Original Article

Tuberculosis Treatment and Factors Associated with Unsuccessful Tuberculosis Treatment Outcome among TB/HIV co-infected Patients in Rwanda: A Retrospective Cohort Study

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Abstract

Introduction

Mycobacterium tuberculosis remains the main cause of death as an infectious agent of Tuberculosis in humans, particularly in resource-poor settings. Worldwide, Tuberculosis is one of the top 10 causes of mortality.

Objective of the study

This study aims to determine the outcomes of TB treatment and assess the factors associated with unsuccessful TB treatment outcome among TB/HIV co-infected patients in Rwanda.

Methods

This was a retrospective cohort study of all TB/HIV co-infected patients reported in the national electronic TB reporting system (e-TB) by all health facilities from July 2019 to June 2020. Frequencies, proportions, bivariate and multivariate logistic regression were performed to determine factors associated with unsuccessful TB treatment.

Results

There were 1,144 people reported in the e-TB, however, only 987 were included in the study because 157 patients did not meet the inclusion criteria.The TB/HIV co-infected patients who were not given nutritional support, OR 7.3, 95%CI [1.4, 37.6] and those who were not on ART,OR15.3, 95%CI [3.6, 69.6],were more likely to have unsuccessful treatment outcome than their counterparts.

Conclusion

Unsuccessful TB treatment outcomes were highly observed among TB/HIV co-infected patients. The study recommended reinforcing nutritional support and early initiation of ART among TB/HIV co-infected patients.

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Keywords: Tuberculosis, TBtreatment, TB/HIV Co-infected patients, Rwanda.

Introduction

Mycobacterium tuberculosis, remains the main cause of death as an infectious agent of Tuberculosis in humans, particularly in resource-poor settings. Worldwide, Tuberculosis is one of the top 10 causes of mortality.[1] The World Health Organization (WHO) Global TB Report of 2020, estimated that 10.0 million new cases of TB were reported in 2019, of which 44% were from South-East Asia and 25% were from Africa. [2] Among the new TB cases reported in 2019,8.2% were people living with HIV. [2] Furthermore, in 2019, there were an estimated 1.4 million TB deaths, 0.2 million of which were people living with HIV.[2] Sub-Saharan Africa accommodates 70% of all TB/HIV co-infected patients worldwide. [3]

The morbidity and mortality due to HIV has increased because of TB.[4] TB is one of the commonest opportunist infections among people living with HIV (PLWHA).[4] People living with HIV have an 18 fold risk of developing active TB than those who are HIV negative.[5]HIV/AIDS suppresses the immune system and it makes PLWHA susceptible to Mycobacterium tuberculosis (MTB) infection.[6,7] HIV also increases the risk of recurrence of TB as well as of quick advancement of latent to active TB.[6,7]Studies have shown a significant association of unsuccessful TB treatment outcomes with TB/HIV co-infection at 29.6% in Thailand,[8] 23.4% in Southwest Ethiopia,[9]15.6%in Nigeria,[10]and 24.5% in South Africa.[11]

In Rwanda, several interventions targeting TB/HIV co-infected patients are implemented, whereby HIV positive TB patients are given anti-TB treatment and ART from the same clinic in "One-stop TB/ HIV service" approach. The recommendation of WHO to initiate ART for all TB/HIV co-infected patients (regardless of their CD4 cell count) is being implemented in Rwanda since July 2016.Furthermore, routine symptoms screening in TB/HIV clinics and regular active TB screening using chest x-ray radiography are conducted among PLWHA. Furthermore, routine symptoms screening in TB/HIV clinics and regular active TB screening using chest x-ray radiography are conducted among PLWHA. In addition, all TB patients with moderate and severe malnutrition (BMI<18.5) are provided with nutritional support composed of Corn-Soya Blend (CSB).TB preventive therapy (TPT), a combination of cotrimoxazole, isoniazid and pyridoxine is given to all HIV positive people to stop TB infection from progression to infection. However, there is paucity of information on TB treatment outcomes among TB/HIV co-infected patients in Rwanda. This study aims to determine the outcomes of TB treatment and assess the factors associated with unsuccessful TB treatment outcome among TB/HIV co-infected patients in Rwanda.

Methods

Study Design

This was a retrospective cohort study of all TB/HIV co-infected patients reported in the national electronic TB reporting system (e-TB) by all health facilities from July 2019 to June 2020 and whose treatment outcome was recorded.

Study Setting

Reporting of TB cases data in the e-TB by health facilities countrywide completely shifted to individual data reporting in July 2019. In Rwanda, all public health facilities have an obligation to report TB cases in the e-TB. There are 571public health facilities (health centers and hospitals) that report TB cases data in the e-TB system countrywide. Each health center and each hospital has a TB focal person responsible for one stop TB-HIV services and a data manager responsible for data registration and reporting including TB data. In addition, each hospital has a TB supervisor responsible for the supervision of TB activities in health centers in the catchment area of that hospital. TB patients' data at health facilities are first registered in TB registers and then transferred to the e-TB.

Each quarter, TB evaluation meetings are held at district hospital (DH) level by the national TB program central level staff with DHs TB supervisors and TB focal persons and health center TB focal persons. During these meetings, the last quarter's TB data are reviewed and crosschecked with the data from the registers and corrections made in case of errors or discrepancies before the final reporting in e-TB is done by each health facility.

Sample Size

All TB/HIV co-infected patients reported in the e-TB during the period of July 2019 to June 2020 and whose treatment outcome was recorded were included in the study. Those TB/HIV co-infected patients who were either bacteriologically confirmed or clinically diagnosed were included. Excluded from the study were TB/HIV co-infected patients who: had not been evaluated, had no treatment outcome recorded, had been put on second line anti-TB treatment, had been classified as lost to follow up before initiation of anti-TB treatment and who had died before initiation of anti TB treatment (Figure 1)

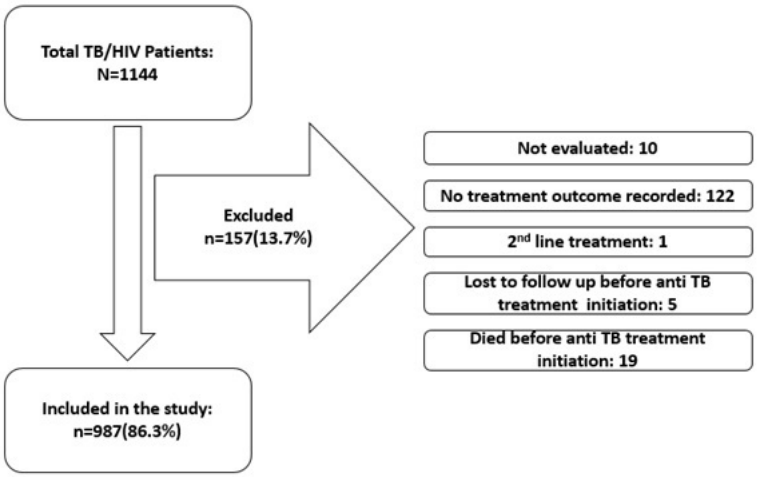

Figure 1.Recruitment of study participant

Data Collection and Analysis

An excel dataset of TB/HIV co-infected patients was extracted from the e-TB reporting system and data was cleaned by the principal investigator. Information collected in the extracted dataset included age, gender, residence, nutritional status, type of TB, TB treatment history, method of TB confirmation, history of HIV, antiretroviral therapy, cotrimoxazole preventive therapy, BMI at initiation of TB treatment, follow up by CHWs and TB Treatment outcomes. The cleaned dataset was then exported to Stata 13 for analysis. Frequencies and proportions were calculated to describe the socio-demographic and clinical factors of the study participants. Logistic regression analysis was performed at 95% confidence interval (C.I) to assess whether there was the association between each exposure and outcome (unsuccessful TB treatment). Multivariable logistic regression was then performed for all variables which were statistically significant in the bivariate analysis to determine independent factors associated with unsuccessful tuberculosis treatment.

Ethical Consideration

The approval of the study was given by the University of Rwanda College of Medicine and Health Sciences Institutional Review Board (IRB) with the approval reference number CMHS/IRB/129/2021;and the authorization to use data was given by Tuberculosis and Other Respiratory Communicable Diseases (TB&ORD) Division in Rwanda Biomedical Center (RBC). Confidentiality was ensured both during and after the study.

Patients' identifiers like names and Tracnet numbers for HIV positive individuals were not included in the analysis and only the principal investigator had access to the dataset.

Key terms used[12]

Successful treatment outcome is defined as the sum of patients who are declared as cured and those that have completed treatment. Unsuccessful treatment outcome is when there is a failure in treating TB patients, lost to follow-up, or death. Cured is when a bacteriologically confirmed pulmonary TB patient at the beginning of treatment was smear- or culture-negative in the last month of treatment and on at least one previous occasion. Treatment completed is when a TB patient 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 performed or because there were no results.

Treatment failure is when sputum smear or culture of TB patients was positive at 5 months or later during the course of treatment. Lost to follow-up is when a TB patient received a treatment for at least four weeks and whose treatment stopped for eight or more weeks consecutively. Not evaluated is when there was no treatment outcome assigned to a TB patient. Died is when there was a TB patient who deceased during the period of treatment because of any reason. A bacteriologically confirmed TB case is one from whom a biological specimen is positive by smear microscopy, culture or WRD (such as Xpert MTB/RIF). A clinically diagnosed TB case is one who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment.

Results

From July 2019 to June 2020, among the 987 TB-HIV co-infected patients who met the inclusion criteria, 617(62.5%) were males and 370(37.5%) were females; their mean (standard deviation) age was 40.4 (12.5) years and 43.8% lived in the capital, Kigali (Table 1). In addition, 853 (86.4%) patients had pulmonary TB, 855 (86.6%) were new TB cases, 921 (93.3%) were on ART, 226 (22.9%) were newly diagnosed with HIV and 508 (51.5%) had a BMI below 18.5 (Table 2).

Table 1. Socio-demographic characteristics of TB/HIV co-infected patients in Rwanda, July 2019 to June 2020, N = 987

Socio-demographic characteristic	Frequency	Percentage (%)
Age		
0-14 Years	21	2.1
≥15 Years	966	97.9
Gender		
Female	370	37.5
Male	617	62.5
Province		
Kigali city	432	43.8
South	183	18.5
West	142	14.4
North	55	5.6
East	175	17.7

Table 2. Clinical factors of TB/HIV co-infected patients in Rwanda, July 2019 to June 2020, N = 987

Clinical Factors	Frequency	Percentage(%)
Nutritional support(n=178)		
Yes	38	21.4
No	140	78.6
Type of TB(n=987)		
Pulmonary	853	86.4
Extra Pulmonary	134	13.6
TB treatment history(n=987)		
New	855	86.6
Previously Treated	132	13.4
Method of TB confirmation(n=987)		
Bacteriologically Confirmed	766	77.6
Clinically diagnosed	221	22.4
Antiretroviral therapy(n=987)		
Yes	921	93.3
No	66	6.7
History of HIV(n=986)		
Newly Diagnosed	226	22.9
Living with HIV	760	77.1
Cotrimoxazole preventive therapy(n=987)		
Yes	815	82.6
No	172	17.4
BMI at start of TB treatment(n=986)		
<18.5	508	51.5
≥18.5	478	48.5
Follow up by CHWs(n=987)		
Yes	308	31.2
No	679	68.8

Successful treatment outcome was achieved in 791 (80.1%) patients (with 54.6% as cured and 25.5% classified as treatment completed), while unsuccessful treatment outcome was reached in196 (19.9%) patients.

The unsuccessful TB treatment outcomes were due to 138 (14.0%) patients who died, 12 (1.2%) who had treatment failure and 46 (4.7%) who were lost to follow up (Figure 2).

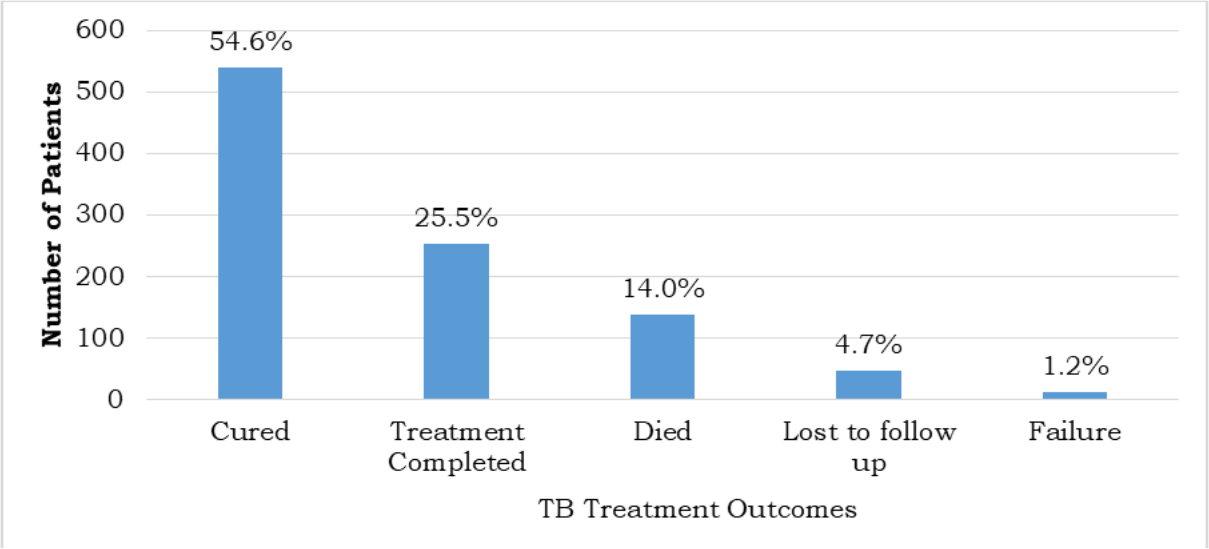

Figure 2. Outcomes of TB treatment among TB/HIV patients in Rwanda, July 2019 to June 2020

In bivariate analysis, TB/HIV co-infected patients who were not given nutritional support were 6.2 times more likely to have unsuccessful TB treatment outcome compared to those who were given nutritional support (p = 0.015). Likewise, patients who were clinically diagnosed were 2.0 times more likely to have unsuccessful treatment outcome compared to those who were bacteriologically confirmed (p<0.001). TB/HIV co-infected patients who were not on antiretroviral therapy (ART) were 5.7 times more likely to have unsuccessful TB treatment compared to those who were not on ART (p < 0.001). Patients who during TB treatment were not followed-up by community health workers (CHWs) were 1.9 times more likely to have unsuccessful TB treatment outcome compared to patients who were followed-up by CHWs (p = 0.001). There was no evidence of association between treatment outcome and age (p = 0.245) or sex (p = 0.456), (Table 3).

In multivariable logistic regression, nutritional support and antiretroviral therapy were the variables independently associated with unsuccessful TB treatment outcome. TB/HIV co-infected patients who were not given nutritional support were 7.3 times more likely to have unsuccessful treatment outcome (adjusted OR 7.3, 95%CI [1.4, 37.6]. Patients who were not on ART were 15.3 times more likely to have unsuccessful treatment outcome (adjusted OR 15.3, 95%CI [3.6, 69.6],(Table 3).

Table 3. Unsuccessful TB treatment outcome by socio-demographic characteristics and clinical factors among TB/HIV co-infected patients in Rwanda, July 2019 to June 2020

			Bivariable			Multivariable		
	Successful Treatment Outcome n(%)	Unsuccessful Treatment Outcome n(%)	cOR[a]	95% CI	p-value	aOR[b]	95% CI[c]	p-value
Overall	791(80.1%)	196(19.9%)						
Demographic factors								
Age group								
0-14 Years	19 (2.4%)	2 (1%)	1.0					
≥15 Years	772 (94.6%)	194 (99%)	2.4	0.6-10.3	0.245			
Gender								
Female	292 (36.9%)	78 (39.8%)	1.0					
Male	499 (63.1%)	118 (60.2%)	0.9	0.6-1.2	0.456			
Province								
Kigali City	346(43.7%)	86 (43.9%)	1.0					
South	151(19.1%)	32 (16.3%)	0.9	0.5-1.3	0.486			
West	111(14.0%)	31(51.8%)	1.1	0.7-1.8	0.622			
North	45(5.7%)	10 (5.1%)	0.9	0.4-1.8	0.762			
East	138(17.5%)	37 (18.9%)	1.1	0.7-1.7	0.732			
Clinical Factors								
Nutritional support(n=178)								
Yes	36(25.7%)	2 (5.3%)	1.0			1.0		
No	104(74.3%)	36 (94.7%)	6.2	1.4-27.2	**0.015**	7.3	1.4-37.6	**0.017**
Type of TB								
Pulmonary	691(87.4%)	162 (82.7%)	1.0					
Extra Pulmonary	100(12.6%)	34 (17.3%)	1.5	0.9-2.2	0.087			
TB treatment history								
New	681(86.1%)	174 (88.8%)	1.0					
Previously treated	110 (13.9%)	22 (11.2%)	0.8	0.5-1.3	0.324			
Method of TB confirmation								
Bacteriologically confirmed	635 (80.3%)	131(66.8%)	1.0			1.0		
Clinically diagnosed	156 (19.7%)	65 (33.2%)	2.0	1.4-2.9	**<0.001**	1.0	0.4-2.3	0.949
Antiretroviral therapy								
Yes	761(96.2%)	160 (81.6%)	1.0			1.0		
No	30 (3.8%)	36 (18.4%)	5.7	3.4-9.5	**<0.001**	15.3	3.6-69.6	**<0.001**
History of HIV								
Living with HIV	607 (76.8%)	153 (78.1%)	1.0					
Newly diagnosed	183 (23.2%)	43 (21.9%)	0.9	0.6-1.4	0.715			
Cotrimoxazole preventive therapy								
Yes	650 (82.2%)	165 (84.2%)	1.0					
No	136 (17.2%)	30 (15.3%)	0.9	0.6-1.3	0.523			
Unknown	5 (0.6%)	1(0.5%)	0.8	0.1-6.8	0.828			
BMI[d]at start of TB treatment								
<18.5	396(50.1%)	112 (57.1%)	1.3	1.0-1.8	0.076			
≥18.5	395(49.9%)	84 (42.9%)	1.0					
Follow up by CHWs[e]								
Yes	267 (33.7%)	41 (20.9%)	1.0			1.0		
No	524 (66.3%)	155 (79.1%)	1.9	1.3-2.8	**0.001**	2.1	0.8-5.5	0.125

[a]cOR: crude odds ratio; [b]aOR: adjusted odds ratio; [c]CI: confidence interval;[d]BMI: body mass index; [e]CHWs: community health workers.

Discussion

In this study, we found that 19.9% of TB/HIV co-infected patients had unsuccessful TB treatment outcome. Our finding was higher than those of other studies previously conducted in Ethiopia which were respectively 13.2%, and 11.8%,[7,13] the Democratic Republic of Congo, 16.7%,[14] and Nigeria,15.6%.[10]However, our study finding was lower than some other studies conducted in Africa: Southwest Ethiopia (23.4%),[9] South Africa (24.5%),[11]Nigeria (34.2%);[15] and South East Asia: Thailand (29.6%),[8]and Malaysia (42.1%).[16] This discrepancy in findings could be as a result of the difference in the number of study participants recruited in the studies, as well as the differences in the death rates, lost to follow-up and treatment failure which may affect the unsuccessful treatment outcome.

Unsuccessful TB treatment outcome among TB/HIV co-infected patients in this study was mainly due to the death rate of 14.0%. This study result is in agreement with another study conducted in Nigeria with death rate of 19%,[15]but higher than results from Cameroon at 6.9%,[6] Ethiopia 8.3%,[13]and Nigeria 10.1%.[10]This finding was slightly lower than the national TB program routine surveillance data reports which reported a death rate of 15.7% and 15.5% among TB/HIV co-infected patients in July 2016 to June 2017 and July 2018 to June 2019 respectively. The differences in death rates might be attributed to different sample sizes used in the studies but also to different care given to TB/HIV co-infected patients in different settings.

The study revealed that the association between non-initiation of ART and unsuccessful TB treatment outcome was statistically significant. TB-HIV co-infected patients who were not on ART had a 15.3-fold high risk of having unsuccessful TB treatment than those on ART. This was in agreement with other studies conducted in Ethiopia,[16,17]and India,[18] which showed that TB/HIV co-infected patients not initiated on ART were more likely to have unsuccessful treatment outcome compared to those on ART. Effective and early initiated antiretroviral therapy improves the longevity and prevents opportunistic infections among people living with HIV.[19]

The study also showed that nutritional support was associated with unsuccessful TB treatment outcome but the association was not significant. TB/HIV co-infected patients who were not given nutritional support had a 7.3 fold risk of having unsuccessful treatment outcome compared to those who received nutritional support. In other studies conducted in Senegal,[20] and India,[21]nutritional support to TB/HIV co-infected TB patients was linked to a reduced risk of having unsuccessful treatment outcome. Nutrition strengthens the immunity that is already suppressed by TB/HIV co-infection and helps the body to heal from infection like TB infection.[22]

Study Limitations

The main limitation of this study results from the use of retrospective secondary data. Whereby for some study participants, there were missing data. In addition, the reporting system did not capture some information about essential variables that might influence the status of TB treatment outcome. These variables includes socioeconomic characteristics (income, marital status, educational status, distance to the health facility), clinical factors (viral load, adherence level), and behavioural (knowledge and attitude about the disease, cigarette smoking, alcohol abuse, illicit drug use).

Conclusion

In this study, we observed that unsuccessful TB treatment outcomes were high among TB/HIV co-infected patients. The mortality rate among TB/HIV co-infected patients was also high. Not receiving nutritional support and non-initiation of ART are risk factors for unsuccessful TB treatment outcomes among TB/HIV co-infected patients. Based on the findings of our study,

it can be stated that reinforcement of nutritional support to TB/HIV co-infected patients, early initiation of ART among TB/HIV co-infected patients irrespective of their CD4 cell count could improve the treatment outcome, Further studies especially prospective studies which can collect all data for all relevant variables should be conducted to identify more factors associated with unsuccessful treatment outcomes. Finally, a study should be conducted to assess the factors associated to mortality among TB/HIV co-infected patients.

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Author contributions
ER and JN conceptualized the study, designed the methods data analysis, analysed the data and drafted the manuscript. CMCS contributed to the data analysis and the general review of the manuscript. All authors provided final approval of the manuscript for its publication.

Conflict of interests
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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