%) had a cure, 323 (28.0%) had treatment completion, 17(1.5%) had failed treatment, 81(7.2%) had died, 89(7.9%) were lost to follow-up, and 136(12.1%) had missing treatment outcome. Overall, 800 (81.1%) of the 987 persons with BC-PTB that had an outcome, were successfully treated. Successful treatment of tuberculosis was less likely to occur among those with HIV infection (Adjusted risk ratio (aRR), 0.88; 95% Confidence Interval (CI), 0.82-0.95), older than 50 years (aRR, 0.89; 95% CI, 0.81-0.97), or male (aRR, 0.92; 95% CI, 0.87-0.98). Mortality was associated with HIV infection (aRR, 4.48; 95% CI, 2.95-6.79), older than 50 years (aRR, 2.93; 95% CI, 1.74-4.92), year of enrollment into treatment from 2015 (aRR, 0.80; 95% CI, 0.66-0.97), and Community-Based Directly Observed Therapy Short Course (aRR, 0.26; 95% CI, 0.13-0.50).

Conclusions

Treatment success rate among adult persons with BC-PTB in rural eastern Uganda is suboptimal and mortality is high. HIV infection and older age reduce the chance of successful treatment of tuberculosis, and increase risk of mortality. Older and HIV infected persons with BC-PTB will require special consideration to optimize treatment success and reduce risk of mortality.

Background

Although tuberculosis is treatable and curable with a standard course of antibiotics, the disease continues to claim millions of lives globally. The 2019 World Health Organization (WHO) Global Tuberculosis report indicates 10 million people developed tuberculosis disease in 2018 and 1.5 million of them died.(1) Therefore WHO recommends that a good performing tuberculosis program should achieve at least 90% treatment success rate and 85% cure rate.(2) These targets contribute to the effective reduction of tuberculosis transmission at household and community levels, and in reducing tuberculosis related complications and mortality.(3) Nonetheless, tuberculosis control programs all over the world have challenges in meeting the recommended treatment success rate particularly for newly diagnosed persons with bacteriologically confirmed pulmonary

tuberculosis. According to current data, global treatment success rate for newly diagnosed persons with BC-PTB has improved from 82% in 2016(4) to 85% in 2017,(1) which is still lower than the desired target of at least 90%.

Sub Saharan Africa has the highest burden of tuberculosis and the slowest decline in tuberculosis incident cases,(5) yet has suboptimal tuberculosis treatment success rate. Recent systematic review and meta-analysis shows successful treatment of tuberculosis in sub Saharan Africa over the past 10 years is 76.2%,(6) far below the global treatment success rate of 85% (1) and the WHO recommended rate of at least 90%.(2) This meta-analysis also shows sub Saharan Africa may be experiencing a gradual but steady decline in tuberculosis treatment success rate.(6). There is a need to conduct research that can inform interventions to improve treatment success rate. Interventions are particularly needed in sub Saharan Africa where the burden of tuberculosis and HIV are both very high. The huge burden of tuberculosis is higher among people living with Human Immunodeficiency Virus (HIV) where it is the number one cause of mortality.(7) More data are needed especially from rural underserved areas on treatment outcomes among persons with tuberculosis to inform interventions.

Therefore, the purpose of this study was to measure treatment outcomes, namely treatment success and mortality, among persons with BC-PTB in rural eastern Uganda, determine whether HIV infection is associated with these treatment outcomes, and identify factors amenable to interventions that can contribute to treatment success.

Methods

Study design

We retrieved and reviewed records for adult persons with BC-PTB across the 10 largest tuberculosis diagnostic and treatment units in the districts of Soroti, Kumi, Ngora, and Serere, all in eastern Uganda. The records are routinely collected by the TB clinics for use in reporting case load, tracking patient outcomes and form part of the National TB and Leprosy program surveillance. The records capture demographics, laboratory and clinical outcomes.

Variables and measurements

The independent variables included the following: district where the tuberculosis patient received treatment, level and location of health facility, health facility ownership type, year of tuberculosis treatment initiation, sex, age category, type of tuberculosis patient (new or retreatment), transfer-in status, baseline pre-treatment bacilli load, type of anti-tuberculosis regimen, HIV sero-status, type of DOTS, availability of a treatment supporter, and patient residence.

In the analysis, we considered two outcomes; primary and secondary. The primary outcome was successful treatment of tuberculosis and the secondary was mortality. Treatment success and mortality were both defined according to the WHO criteria.(8) We computed treatment success as the percentage of adult BC-PTB cases registered under directly observed therapy (DOTs) in a given year who completed tuberculosis treatment with bacteriologic evidence of success (cured) or no cure but had completed treatment. Mortality was computed as the percentage of adult persons with BC-PTB who died from any cause during tuberculosis treatment.

Inclusion and exclusion criteria

We included all adult (15 years and older) persons with BC-PTB, diagnosed and treated between January 2015 and June 2018. The patients were either newly diagnosed with tuberculosis or had previously been treated for tuberculosis, and if they were transferred-in, this should not have happened after two months of treatment at the preceding health facilities. This study excluded participants with no treatment outcome evaluation namely those who were transferred to other health facilities, or had missing treatment outcomes in the tuberculosis unit registers.

Data analysis

In the Univariate analysis, we computed frequencies and percentages for categorical variables, and means with standard deviations for numerical data. In the bivariate analysis, we assessed differences in observed and expected frequencies in categorical variables between participants with successful versus non-successful tuberculosis treatment, and between persons with BC-PTB who died versus those who survived using the Chi-squared test for expected cell counts above five, or the Fisher's exact test for expected cell counts less than five. For numeric data, we used Student's t-test to assess differences in their means. We used modified Poisson regression analysis with robust standard errors to perform multivariate analysis for all statistically significant variables identified at the bivariate analysis and reported the results as risk ratios (RR). The RR was a better measure of effect over the odds ratio (OR) for two reasons: 1) Our outcome variables had prevalence greater than 10%, and therefore with this over dispersion, the OR overestimates the degree of association compared to the RR; 2) when an outcome is rare or less than 10%, both RR and OR estimates are comparable.(9) Since one of the outcomes was large and another was small, the RR provides an unbiased measure of effect and ensures harmonized reporting. Each RR was reported with the corresponding 95% confidence interval (CI), for both the unadjusted and adjusted results. We performed data analysis in R programing language and statistical software version 3.5.2(10) at the 5% level of significance.

Human subjects' issues and ethics approval

The study was reviewed and approved by Mbarara University of Science and Technology Research Ethics Committee (Reference number 03/11-18), and the Uganda National Council for Science and Technology (Reference number HS 2531).

The need for patient consent was waived by the ethics committee because data collection involved retrieval of records from large numbers of persons with BC-PTB, for whom it would have been logistically impractical to reach and seek individual consent. Data were handled confidentially and personal identifiers were not abstracted.

Results

Characteristics of participants with successful treatment outcome

We retrieved 1,123 records, present and compare the characteristics of participants with and without successful treatment of tuberculosis and the results are shown in Table 1. Participants who were successfully treated were on average younger than those who were not successfully treated: 37.89 (SD = 15.15) years versus 41.20 (SD = 15.70), p = 0.008. Most of the successfully treated participants were males (510 (63.7%)), aged 15 to 34 years (387 (48.4%)), and new tuberculosis cases (708 (88.5%)). Participant characteristics namely sex, age, and HIV status differed between those successful treated and those unsuccessfully treated.

Table 1

Baseline characteristics of successfully and unsuccessfully treated participants

		Tuberculosis treatment outcome		
Characteristics	Level	Unsuccessful (No. (%))	Successful (No. (%))	P-value
All participants		187 (18.9)	800 (81.1)	
District	Soroti	104 (55.6)	359 (44.9)	< 0.001
	Kumi	49 (26.2)	179 (22.4)	
	Ngora	26 (13.9)	115 (14.4)	
	Serere	8 (4.3)	147 (18.4)	
Level of health facility	Health Center IV	67 (35.8)	341 (42.6)	0.221
	General Hospital	40 (21.4)	161 (20.1)	
	Referral Hospital	80 (42.8)	298 (37.2)	
Location of health facility	Rural	45 (24.1)	230 (28.7)	0.232
	Urban	142 (75.9)	570 (71.2)	
Type of health facility ownership	Public	173 (92.5)	707 (88.4)	0.132
	Private not-for-profit	14 (7.5)	93 (11.6)	
Year of tuberculosis treatment	2015	69 (36.9)	298 (37.2)	0.322
	2016	45 (24.1)	172 (21.5)	
	2017	47 (25.1)	176 (22.0)	
	2018	26 (13.9)	154 (19.2)	
Sex	Female	46 (24.6)	290 (36.2)	0.003
	Male	141 (75.4)	510 (63.7)	
Age category	15–34	73 (39.0)	387 (48.4)	0.037
	35–50	66 (35.3)	262 (32.8)	
	More than 50	48 (25.7)	151 (18.9)	
Age (mean (SD))		41.20 (15.70)	37.89 (15.15)	0.008
Type of patient	New	154 (82.4)	708 (88.5)	0.031

Note: 1) 2RHZE/4RH: 2 months of Rifampicin (R), Isoniazid (H), Pyrazinamide (Z),Ethambutol / 4 months of RH; 2) 2RHZE/6EH: 2 months of RHZE)/ 6 months of EH; 3) 2RHZES/IRHZE/5RHE: 2 months of RHZE, Streptomycin/One month of RHZE/ 5 months of RHE

		Tuberculosis treatment outcome		
	Previously treated	33 (17.6)	92 (11.5)	
Pre-therapy bacilli	1+	25 (13.4)	117 (14.6)	0.634
	2+	43 (23.0)	215 (26.9)	
	3+	64 (34.2)	251 (31.4)	
	Diagnosis by GeneXpert	55 (29.4)	217 (27.1)	
Anti-tuberculosis regimen	2RHZE/4RH	105 (56.1)	496 (62.0)	0.172
	2RHZE/6HE	63 (33.7)	250 (31.2)	
	2RHZES/1RHZE/5RHE	19 (10.2)	54 (6.8)	
HIV status	Negative	113 (60.4)	591 (73.9)	< 0.001
	Positive	74 (39.6)	209 (26.1)	
Type of Directly Observed Therapy Short Course	Health facility	12 (6.4)	33 (4.1)	0.247
	Community	175 (93.6)	767 (95.9)	
Treatment supporter availability	No	24 (12.8)	98 (12.2)	0.924
	Yes	163 (87.2)	702 (87.8)	
Lives in same sub-county where health facility is located	Yes	60 (39.5)	312 (45.4)	0.214
	No	92 (60.5)	375 (54.6)	

Note: 1) 2RHZE/4RH: 2 months of Rifampicin (R), Isoniazid (H), Pyrazinamide (Z),Ethambutol / 4 months of RH; 2) 2RHZE/6EH: 2 months of RHZE)/ 6 months of EH; 3) 2RHZES/IRHZE/5RHE: 2 months of RHZE, Streptomycin/One month of RHZE/ 5 months of RHE

Table 2

Study profile and tuberculosis treatment outcomes by district in eastern Uganda

Characteristics	Soroti n = 541	Kumi n = 279	Ngora n = 148	Serere n = 155	Total n = 1,123
Treatment outcomes (n = 1,123)	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)
Cured	247 (45.7)	122 (43.7)	31 (20.9)	77 (49.7)	477 (42.5)
Completed treatment	112 (20.7)	57 (20.4)	84 (56.8)	70 (45.2)	323 (28.8)
Failed treatment	10 (1.8)	6 (2.2)	0 (0.0)	1 (0.6)	17 (1.5)
Died	45 (8.3)	15 (5.4)	16 (10.8)	5 (3.2)	81 (7.2)
Lost to follow-up	49 (9.1)	28 (10.0)	10 (6.8)	2 (1.3)	89 (7.9)
Treatment outcome missing	78 (14.4)	51 (18.3)	7 (4.7)	0 (0.0)	136 (12.1)
Tuberculosis treatment outcome available n = 987	Soroti n = 463	Kumi n = 228	Ngora n = 141	Serere n = 155	Total n = 987
Unsuccessful	104 (22.5)	49 (21.5)	26 (18.4)	8 (5.2)	187 (18.9)
Successful	359 (77.5)	179 (78.5)	115 (81.6)	147 (94.8)	800 (81.1)
Total	463	228	141	155	987

Note: In computation of mortality and treatment success, participants with missing treatment outcome (n = 136) were excluded.

The treatment outcomes for the 1,123 records were as follows: 477 (42.5%) cured, 323 (28.8%) completed treatment with no cure, 17 (1.5%) failed treatment, 81 (7.2%) died, 89 (7.9%) lost to follow-up, and 136 (12.1%) had no treatment outcome data in the records. Table 1 shows the results of the treatment outcome stratified by district of assessment. After excluding participants with missing treatment outcome, revised analysis showed 800 (81.1%) were successfully treated.

Factors associated with successful treatment of tuberculosis

Table 3 is a summary of results at unadjusted and adjusted analyses. In unadjusted analysis, participants from Serere district had increased chances of successful treatment of tuberculosis compared to those from Soroti district (RR, 1.22; 95% CI, 1.15–1.30). However, successful treatment of tuberculosis was lower among males compared to females (RR, 0.91; 95% CI, 0.86–0.96), more than 50 years of age than 15 to 34 years of age (RR, 0.88; 95% CI, 0.81–0.97), retreatment persons with BC-PTB compared to new ones (RR, 0.90; 95% CI, 0.80-1.00), and HIV infected than HIV non-infected (RR, 0.88; 95% CI, 0.81–0.95).

Table 3

Factors associated with successful tuberculosis treatment at unadjusted and adjusted analysis

		Tuberculosis treatment outcome		Modified Poisson regression analysis			
Characteristics	Level	Unsuccessful (No. (%))	Successful (No. (%))	Unadjusted analysis		Adjusted analysis	
Participants		187 (18.9)	800 (81.1)	RR	95% CI	aRR	95% CI
District	Soroti	104 (55.6)	359 (44.9)	Ref		Ref	
	Kumi	49 (26.2)	179 (22.4)	1.01	(0.93,1.10)	1.02	(0.94,1.11)
	Ngora	26 (13.9)	115 (14.4)	1.05	(0.96,1.15)	1.04	(0.95,1.14)
	Serere	8 (4.3)	147 (18.4)	1.22***	(1.15,1.30)	1.22***	(1.14,1.30)
Sex	Female	46 (24.6)	290 (36.2)	1		1	
	Male	141 (75.4)	510 (63.7)	0.91**	(0.86,0.96)	0.92**	(0.87,0.98)
Age group	15–34	73 (39.0)	387 (48.4)	1		1	
	35–50	66 (35.3)	262 (32.8)	0.98	(0.92,1.05)	0.97	(0.91,1.04)
	More than 50	48 (25.7)	151 (18.9)	0.88**	(0.81,0.97)	0.89**	(0.81,0.97)
Type of persons with tuberculosis	New	154 (82.4)	708 (88.5)	1		1	
	Retreatment	33 (17.6)	92 (11.5)	0.90*	(0.80,1.00)	0.94	(0.84,1.05)
HIV status	Negative	111 (60.0)	583 (73.6)	1		1	
	Positive	74 (40.0)	209 (26.4)	0.88**	(0.81,0.95)	0.88**	(0.82,0.95)

Note: 95% confidence intervals for risk ratio (RR) in brackets; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; RR: Unadjusted risk ratio; aRR: Adjusted risk ratio

When we adjusted for all statistically significant factors, successful treatment of tuberculosis was independently associated with being male (aRR, 0.92; 95% CI, 0.87–0.98), older than 50 years of age (aRR, 0.89; 95% CI, 0.81–0.97), being HIV infected (aRR, 0.88; 95% CI, 0.82–0.95) and a resident from Serere compared to Soroti district (aRR, 1.22; 1.14–1.30),

Baseline characteristics of persons with BC-PTB by survival status

Table 4 shows the distribution of participant characteristics stratified by survival, namely alive or died. Of 987 participants whose treatment outcomes were evaluated, 81 (8.2%) died. Most of the deaths were at referral hospital level (40/81 or 49.4%) and in 2015 (35/81 or 43.2%). Participants who died were on average older than

those who were alive: 44.80 ± 16.82 versus 37.95 ± 15.05 years, $p < 0.001$. There was a statistically significant difference in mortality based on the district where treatment was received, level of health facility, year of tuberculosis treatment, participants' age, participant HIV sero-status, and form of DOTs.

Table 4
Baseline characteristics of alive and dead participants

Characteristics	Level	Patient alive n = 906 (91.8%)	Patient died n = 81 (8.2%)	P-value
District	Soroti	418 (46.1)	45 (55.6)	0.027
	Kumi	213 (23.5)	15 (18.5)	
	Ngora	125 (13.8)	16 (19.8)	
	Serere	150 (16.6)	5 (6.2)	
Level of health facility	Health Center IV	386 (42.6)	22 (27.2)	0.023
	District Hospital	182 (20.1)	19 (23.5)	
	Referral Hospital	338 (37.3)	40 (49.4)	
Location of health facility	Rural	252 (27.8)	23 (28.4)	1.000
	Peri-urban	654 (72.2)	58 (71.6)	
Type of health facility ownership	Public	808 (89.2)	72 (88.9)	1.000
	Private not for profit	98 (10.8)	9 (11.1)	
Year of tuberculosis treatment	2015	332 (36.6)	35 (43.2)	0.022
	2016	192 (21.2)	25 (30.9)	
	2017	209 (23.1)	14 (17.3)	
	2018	173 (19.1)	7 (8.6)	
Age category (years)	15–34	436 (48.1)	24 (29.6)	0.002
	35–50	297 (32.8)	31 (38.3)	
	> 50	173 (19.1)	26 (32.1)	
	Mean (SD)	37.95 (15.05)	44.80 (16.82)	< 0.001
Sex	Male	593 (65.5)	58 (71.6)	0.319
	Female	313 (34.5)	23 (28.4)	
Type of tuberculosis patient	New	792 (87.4)	70 (86.4)	0.933
	Previously treated	114 (12.6)	11 (13.6)	
Transfer in	No	830 (91.6)	73 (90.1)	0.801

Note: 1) 2RHZE/4RH: 2 months of Rifampicin (R), Isoniazid (H), Pyrazinamide (Z),Ethambutol / 4 months of RH; 2) 2RHZE/6EH: 2 months of RHZE)/ 6 months of EH; 3) 2RHZES/IRHZE/5RHE: 2 months of RHZE, Streptomycin/One month of RHZE/ 5 months of RHE

Characteristics	Level	Patient alive n = 906 (91.8%)	Patient died n = 81 (8.2%)	P-value
	Yes	76 (8.4)	8 (9.9)	
Pre-therapy bacilli load	1+	130 (14.3)	12 (14.8)	0.948
	2+	238 (26.3)	20 (24.7)	
	3+	287 (31.7)	28 (34.6)	
	GeneXpert	251 (27.7)	21 (25.9)	
Anti-tuberculosis regimen	2RHZE/4RH	560 (61.8)	41 (50.6)	0.136
	2RHZE/6HE	280 (30.9)	33 (40.7)	
	2RHZES/1RHZE/5RHE	66 (7.3)	7 (8.6)	
HIV status	Negative	673 (74.3)	31 (38.3)	< 0.001
	Positive	233 (27.7)	50 (61.7)	
Type of Directly Observed Therapy Short Course	Health facility	36 (4.0)	9 (11.1)	0.008
	Community	870 (96.0)	72 (88.9)	
Treatment support availability	No	111 (12.3)	11 (13.6)	0.864
	Yes	795 (87.7)	70 (86.4)	

Note: 1) 2RHZE/4RH: 2 months of Rifampicin (R), Isoniazid (H), Pyrazinamide (Z),Ethambutol / 4 months of RH; 2) 2RHZE/6EH: 2 months of RHZE)/ 6 months of EH; 3) 2RHZES/IRHZE/5RHE: 2 months of RHZE, Streptomycin/One month of RHZE/ 5 months of RHE

Factors associated with mortality among persons with BC-PTB

Table 5 presents results for factors associated with mortality. In unadjusted analysis, mortality was lower among participants who received treatment under community-based DOTS than facility-based DOTS (RR, 0.38; 95% CI, 0.20–0.71). However, mortality was more likely to occur when treatment of tuberculosis was given at a Referral Hospital compared to a Health Center IV level (RR, 1.96; 95% CI, 1.19–3.24), persons with BC-PTB older than 50 years of age compared to 15 to 34 years (RR, 2.50; 95% CI, 1.47–4.25), and HIV infected compared to HIV non-infected (RR, 4.01; 95% CI, 2.62–6.15).

Table 5

Factors associated with mortality among persons with BC-PTB in rural eastern Uganda

Characteristics	Level	Patient alive n = 906 (91.8%)	Patient died n = 81 (8.2%)	Modified Poisson regression analysis			
				Unadjusted analysis (RR, 95% CI)		Adjusted analysis (RR, 95% CI)	
District	Soroti	418 (46.1)	45 (55.6)	Ref		Ref	
	Kumi	213 (23.5)	15 (18.5)	0.68	(0.39,1.19)	0.74	(0.25,2.18)
	Ngora	125 (13.8)	16 (19.8)	1.17	(0.68,2.00)	1.74	(0.63,4.82)
	Serere	150 (16.6)	5 (6.2)	0.33*	(0.13,0.82)	0.57	(0.18,1.88)
Level of health facility	Health Center IV	386 (42.6)	22 (27.2)	Ref		Ref	
	District Hospital	182 (20.1)	19 (23.5)	1.75	(0.97,3.16)	1.38	(0.69,2.75)
	Referral Hospital	338 (37.3)	40 (49.4)	1.96**	(1.19,3.24)	1.99	(0.81,4.89)
Year of tuberculosis treatment	2015			Ref		Ref	
	One year increase			0.78**	(0.64,0.93)	0.80*	(0.66,0.97)
Age group	15–34	436 (48.1)	24 (29.6)	Ref		Ref	
	35–50	297 (32.8)	31 (38.3)	1.81*	(1.08,3.03)	1.56	(0.96,2.55)
	> 50	173 (19.1)	26 (32.1)	2.50***	(1.47,4.25)	2.93***	(1.74,4.92)
HIV status	Negative	673 (74.3)	31 (38.3)	Ref		Ref	
	Positive	233 (27.7)	50 (61.7)	4.01***	(2.62,6.15)	4.48***	(2.95,6.79)
Type of Directly Observed Therapy Short Course	Facility	36 (4.0)	9 (11.1)	Ref		Ref	

Note: 95% confidence intervals for risk ratio (RR) in brackets; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; RR: Unadjusted risk ratio; aRR: Adjusted risk ratio.

Characteristics	Level	Patient alive n = 906 (91.8%)	Patient died n = 81 (8.2%)	Modified Poisson regression analysis			
	Community	870 (96.0)	72 (88.9)	0.38**	(0.20,0.71)	0.26***	(0.13,0.50)

Note: 95% confidence intervals for risk ratio (RR) in brackets; * p < 0.05, ** p < 0.01, *** p < 0.001; RR: Unadjusted risk ratio; aRR: Adjusted risk ratio.

In the adjusted analysis, mortality was lower when tuberculosis treatment was initiated in the years after 2015, with a 20% reduction for every one year lapse from 2015 up to 2018 when the last data were retrieved (aRR, 0.80; 95% CI, 0.66–0.97). Delivery of tuberculosis treatment under community DOTS was protective of mortality (aRR, 0.26; 95% CI, 0.13–0.50). But mortality was higher among persons with BC-PTB aged 50 years and older (aRR, 2.93; 95% CI, 1.74–4.92) and those who were HIV infected (aRR, 4.48; 95% CI, 2.95–6.79).

Discussion

Our data from rural eastern Uganda show that treatment success rate for tuberculosis is suboptimal and mortality rate is high. Our data also show that HIV infection and older age are associated with poor treatment outcomes including mortality but patients who had CB-DOTS were less likely to die. The treatment success rate reported here is no different from that recently reported in a meta-analysis of tuberculosis treatment success for sub Saharan Africa, which was 76.2%.(6) Since the treatment success rate in eastern Uganda falls below the desired target of at least 90%, site-specific measures are needed to address barriers to achieving high rates of treatment success.

Mortality was high in this cohort of adult persons with BC-PTB. We were not able to ascertain the exact date of death from the records, therefore it is not clear whether mortality occurred early or later during treatment. The mortality rate is comparable to that observed in other cohorts of persons with tuberculosis in sub Saharan Africa such as examples from Ethiopia.(11) However, some cohorts from sub Saharan Africa have reported significantly lower mortality rates of less than 5%.(12, 13) It is clear there is a wide variation in mortality rates in the treatment cohorts in sub Saharan Africa. These differences may be explainable by prevalence of HIV in the different countries across the continent, especially given the relationship between HIV and mortality in that we found in our cohort.

Our study shows HIV infected persons with BC-PTB have reduced chances of achieving successful treatment and increased risk of mortality. These findings are not unique because the relationship between HIV and tuberculosis is well-established.(14) HIV is a known strong risk factor for tuberculosis disease, alters the clinical presentation, progression, and prognosis of tuberculosis as well as response to its treatment.(15) In addition, tuberculosis disease is the commonest opportunist infection among people living with HIV, and the leading cause of mortality.(7) Dual treatment of tuberculosis and HIV is associated with increased pill burden and this may lead to medication fatigue potentially leading to non-adherence.(16, 17) Non-adherence to anti-tuberculosis medications is associated with reduced chances of successful treatment(18) and increased chances of mortality.(19) In general, several pathways could explain the observed relationship. Several studies in sub Saharan Africa(20–25)

indicate that people living with HIV have increased chances of unsuccessful treatment of tuberculosis. Our findings are also in agreement with previous studies in sub Saharan Africa.(26–28)

HIV infected persons with BC-PTB might hence benefit from closer clinical and laboratory monitoring and treatment adherence support so as to improve the rates of treatment success and reduce mortality. At programing level, it appears strengthening the collaboration between tuberculosis and HIV care would improve the management of HIV infected persons with tuberculosis which might enhance successful treatment of tuberculosis and reduced mortality.

We found persons with BC-PTB who were older than 50 years old had reduced chances of achieving treatment success rate and had increased risk of mortality. Studies in several parts of sub Saharan, (20, 22, 23, 25, 27, 29–31) all indicate older or increasing age is associated with reduced chances of successful treatment of tuberculosis. This could be because older persons interrupt treatment adherence more than younger persons, are challenges by several health determinants such as low socio-economic status as well as low immunity that cannot effectively fight infections.(25)

Comparable to our findings, a systematic review with no meta-analysis(32) report persons who are at least 30 years of age do not adhere to anti-tuberculosis medication. The increased risk of mortality among persons with BC-PTB above 40 years of age observed in this study is consistent with earlier studies.(27, 33, 34) This might be due to medical complications that comes along with ageing. Older persons with tuberculosis might therefore benefit from closer monitoring of response to tuberculosis treatment.(35)

Our study indicates males have reduced chances of successful treatment of tuberculosis as compared to females. This finding is consistent with several studies in Africa.(22, 25, 27) In particular, the study in Nigeria,(27) reports gender disparities in treatment outcomes where men were more likely to fail to sputum smear convert at two and five months of treatment, to fail treatment, and to register increased chances of unsuccessful tuberculosis treatment. Another study in Benin also showed that men are more likely to fail treatment,(36) and treatment failure is known to translate to unsuccessful tuberculosis treatment. The observed difference could be attributed to men's poor healthcare seeking behavior compared to women,(37) that translates to late diagnosis of tuberculosis and missing of drug refill days hence treatment non-adherence and ultimately unsuccessful treatment of tuberculosis. Our findings suggests the need to design gender-specific interventions across tuberculosis programs.

The lower mortality rate as the year progresses may be attributable to improvements in healthcare system over time: better staffing and improved healthcare provider competence and confidence to manage persons with BC-PTB through mentorships and coaching, and better counseling among others. Elsewhere,(38) healthcare providers indicted that tuberculosis clinics have been introduced across most health facilities so that more time is accorded to persons with tuberculosis with respect to understanding their challenges and solving them. In addition, continuous quality improvement interventions have been introduced to tackle operational challenges in tuberculosis programing. These initiatives have strengthened the healthcare system.

Our study indicates community-based DOTS is associated with reduced mortality compared to facility-based DOTS. Our results are consistent with those from systematic reviews and meta-analyses where community-based DOTS was shown to improve treatment completion, cure and reduce risk of mortality. (39–42) In the community-based DOTS, persons with tuberculosis take medications under the direct supervision of a treatment supporter at

home or in their community,(43) and this is likely to result into better treatment adherence(44) and completion hence better cure rates and reduced mortality. A meta-analysis reported that community-based DOTS is associated with better treatment outcomes such as lower mortality compared to facility-based DOTS.(45)

Study Strengths And Limitations

Our study has several strengths. First, we had a large sample size that provided adequate statistical power to detect differences, and data spanned a period of three years, which was sufficient to demonstrate a possible trend in tuberculosis treatment outcomes. However, there are some limitations that should be considered. This study was performed in a rural setting hence the findings may not apply to an urban setting due to variations in socio-economic and structural challenges associated with rural dwelling such as longer distances to health facilities. Second, our results do not apply to persons with tuberculosis who are below 15 years of age as well as forms of tuberculosis other than BC-PTB.

Conclusions And Recommendations

In conclusion, we have shown that adult persons with BC-PTB in rural eastern Uganda have suboptimal treatment success rate and high mortality rate. Tuberculosis and HIV co-infection and older age were associated with reduced chances of treatment success and increased risk of mortality.

Integration of tuberculosis and HIV prevention should be enhanced; particularly early screening and prophylaxis for tuberculosis among HIV infected persons, especially those who are older as they have poorer prognosis with TB disease. Community-based DOTs should be implemented widely and more research should be done to examine successful ways for implementation of Community-based DOTS especially in rural areas such as those where our study was conducted.

List Of Abbreviations

aRR: Adjusted Risk Ratio

BC-PTB: Bacteriologically Confirmed Pulmonary Tuberculosis

DOTS: Directly Observed Therapy Short Course

HIV: Human Immunodeficiency Virus

uRR: Unadjusted Risk Ratio

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

This study was approved by Mbarara University of Science and Technology Research Ethics Committee Reference number 03/11-18) and the Uganda National Council for Science and Technology (Reference number HS 2531). The need for patient consent was waived by the ethics committee because data collection involved retrieval of

records from large numbers of persons with tuberculosis, for whom it would have been logistically impractical to reach and seek individual consent.

Consent to publish

Not applicable

Availability of data and materials

The dataset used/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author contributions

JI, IKT, and FB conceptualized and designed the study.

JI obtained the data.

JI, IKT and FB analyzed the data and interpreted the results.

JI, IKT, and FB drafted the manuscript.

IKT and FB performed critical revisions of the manuscript.

JI, IKT, and FB all approved the final manuscript.

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