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Diagnosis and treatment outcomes of adult tuberculosis in an urban setting with high HIV prevalence in Sierra Leone: A retrospective study

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ABSTRACT

Objective: To assess the diagnosis, treatment outcomes, and predictors of mortality in adult tuberculosis (TB) patients in an urban setting with a high HIV prevalence.
Methods: A retrospective study was conducted of adult TB patients aged ≥15 years who were treated at Connaught Hospital in Freetown, Sierra Leone from January through December 2017. Multivariate logistic regression was used to identify predictors of mortality.
Results: Of 1127 TB cases notified in 2017, 1105 (98%) were tested for HIV, yielding a TB/HIV co-infection rate of 32.0%. Only HIV-tested cases (n = 1105) were included in the final analysis. The majority were male (69.3%), aged 25–34 years (29.2%), and had pulmonary TB (96.3%). Treatment outcomes were as follows: 29.0% cured, 29.0% completed, 0.5% treatment failure, 24.2% lost to follow-up, 12.8% transferred/not evaluated, and 4.5% died. The majority of deaths (80.0%, 40/50) occurred within 2 months of TB treatment initiation. Age 65 years or older (adjusted odds ratio 3.48, 95% confidence interval 1.15–10.56; p = 0.027) and HIV-positive status (adjusted odds ratio 3.50, 95% confidence interval 1.72–7.12; p = 0.001) were independent predictors of mortality.
Conclusions: Suboptimal TB treatment outcomes were observed in Sierra Leone in 2017. More local and international action is warranted to help achieve the 2035 global TB elimination targets.

1. Introduction

Tuberculosis (TB) is a leading cause of morbidity and is among the top 10 causes of death globally, ranking above HIV as a single infectious cause of death (World Health Organization, 2018a). Based on recent estimates from 2017, there were 10 million incident TB cases and 1.6 million TB-related deaths worldwide, despite a 2% decline in incidence rates annually in recent years (World Health Organization, 2018a). In an attempt to definitively address this enduring global scourge, the World Health Organization (WHO) launched the End TB Strategy in 2014, with the goal of reducing global TB incidence by 90%, reducing mortality by 95%, and eliminating catastrophic treatment costs by the year 2035 (World Health Organization, 2015). The importance of this global

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initiative was further underscored in 2015 by the high-profile incorporation of accelerated health targets into the United Nations Sustainable Development Goals, which aim to achieve an 80% reduction in global TB incidence and a 90% reduction in deaths by the year 2030 (United Nations, 2015).

Notwithstanding the groundswell of international support for achieving the set health targets, global TB prevention and control efforts are now being threatened by myriad challenges. These include significant gaps in funding, lack of access to diagnostic and treatment services in many resource-limited settings, the emergence and transmission of multidrug-resistant TB (MDR-TB) strains in endemic countries across Sub-Saharan Africa (SSA), Asia, and Eastern Europe (World Health Organization, 2018a; World Health Organization, 2018b), and the unique challenges that are being presented by the intersection of TB with the global HIV pandemic.

Sierra Leone is one of only 30 high TB burden countries that collectively accounted for 87% of all new TB cases globally in 2017 (World Health Organization, 2018a; World Health Organization, 2018b), yet studies are lacking on the TB epidemic in this country. According to 2017 estimates, Sierra Leone registered 16 142 TB cases (incidence rate of 301 per 100 000 of the population) and 3000 TB-related deaths (case fatality ratio of 0.17) (World Health Organization, 2018a; World Health Organization, 2018b). Ninety-eight percent of all TB patients were tested for HIV infection, yielding a TB/HIV co-infection prevalence of 12% (World Health Organization, 2018a; World Health Organization, 2018b). Although there is a well-outlined national policy to provide treatment for all TB patients in Sierra Leone cost-free, only 70% of incident cases received anti-TB treatment in 2017, with a treatment success rate of 89% (World Health Organization, 2018a; World Health Organization, 2018b). Currently, the Global Fund provides 70% of TB control program costs in Sierra Leone, with other local and international agencies providing additional technical and logistical support towards control efforts (The Global Fund, 2019). Thus, significant challenges remain in place (Bah et al., 2017; Ansumana et al., 2017), including overlapping gaps in the local HIV care continuum that need closing if this high TB burden country is to meet the global health targets for 2030 and 2035 (Yendewa et al., 2018a; Yendewa et al., 2018b; Lakoh et al., 2019a; Lakoh et al., 2019b; Oxner et al., 2019).

The characteristics of the TB epidemic in Sierra Leone are poorly understood and have not previously been investigated in detail. In this study, we describe the demographic characteristics, clinical presentation, treatment outcomes, and predictors of TB-related mortality at the largest TB clinic in an urban setting with high HIV prevalence in Sierra Leone (Lakoh et al., 2019b), using secondary data extracted from medical records of patients who started TB treatment at the facility during 2017.

2. Materials and methods

2.1. Study design, population, and setting

A retrospective study was conducted using secondary data extracted from the medical records of patients who were diagnosed with TB and received treatment at the Chest Clinic at Connaught Hospital in Freetown, Sierra Leone from January through December 2017. Connaught Hospital is a 300-bed academic facility that is affiliated with the College of Medicine and Allied Health Sciences of the University of Sierra Leone and is the country's main tertiary referral health center. The Chest Clinic at Connaught Hospital offers outpatient and inpatient TB diagnostic and treatment services, including a directly observed therapy, short-course (DOTS) program. Due to its location within the country's main referral hospital, the Chest Clinic is the largest TB treatment center in Sierra Leone.

2.2. Clinical data collection and definitions

Study inclusion criteria were age $\geq$15 years, documented TB and HIV status, and documented treatment outcome. Patients without documented HIV status were excluded from the analysis.

Mode of referral was assigned to cases on the basis of how the patient initially presented to the Chest Clinic at Connaught Hospital. Self-reporting cases referred to patients presenting directly to the TB clinic on their own, reporting the classic symptoms of cough, night sweats, weight loss, or generally not feeling well. Community member-initiated cases referred to patients presenting directly to the TB clinic urged by their family members or peers in the community who suspected they had TB on the basis of their symptoms. Private health facility or public health facility referrals consisted of cases that were secondarily referred to the TB clinic for further evaluation of suspected TB after initially presenting to outside privately run clinics or public health facilities, respectively.

TB disease was defined as fulfilment of any one of the following criteria: (1) bacteriologically or microscopically confirmed pulmonary TB (PTB), i.e., positive culture and/or at least one sputum sample with a positive acid-fast bacillus (AFB) test; (2) clinically diagnosed PTB, i.e., AFB-negative sputum in the presence of epidemiological exposure, compatible clinical symptoms, and suggestive chest radiographic findings; or (3) extrapulmonary TB (EPTB), i.e., TB confirmed or suspected to have spread outside the lungs. In keeping with standard practice, patients were treated with an intensive initial phase four-drug regimen consisting of rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA), and ethambutol (EMB) for 2 months, followed by a continuation phase two-

Table 1
Definitions of treatment outcomes for TB patients[a]

Outcome	Definition
Cured	A pulmonary TB 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.
Treatment completed	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.
Treatment failed	A TB patient whose sputum smear or culture is positive at month 5 or later during treatment.
Died	A TB patient who dies for any reason before starting or during the course of treatment.
Lost to follow-up	A TB patient who did not start treatment or whose treatment was interrupted for 2 consecutive months or more.
Not evaluated	A TB patient for whom no treatment outcome is assigned. This includes cases 'transferred out' to another treatment unit as well as cases for whom the treatment outcome is unknown to the reporting unit.
Treatment success	The sum of 'cured' and 'treatment completed'.

TB, tuberculosis.
[a] Reproduced from the World Health Organization, Geneva, Switzerland, 2013 (World Health Organization, 2014a).

drug regimen consisting of INH/RIF intended for the standard duration of at least 6 months.

Treatment outcomes were ascertained by reviewing the patient medical records and were assigned in accordance with the standard WHO definitions and reporting framework for tuberculosis document (World Health Organization, 2014a) (Table 1). Treatment success was defined as the sum of all patients who achieved 'cured' or 'completed treatment'. Death was confirmed by reviewing the death certificates or entries in the medical records and death register at Connaught Hospital.

2.3. Statistical analysis

The statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Categorical variables were reported as frequencies and percentages and compared using Pearson's Chi-square test. Continuous variables were recorded as medians and interquartile ranges (IQR) and compared using the non-parametric independent samples Mann–Whitney *U*-test or Kruskal–Wallis test, as appropriate. A logistic regression model was used to identify risk factors and predictors of TB-related mortality in the univariable (unadjusted) and multivariable (adjusted) analyses. All variables were included in the multivariable model regardless of the *p*-value attained in the preliminary univariable analysis, given the relatively limited number of variables being assessed–all of which have been shown to be plausibly associated with TB-related mortality. Lastly, odds ratios (OR) and adjusted odds ratios (AOR) were presented with 95% confidence intervals (CI). In all analyses, statistical significance was set at $p < 0.05$.

2.4. Ethical considerations

Ethical approval for the study was obtained from the Sierra Leone Ethics Scientific and Research Committee. All patient personal information was de-identified before entry into a password-protected spreadsheet accessible only to study personnel.

3. Results

Medical records were available for 1127 patients who were diagnosed with TB at the Chest Clinic at Connaught Hospital in Freetown, Sierra Leone from January through December 2017. Of these, 22 patients did not have documented HIV status, yielding an HIV testing rate of 98% (1105/1127). Given the large study population size, this was assumed to be due to random chance; therefore, the 22 patients without documented HIV status were excluded from the study.

3.1. Baseline demographic and clinical characteristics of the study population

The 1105 TB cases with documented HIV status were included in the final statistical analysis (Table 2). The overall prevalence of TB/HIV co-infection was 32.0% (352/1105). The majority of patients were male (69.3%, 766/1105) and belonged to the 25–34 years age group (29.2%, 323/1105). Most were newly diagnosed (87.8%, 971/1105), except for 9.8% (108/1105) who were re-engaging with treatment after previously being lost to follow-up (LTFU) and a relatively small proportion (2.4%, 26/1105) who were returning after failing previous treatment. Over half of the patients (50.3%, 556/1105) were referred from a public health facility, nearly one-third (31.5%, 348/1105) were referred by community members, 14.6% (161/1105) were self-referrals, and 3.6% (40/1105) were referred from privately run health facilities.

Table 2
Characteristics of study population and treatment outcomes

Characteristics	Frequency	Percentage
Sex		
Male	766	69.3
Female	339	30.7
Age, years		
15–24	237	21.5
25–34	323	29.2
35–44	237	21.4
45–54	157	14.2
55–64	83	7.5
65 and older	68	6.2
Patient type		
New diagnosis	971	87.8
Lost to follow-up	108	9.8
Failed previous treatment	26	2.4
Mode of referral		
Self-reporting	161	14.6
Community member-initiated	348	31.5
Private health facility	40	3.6
Public health facility	556	50.3
Type of TB		
Pulmonary	1064	96.3
Extrapulmonary	41	3.7
Lymph node	12	1.1
Spinal	7	0.6
Pericardial	7	0.6
Abdominal	5	0.5
Pleural	4	0.4
Meningeal	2	0.2
Bone and joints	1	0.1
Other	3	0.3
Smear positivity at diagnosis		
Positive	537	48.6
Negative	478	43.3
Not done	90	8.1
Chest X-ray findings		
Suggestive of PTB	500	45.2
Not suggestive of PTB	463	41.9
Not available	142	12.9
HIV status		
Positive	352	31.9
Negative	753	68.1
Treatment duration, months		
2 or less	368	33.3
3–5	93	8.4
6 or more	644	58.3
Treatment outcome		
Cured	320	29.0
Completed	320	29.0
Failed treatment	5	0.5
Transferred/not evaluated	142	12.9
Lost to follow-up	268	24.3
Died	50	4.5

TB, tuberculosis; PTB, pulmonary tuberculosis.

The vast majority of patients were diagnosed with PTB (96.3%, 1064/1105). Of the remaining 3.7% (41/1105) who were diagnosed with EPTB, lymph node was the most frequent (1.1%, 12/1105), followed by spinal and pericardial TB (0.5%, 7/1105 each). Chest imaging findings were reported as 'suggestive' of PTB in 45.2% (500/1105) and 'not suggestive' of PTB in 41.9% (463/1105) of cases; no imaging was available for 12.9% (142/1105) of patients.

3.2. Microbiological characteristics and treatment duration

Sputum AFB smear by microscopy was obtained at treatment initiation (month 0) and subsequently at months 2, 3, and 5 into treatment (Fig. 1). At month 0, sputum AFB smears were reported for 92.0% (1015/1105) of the patients, with a smear positivity rate of 52.9% (537/1015). At the end of month 2, the smear positivity rate had decreased 5-fold to 11.6% (85/734). This trend was sustained,

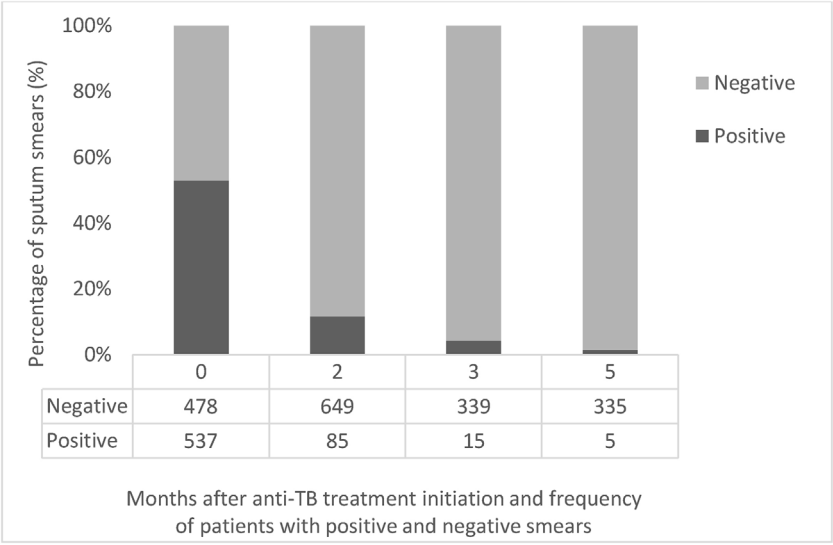

Fig. 1. Microbiological characteristics of treated patients based on sputum smear positivity. Number of positive and negative smears by microscopy at months 0, 2, 3, and 5 after treatment initiation.

with smear positivity rates of 4.2% (15/354) at the end of month 3 and 1.5% (5/340) at the end of month 5.

The durations of treatment are presented in Table 2. The majority (58.3%, 644/1105) completed the standard treatment duration of 6 months or more (for patients who had positive smears at 5 months into treatment). In contrast, one-third (33.4%, 369/1105) of patients received treatment for 2 months or less, i.e., did not complete the intensive four-drug initial phase of treatment, while 8.4% (93/1105) completed between 3 and 5 months of treatment.

3.3. Treatment outcomes

Table 3 presents the treatment outcomes for all patients based on demographic and clinical parameters. Based on the standard WHO definitions for reporting TB treatment outcomes (World Health Organization, 2014a), 29.0% (320/1105) achieved cure, while a similar proportion (29.0%, 320/1105) completed the treatment course, yielding a treatment success rate of 58.0% (640/1105). The rates of treatment failure, LTFU, and transferred/not evaluated were 0.5% (5/1105), 24.2% (268/1105), and 12.8%

Table 3
Treatment outcomes based on demographic and clinical variables

Characteristics	Cured (n = 320)	Completed treatment (n = 320)	Failed treatment (n = 5)	Lost to follow-up (n = 268)	Not evaluated/transferred (n = 142)	Died (n = 50)	p-Value
Sex							
Male	245 (32.0)	208 (27.2)	4 (0.5)	165 (21.5)	110 (14.4)	34 (4.4)	<0.001
Female	75 (22.1)	112 (33.0)	1 (0.3)	103 (30.4)	32 (9.4)	16 (4.7)	
Age, years							
15–24	71 (30.0)	77 (32.5)	2 (0.8)	61 (25.7)	18 (7.6)	8 (3.4)	<0.001
25–34	114 (35.3)	78 (24.1)	1 (0.3)	78 (24.1)	39 (12.1)	13 (4.0)	
35–44	65 (27.4)	63 (26.6)	2 (0.8)	53 (22.4)	39 (16.5)	15 (6.3)	
45–54	48 (30.6)	37 (23.6)	-	36 (22.9)	32 (20.4)	4 (2.5)	
55–64	16 (19.3)	35 (42.2)	-	20 (24.1)	9 (10.8)	3 (3.6)	
65 or above	6 (8.8)	30 (44.1)	-	20 (29.4)	5 (7.4)	7 (10.3)	
Mode of referral							
Self-reporting	62 (38.5)	46 (28.6)	1 (0.6)	30 (18.6)	17 (10.60	5 (3.1)	<0.001
Community member-initiated	154 (44.3)	96 (27.6)	2 (0.6)	55 (15.8)	29 (8.3)	12 (3.4)	
Private health facility	8 (20.0)	16 (40.0)	-	5 (12.5)	6 (15.0)	5 (12.5)	
Public health facility	96 (17.3)	162 (29.1)	2 (0.4)	178 (32.0)	90 (16.2)	28 (5.0)	
Patient type							
New diagnosis	272 (28.0)	287 (29.6)	-	234 (24.1)	131 (13.5)	47 (4.8)	<0.001
Lost to follow-up	33 (30.6)	32 (29.6)	2 (1.9)	29 (26.9)	9 (8.3)	3 (2.8)	
Failed previous treatment	15 (57.7)	1 (3.8)	3 (11.5)	5 (19.2)	2 (7.7)	-	
Type of TB							
Pulmonary	320 (30.1)	305 (28.7)	5 (0.5)	251 (23.6)	135 (12.7)	48 (4.5)	0.009
Extrapulmonary	-	15 (36.6)	-	17 (41.5)	7 (17.0)	2 (4.9)	
Smear positivity at diagnosis							
Positive	311 (57.9)	31 (5.8)	5 (0.9)	113 (21.0)	58 (10.8)	19 (3.5)	<0.001
Negative	9 (1.9)	273 (57.1)	-	103 (21.5)	70 (14.6)	23 (4.8)	
Not done	-	16 (17.8)	-	52 (57.8)	14 (15.6)	8 (8.9)	
HIV status							
Positive	60 (17.0)	96 (27.3)	-	29 (8.2)	107 (30.4)	60 (17.0)	<0.001
Negative	260 (34.5)	224 (29.7)	5 (0.7)	21 (2.8)	161 (21.4)	82 (10.9)	

TB, tuberculosis.

(142/1105), respectively. Fifty deaths were notified, yielding a mortality rate of 4.5% (50/1105). The majority of deaths (80%, 40/50) were recorded within 2 months of initiation of anti-TB treatment.

3.4. Predictors of TB mortality

Risk factors of TB mortality were assessed by comparing patients who died with those who were successfully treated (Table 4). In the univariate analysis, age 65 years or above (OR 2.73, 95% CI 1.15–6.45; $p = 0.018$) and HIV-positive status (OR 4.32, 95% CI 2.40–7.80; $p < 0.001$) were significantly associated with death. After controlling for covariates in the multivariate logistic regression model, age 65 years or older (AOR 3.48, 95% CI 1.15–10.56; $p = 0.027$) and HIV-positive status (AOR 3.50, 95% CI 1.72–7.12; $p = 0.001$) were identified as independent predictors of mortality.

4. Discussion

This study assessed a cohort of 1127 patients who were diagnosed with TB and received treatment at the largest TB treatment center in Sierra Leone during 2017. Of these 1127 patients, 98% with a documented HIV status were included in a detailed statistical analysis. The proportion of HIV-tested patients at this treatment center surpassed the reported average of 86% in the African region in 2017 and was equaled or bettered only by Zimbabwe (100%), Tanzania (98%), and Namibia (98%) among the 30 high TB burden countries (World Health Organization, 2018a; World Health Organization, 2018b). This finding is encouraging and may be a reflection of the increasing emphasis on integrating TB and HIV services in SSA countries, as recommended by the WHO through its policy on collaborative TB/HIV activities (World Health Organization, 2012).

HIV infection is a well-established risk factor for activation of latent TB infection, as it is known to increase the odds of progression to full-blown TB disease 9- to 27-fold (Guelar et al., 1993; Antonucci et al., 1995; World health Organization, 2018ca). A substantial proportion of patients at this health center were TB/HIV co-infected, i.e., 32%, which is 2.7-fold higher than the country average of 12% reported in 2017 (World Health Organization, 2018a). Several studies from SSA have reported the prevalence of TB/HIV co-infection as increasing. A recent systematic review and meta-analysis from SSA reported a pooled HIV prevalence of 31.8% among TB patients, with the highest co-infection prevalence rates found in the high HIV burden East and Southern African countries (Gelaw et al., 2019). Within our West African sub-region, studies from Togo, Ghana, and Nigeria have noted widely varying TB/HIV co-infection prevalence rates, ranging from 18.2% to 72% (Dagnra et al., 2011; Chinedu et al., 2017; Osei et al., 2017; Gomerep et al., 2015). Locally in Sierra Leone, we have previously documented a relatively high burden of HIV infection among voluntary testers (Lakoh et al., 2019b), as well as a high prevalence of late stage HIV presentation at this referral hospital (Yendewa et al., 2018b), which may partly explain the high TB incidence in this particular urban setting. Taken all together, these studies appear to signify similar weaknesses in TB/HIV surveillance and control policies in SSA, thus warranting more coordinated and sustained regional action by member countries, as directed by the WHO TB/HIV Working Group of the Global Partnership to stop TB (World Health Organization, 2014b).

The diagnosis of TB is definitively established by the isolation of *Mycobacterium tuberculosis* in culture from respiratory secretions or a tissue biopsy specimen (Pai et al., 2016). In routine clinical practice, however, TB diagnosis is established based on a combination of epidemiological, clinical, radiological, microbiological, and histopathological approaches (Sia and Wieland, 2011). In the majority of cases in this study, microscopy was used to confirm the diagnosis. We observed a smear positivity rate of 52.9% from the 92.0% (1015/1105) of patient sputum samples that initially underwent microscopy, which achieved parity with the global smear positivity rate of 56% among confirmed TB cases in 2017 (World Health Organization, 2018a). The remaining PTB cases were diagnosed radiographically, while EPTB case diagnoses were based exclusively on clinical suspicion, due to the lack of histopathological diagnostic facilities at this treatment center. Although useful in the initial triaging of suspected PTB cases, over-reliance on chest radiography as a diagnostic tool is a concern. Chest radiography has low specificity and sensitivity, due in part to the unavoidable inter-observer variabilities that occur in interpreting imaging findings,

Table 4
Univariate and multivariate analysis of associated risk factors of tuberculosis mortality

Characteristics	Treatment outcome		Univariable analysis		Multivariable analysis	
	Died ($n = 50$)	Successfully treated ($n = 640$)	Unadjusted odds ratio (95% CI)	p-Value	Adjusted odds ratio (95% CI)	p-Value
Sex						
Male	34 (7.0)	453 (93.0)	Ref.		Ref.	
Female	16 (7.9)	187 (92.1)	1.14 (0.61–2.12)	0.678	1.74 (0.76–3.99)	0.189
Age, years						
15–64	43 (6.6)	604 (93.4)	Ref.		Ref.	
65 or above	7 (16.3)	36 (83.7)	2.73 (1.15–6.45)	0.018	3.48 (1.15–10.56)	0.027
Patient type						
New diagnosis	46 (7.6)	560 (92.4)	1.64 (0.58–4.69)	0.353	2.20 (0.50–9.65)	0.297
Other	4 (4.8)	80 (95.2)	Ref.		Ref.	
Type of TB						
Pulmonary	48 (7.1)	628 (92.9)	0.46 (0.10–2.11)	0.317	0.24 (0.03–2.30)	0.218
Extrapulmonary	2 (14.3)	12 (85.7)	Ref.		Ref.	
Smear positivity at diagnosis						
Negative	23 (7.5)	283 (92.5)	1.47 (0.78–2.75)	0.229	1.05 (0.49–2.25)	0.893
Positive	19 (5.20)	343 (94.8)	Ref.		Ref.	
Chest X-ray findings						
Suggestive of PTB	24 (8.1)	273 (91.9)	1.30 (0.69–2.42)	0.415	1.14 (0.56–2.31)	0.722
Not suggestive of PTB	19 (6.4)	280 (93.6)	Ref.		Ref.	
HIV status						
Positive	29 (15.8)	155 (84.5)	4.32 (2.40–7.80)	<0.001	3.50 (1.72–7.12)	0.001
Negative	21 (4.2)	485 (95.8)	Ref.		Ref.	

CI, confidence interval; TB, tuberculosis; PTB, pulmonary tuberculosis.

especially in HIV-infected patients who tend to have atypical presentations (Perlman et al., 1997; Yang et al., 2004; World Health Organization, 2016).

To partially address unmet diagnostic needs in resource-limited settings, new point-of-care molecular detection modalities with higher sensitivity and specificity that have gained WHO approval are increasingly being deployed in TB care (e.g., Xpert MTB/RIF and lateral flow assay urine lipoarabinomannan tests) (World Health Organization, 2014c; World Health Organization, 2019). The major drawbacks of these new technologies are that they remain cost-prohibitive and are not widely accessible in most places. Of note, the Global Fund started implementing Xpert MTB/RIF technology in Sierra Leone in 2017 for use in patients meeting any one of the following criteria: (1) initial AFB-negative smear, (2) previously treated TB, (3) HIV-positive status, or (4) contact with a patient with known RIF-resistant TB (The Global Fund, 2018; Hamilton et al., 2019). Two recent studies from district-level public health facilities in Sierra Leone have demonstrated its feasibility and applicability in TB and/or HIV care (Oxner et al., 2019; Hamilton et al., 2019). However, Xpert MTB/RIF was not used to establish the TB diagnosis in the patients in this study.

One of the major challenges of TB service delivery in Sierra Leone is that it relies heavily on public health facility-based intensified case-finding approaches, despite the WHO recommendations for increasing community-based TB intervention activities (World Health Organization, 2006) and for more multi-sectoral engagement in TB control efforts (World Health Organization, 2018cb). In this study, public health facility referrals accounted for more than half of all diagnosed cases (50.3%), compared with community-based referrals at 31.5% and private health facility-based referrals at 3.6%. Community-based TB screening activities have been found to be beneficial in some studies from SSA, especially in high HIV prevalence settings (Ssemmondo et al., 2016; Shapiro et al., 2018). In a Cochrane review, community-based TB screening using a house-to-house visit strategy was shown to increase TB case detection and lower the risk of attrition from treatment (Mhimbira et al., 2017). Using a probabilistic sensitivity analysis in South Africa, community-based active TB case finding was predicted to be cost-effective and led to increased TB case detection in rural settings (Gilbert et al., 2016). Thus, scaling up of community-based TB diagnosis, prevention, and treatment activities, as well as encouraging more private–public sector cooperation may benefit TB control efforts in Sierra Leone.

Suboptimal treatment outcomes were observed at this treatment facility, with a treatment success rate of 58% (cured and completed combined), which was well below the reported national average of 89% in 2017 (World Health Organization, 2018a). Additionally, there was a high treatment attrition rate (i.e., 33% of patients were LTFU or transferred) and substantial mortality (4.5%) in this cohort of patients. HIV-positive status increased the odds of death 3.50-fold (95% CI 1.72–7.12; $p = 0.001$), whereas it was 3.48-fold higher (95% CI 1.15–10.56; $p = 0.027$) among patients who were aged 65 years or older. These findings were not unexpected. Worldwide, TB is the most common initial presentation of HIV infection and remains the commonest cause of death among HIV-infected individuals (World health Organization, 2018ca); however, due to incomplete data, a detailed statistical analysis of the TB/HIV co-infected subgroup was not conducted in this cohort. More generally, however, studies have shown that specific patient factors leading to adverse TB treatment outcomes and/or mortality include male sex (Romanowski et al., 2019), homelessness (Agarwal et al., 2019; Ranzani et al., 2016), low socio-economic status (Pizzol et al., 2018; Christian et al., 2019), smoking (Gajalakshmi et al., 2003; Amere et al., 2018), diabetes mellitus (Degner et al., 2018; van Crevel et al., 2018), and acquired drug resistance to INH and/or RIF (Ershova et al., 2014; Lew et al., 2008). In one study from Sierra Leone, Sesay (2017) highlighted the location of TB treatment facility as significantly impacting treatment outcomes in Sierra Leone (Sesay, 2017). More rigorous studies are therefore needed to better understand the specific patient factors and socio-economic and cultural determinants influencing TB treatment outcomes and mortality in the local Sierra Leone context, to help inform effective, evidence-based TB prevention and control policies.

This study has several limitations. It was a single site urban study at a national referral health center that generally serves a much sicker population; thus, the findings, especially as they relate to treatment outcomes, may not apply to the general TB care cascade in the country. As a retrospective study design was used, it was not possible to undertake an in-depth assessment of factors affecting treatment success. Due to the lack of a central electronic medical records system, it was not possible to ascertain the clinical outcomes of patients who were transferred out of the facility or LTFU, potentially resulting in under-estimation of the mortality rate. Furthermore, data on RIF resistance were lacking, as the piloting of the Xpert MTB/RIF system in this facility started late in 2017. Notwithstanding the aforesaid limitations, the findings from this large cohort of patients merit attention and may have important clinical and policy implications for TB prevention and control efforts in Sierra Leone.

In summary, a high TB/HIV co-infection prevalence (32%) and suboptimal treatment outcomes characterized by low treatment success (58%), high treatment attrition rate (33%), and substantial mortality (4.5%), coupled with minimal engagement with the private health sector, were observed among 1105 TB patients at the Chest Clinic at Connaught Hospital in Freetown in 2017. These findings highlight significant gaps in the TB care continuum in Sierra Leone. More local and international support is needed to enable this high TB burden country to meet the global 2030 and 2035 health targets for eliminating TB as a public health threat.

Declarations

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Conflict of interest: We have no competing interest to declare.

Author contributions

SL, DFJ, and GAY designed the study; DFJ and SL collected the data; SL and GAY conducted the statistical analysis and interpreted the data; SL, EP, and GAY wrote the initial draft; all authors contributed intellectual content and edited the final manuscript draft.

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