Published in final edited form as:
AIDS. 2010 June 1; 24(9): 1323–1328. doi:10.1097/QAD.0b013e3283390dd1.

Tuberculosis during the first year of antiretroviral therapy in a South African cohort using an intensive pretreatment screening strategy

Stephen D Lawn[a,b], **Katharinaa Kranzer**[b], **David J Edwards**[a], **Matthew McNally**[c], **Linda-Gail Bekker**[a], and **Robin Wood**[a]

[a]The Desmond Tutu HIV Centre, Institute for Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa

[b]Clinical Research Unit, Department of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

[c]Hannan Crusaid Antiretroviral Treatment Clinic, Gugulethu, Cape Town, South Africa.

Abstract

Objective: To determine the baseline prevalence of tuberculosis (TB) in a cohort using a strategy of intensive pretreatment screening for TB and the subsequent incidence rate and temporal distribution of cases during the first year of antiretroviral therapy (ART).

Design: Prospective observational community-based ART cohort in South Africa.

Methods: Adults enrolling for ART and who did not have a current TB diagnosis were intensively screened for TB at baseline using culture of two sputum samples, chest radiography and investigations for extrapulmonary disease as required. Patients who developed symptoms consistent with incident TB during ART were similarly investigated.

Results: Two hundred forty-one patients had a median CD4 cell count of 125 cells/μl (interquartile range 70–186) and 200 (83%) started ART. TB was diagnosed in 87 (36%) patients, with 82% of pulmonary cases being culture-proven. Most TB cases (87%) were prevalent disease detectable at baseline, whereas just 11 (13%) were incident cases that presented during the first year of ART. The incidence rate during 0–4 months of ART was similar to the rate during months 5–12 of ART [10.9 (95% confidence interval [CI] 4.6–23.3) cases per 100 person-years versus 8.1 (95% CI 3.6–18.0) cases per 100 person-years].

Conclusion: Systematic culture-based screening detected a very high burden of prevalent TB present at baseline. This intensified screening strategy was associated with an approximately two-fold lower incidence rate in the first 4 months of ART than previously observed in this cohort. This suggests that many incident cases of symptomatic TB presenting during early ART can be detected as prevalent disease prior to ART initiation using sensitive diagnostic tests.

Correspondence to Stephen D. Lawn, Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Anzio Road, Observatory 7925, Cape Town, South Africa. Tel: +27 21 650 6970; fax: +27 21 650 6963; stevelawn@yahoo.co.uk.

Author contributions: S.D.L. designed the study, collected the data, designed the analyses and wrote the paper with input from R.W. D.J.E. collected the data. K.K. did the statistical analyses. M.M. oversaw the field site and L.-G.B. and R.W. were responsible for research infrastructure. All authors contributed to and approved the final version of the article.

Introduction

Tuberculosis (TB) is a key challenge for antiretroviral treatment (ART) services in sub-Saharan Africa [1-3]. Among patients enrolling for ART, the prevalence of disease at baseline and the subsequent incidence rate during the initial months of ART are both very high [1,2,4]. Thereafter, incidence rates fall steeply as CD4 cell counts improve [1,2,4,5]. Both prevalent and early incident TB cause much morbidity, complicate delivery of ART and are associated with substantial mortality [1,2,6-9]. In addition, there is high risk of nosocomial TB transmission in ART clinics [10,11]. Strategies to reduce the impact of TB are urgently needed.

The WHO '3Is' strategy aims to reduce the burden of TB in people living with HIV through implementation of intensified case finding, infection control and isoniazid preventive therapy [12]. Intensified case finding permits early case detection and treatment of active cases and may thereby reduce morbidity, mortality and TB transmission risk in ART services. However, the yield and associated benefits of intensified case finding may vary greatly according to the screening strategy used, patient CD4 cell count and the diagnostic tests available [13,14]. Patients enrolling for ART in Africa typically have advanced immunodeficiency and available TB diagnostics are often very limited. Most disease is sputum smear-negative culture-positive and diagnosis is therefore very challenging [15-18].

Our hypothesis a priori was that routine systematic intensive screening of all patients using automated liquid culture of sputum samples would identify a high yield of prevalent TB at baseline and that much of the burden of incident TB cases presenting during the initial months of ART would be detected as prevalent disease at baseline. We therefore examined the yield of intensive TB case finding at baseline among patients enrolling in a well characterized ART cohort in South Africa and the subsequent incidence and temporal distribution of TB cases during the first year of treatment.

Methods

Setting

This study arises from a body of research conducted in a South African ART cohort aiming to ascertain the true burden of TB disease, identify optimal means of screening for TB in those preparing for ART, evaluate new TB diagnostics and ascertain the impact of these interventions on patient outcomes. Data from these studies have been previously been reported in part elsewhere [17,19].

The ART cohort is based in Gugulethu township in Cape Town where the HIV prevalence and TB notification rate are very high [1,20]. The national ART programme provided treatment for those with WHO stage 4 disease or a blood CD4 cell count less than 200 cells/μl. The extraordinarily high burden of TB diagnosed during routine clinical practice in this service has been previously characterized in detail [1,4,17,21]. All patients gave written informed consent and this study was approved by the Research Ethics Committee of the Faculty of Health Sciences of the University of Cape Town.

Patients, laboratory investigations and follow-up

Eligible patients were ART-naive adults (≥18 years of age) referred to start ART and who did not have a current diagnosis of TB. As previously described, the time between enrolment of a patient in this service and initiation of ART is typically 28 days, permitting thorough evaluation of patients for possible active TB and other co-morbidity as well as preparation for ART [20].

Patients completed a symptom-screening questionnaire and chest radiographs were submitted for specialist reporting. All patients provided two sputum samples, with one or both being induced using nebulized hypertonic (3%) saline. Further investigations such as abdominal ultrasonography, lumbar puncture and fine-needle aspiration of lymphadenopathy for cytology were done when required. Outcomes of all patients were prospectively recorded in a research database as previously described [1,20].

Sputum samples were analysed within accredited laboratories using standardized protocols and quality control procedures as described elsewhere [17,22]. In brief, centrifuged sputum deposits were examined for acid-fast bacilli (AFB) using auramine O fluorescent stain and cultured using mycobacterial growth indicator tubes (MGIT; Becton-Dickinson, Sparks, Maryland, USA). Positive cultures were speciated and isolates of Mycobacterium tuberculosis underwent spoligotyping to assess possible cross-contamination.

Definitions

Prevalent TB was defined as all TB diagnoses established in the interval between enrolment and initiation of ART; TB diagnoses established during early ART, but for which symptoms were present and investigations were initiated before starting ART; and TB diagnoses established during early ART in asymptomatic patients with positive baseline sputum cultures and who remained asymptomatic at the time of cultures were identified as positive. Incident TB was defined as occurring in patients with new TB diagnoses for which symptom onset and date of diagnosis were both after ART initiation.

Culture-positive TB was diagnosed on the basis of at least one positive culture of M. tuberculosis. Diagnoses of sputum culture-negative TB were based on negative smears and cultures for M. tuberculosis in the context of clinically and radiologically compatible illness that did not respond to administration of simple antibiotics but did respond to subsequent antituberculosis treatment. Diagnosis of extrapulmonary TB was based on a combination of clinical, radiological, histopathological findings and response to antituberculosis treatment.

Data analysis

Data were analysed using STATA version 10.0 (STATA, College Station, Texas, USA). Wilcoxon rank-sum test, $\chi 2$-test and Fisher's exact test were used to compare medians and proportions as appropriate. We calculated TB incidence rates from ART initiation. Person-time was censored at death, loss to follow-up or after 12 months of ART and person-time accrued during TB treatment was excluded from the time denominator. Rates, rate ratios and 95% confidence intervals were calculated. A Kaplan–Meier plot of TB-free survival through time was used to illustrate the temporal distribution of incident TB cases. All statistical tests were two-sided at $\alpha = 0.05$.

Results

Patient characteristics and tuberculosis diagnoses

Patients (n = 241) who were screened for TB had a median age of 33 years [interquartile (IQR) 29–39 years] and 72% were women, 14% of whom were pregnant. The median CD4 cell count was 125 cells/μl (IQR 70–186) and 54% had WHO stage 3 or 4 disease. ART was started by 200 (83%) patients after a median of 29 days (26–56 days) from enrolment. ART was not started by 41 (17%) patients because of death (n = 8), ART ineligibility (n = 5), loss to follow-up (n = 18) or transfer-out to another ART clinic (n = 10).

TB was diagnosed in 87 (36%) patients between enrolment and completion of 1 year of ART. Pulmonary involvement was observed in 77 (89%) patients. Of these, 63 (82%)

patients were culture-proven, but only 11 (14%) were sputum smear-positive. The median time to culture-positivity was 22 days (18–29 days). Molecular fingerprinting of cultured isolates of M. tuberculosis provided no evidence of cross-contamination. Disease was exclusively extrapulmonary in 10 (11%) patients, which was characterized as either pleural (n = 5), abdominal (n = 2), peripheral lymphadenopathy (n = 1), a psoas abscess (n = 1) or septic arthritis (n = 1).

Prevalent tuberculosis

The vast majority (n = 76; 87%) of TB cases diagnosed were prevalent disease detectable at baseline with a prevalence of 31.5% (Table 1). Patients with prevalent TB tended to have lower CD4 cell counts, more advanced WHO stage of disease and higher viral loads at baseline compared with those who remained TB-free. The sensitivity of symptom screening was poor with cough for 2 weeks or more, sputum production, significant recent weight loss, fever and night sweats having sensitivities for prevalent TB of 39, 34, 58, 21 and 39%, respectively. Use of a combined screening of any one of these symptoms had a sensitivity of 77% [95% confidence interval (CI) 66–86] and a specificity of 42% (95% CI 34–50).

Only 59% of those who had prevalent TB at baseline remained in this service alive on ART at the end of 1 year compared with 73% of those who did not have prevalent TB (P = 0.024) (Table 1). Of the eight patients who died prior to ART initiation, six (75%) had prevalent TB and of the 18 patients lost to follow-up pre-ART, nine (50%) had prevalent TB. Those with prevalent TB were more likely to die or be lost to follow-up pre-ART compared with those who remained TB-free (19.7 versus 8.4%, respectively; P = 0.018). Five patients with prevalent TB developed paradoxical TB immune reconstitution disease during ART as described previously [17]. However, no cases of incident TB were associated with immune reconstitution disease.

Incident tuberculosis

During ART, only 11 cases of incident TB were diagnosed, accounting for just 13% of total TB diagnoses (Table 1). A Kaplan–Meier plot showed that, in marked contrast to previous observations in this cohort [1,4], these cases were evenly distributed during the first year of ART (Fig. 1). The median duration of ART at the time of symptom onset was 5.1 months (IQR 1.4–9.1 months). The overall TB incidence rate was 9.2 cases per 100 person-years (95% CI 5.1–16.6). The rate in months 0–4 of ART was 10.9 cases per 100 person-years (95% CI 4.6–23.3) and was similar to the rate of 8.1 cases per 100 person-years in months 5–12 of ART (95% CI 3.6–18.0).

Discussion

We have previously documented the enormous burden of TB diagnosed in this South African ART service under routine programme conditions during which investigations for TB are usually initiated based on clinical suspicion [1,4]. However, in this study, all patients, regardless of clinical status, were systematically investigated at baseline for TB using automated liquid sputum culture. A TB diagnosis was made in over one-third of patients between enrolment and up to 1 year of ART. However, the vast majority of these diagnoses (87%) were prevalent disease detectable at baseline with a prevalence of 31.5%. The data from this study suggest that many incident cases of symptomatic TB presenting during early ART can be detected as prevalent disease at baseline by routine screening using sensitive diagnostic tests.

Previous data from this cohort have suggested that, under routine programme conditions, approximately 40% of TB cases presenting in the first 4 months of ART are due to ART-

induced ‘unmasking’ of subclinical active TB that was not diagnosed at baseline [4]. The present data are entirely consistent with this, showing that with use of a routine intensive screening strategy, the TB incidence rate in this period (10.9 cases per 100 person-years) was approximately two-fold lower than previously observed [1,4]. This suggests that approximately half the incident TB cases that present during months 0–4 of ART under routine programme conditions can be diagnosed at baseline by effective screening. Expediting the diagnosis of these cases in this way would explain the strikingly even temporal distribution of TB cases that was observed during the first year of ART.

TB diagnosis remains a huge challenge in this clinical setting. Symptom screening and sputum microscopy were very insensitive as reported in a similar study from elsewhere in South Africa [18]. Most cases in the present study were sputum smear-negative culture-positive and 32% of culture-confirmed pulmonary TB cases in this cohort have an entirely normal chest radiograph [19]. Using a large meta-analysis of studies, a symptom-screening algorithm has been developed by the WHO and Centers for Disease Control and Prevention to identify TB suspects among HIV-infected patients [23]. However, the very low specificity of this algorithm in those with CD4 cell counts less than 200 cells/μl results in the need to investigate most patients. Furthermore, limited sensitivity also results in some cases being missed. In light of these observations and the extremely high TB prevalence, there is a strong rationale for routine culture-based screening at the first ART clinic visit in this setting. Availability of culture-based TB diagnosis is currently extremely limited in sub-Saharan Africa, but there is an international policy initiative for this to be expanded [24].

In sub-Saharan Africa, mortality is extremely high in patients just prior to starting ART and during the initial months of treatment [25]; two key causes of death are TB and cryptococcal disease. The present data and those from a study of screening for cryptococcal antigenaemia [26] suggest that baseline screening for these diseases may be key interventions to address this. It was striking that of 75% of pre-ART deaths in this study had culture-proven prevalent TB. This is consistent with previous observations that a large proportion of patients dying with HIV/AIDS in sub-Saharan Africa have active TB [27,28].

Despite high sensitivity, automated liquid sputum culture was slow with a median time to a positive result of over 3 weeks. This is likely to reflect very low mycobacterial numbers in sputum samples and the time to positivity needs to be shortened, for example, by using simple growth supplementation in the culture medium [29]. Availability of novel rapid diagnostic assays for routine screening such as urine lipoarabinomannan detection [17,30] or nucleic acid amplification tests [16] may further expedite diagnosis and treatment initiation and thereby avert some of these deaths. However, diagnostic sensitivity remains a key challenge in this patient group.

Although clinical observation suggests that the majority of cases of ‘unmasking TB’ have an unremarkable presentation [31], a minority of cases may be severe and even result in death from immune reconstitution disease [32,33]. This complication might be effectively prevented by baseline screening. The frequency of paradoxical immune reconstitution disease events occurring among TB cases identified using this screening strategy was broadly similar to that described previously in this cohort [21].

Nosocomial TB transmission poses a grave threat to ART services in Africa, especially with regard to multidrug-resistant TB [10,11]. Early case detection through baseline screening is clearly one of the most important strategies to address this. Studies are needed to quantify the overall costs and benefits of routine TB screening in this clinical setting.

Strengths of this study include the well characterized study cohort in which the TB disease burden has previously been described in detail. Most TB cases were culture-proven.

Weaknesses include the absence of a direct comparator group in which intensive screening was not used. Although the overall cohort size was small, the disease frequency was very high. The overall impact of routine screening on clinical management, mortality and nosocomial TB transmission risk remains to be quantified in future studies.

In summary, a large majority of the TB diagnosed during the first year of ART in this setting can be detected as prevalent disease at baseline using a strategy of systematic screening using sensitive diagnostics. Sputum culture-based screening should be used more widely in this clinical setting pending development of simpler and more rapid diagnostic assays.

Acknowledgments

S.D.L. and K.K. are funded by the Wellcome Trust, London, UK. R.W. and L.-G.B. are funded in part by the National Institutes of Health (NIH) through a CIPRA grant 1U19AI53217-01 and RO1 grant (A1058736-01A1). D.J.E. is funded by the NIH through the International Clinical Research Fellows Program at Vanderbilt (R24 TW007988). The authors gratefully acknowledge the dedicated staff of the Hannan Crusaid ART clinic and the Desmond Tutu HIV Centre.

References

1. Lawn SD, Myer L, Bekker LG, Wood R. Burden of tuberculosis in an antiretroviral treatment programme in sub-Saharan Africa: impact on treatment outcomes and implications for tuberculosis control. AIDS. 2006; 20:1605–1612. [PubMed: 16868441]
2. Moore D, Liechty C, Ekwaru P, Were W, Mwima G, Solberg P, et al. Prevalence, incidence and mortality associated with tuberculosis in HIV-infected patients initiating antiretroviral therapy in rural Uganda. AIDS. 2007; 21:713–719. [PubMed: 17413692]
3. Bonnet MM, Pinoges LL, Varaine FF, Oberhauser BB, O'Brien DD, Kebede YY, et al. Tuberculosis after HAART initiation in HIV-positive patients from five countries with a high tuberculosis burden. AIDS. 2006; 20:1275–1279. [PubMed: 16816556]
4. Lawn SD, Myer L, Edwards D, Bekker LG, Wood R. Short-term and long-term risk of tuberculosis associated with CD4 cell recovery during antiretroviral therapy in South Africa. AIDS. 2009; 23:1717–1725. [PubMed: 19461502]
5. Lawn SD, Kranzer K, Wood R. Antiretroviral therapy for control of the HIV-associated tuberculosis epidemic in resource-limited settings. Clin Chest Med. 2009; 30:685–699. [PubMed: 19925961]
6. Koenig SP, Riviere C, Leger P, Joseph P, Severe P, Parker K, et al. High mortality among patients with AIDS who received a diagnosis of tuberculosis in the first 3 months of antiretroviral therapy. Clin Infect Dis. 2009; 48:829–831. [PubMed: 19207078]
7. Lawn SD, Edwards DJ, Wood R. Concurrent drug therapy for tuberculosis and HIV infection in resource-limited settings: present status and future prospects. Future HIV Ther. 2007; 1:387–398.
8. Harries AD, Zachariah R, Lawn SD. Providing HIV care for co-infected tuberculosis patients: a perspective from sub-Saharan Africa. Int J Tuberc Lung Dis. 2009; 13:6–16. [PubMed: 19105873]
9. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. AIDS. 2008; 22:1897–1908. [PubMed: 18784453]
10. Bock NN, Jensen PA, Miller B, Nardell E. Tuberculosis infection control in resource-limited settings in the era of expanding HIV care and treatment. J Infect Dis. 2007; 196(Suppl 1):S108–S113. [PubMed: 17624819]
11. Gandhi NR, Moll A, Sturm AW, Pawinski R, Govender T, Lalloo U, et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. Lancet. 2006; 368:1575–1580. [PubMed: 17084757]
12. World Health Organization. WHO three I's meeting. Report of a joint WHO HIV/AIDS and TB Department Meeting. Geneva; WHO: 2008. http://www.who.int/hiv/pub/meetingreports/WHO_3Is_meeting_report.pdf. [Accessed 12 December]

13. Kranzer K, Houben RMG, Glynn JR, Bekker L- G, Wood R, Lawn SD. Yield of HIV-associated tuberculosis during intensified case finding in resource-limited settings: a systematic review and meta-analysis. Lancet Infect Dis. 2010; 10:93–102. [PubMed: 20113978]
14. Reid MJ, Shah NS. Approaches to tuberculosis screening and diagnosis in people with HIV in resource-limited settings. Lancet Infect Dis. 2009; 9:173–184. [PubMed: 19246021]
15. Getahun H, Harrington M, O'Brien R, Nunn P. Diagnosis of smear-negative pulmonary tuberculosis in people with HIV infection or AIDS in resource-constrained settings: informing urgent policy changes. Lancet. 2007; 369:2042–2049. [PubMed: 17574096]
16. Perkins MD, Cunningham J. Facing the crisis: improving the diagnosis of tuberculosis in the HIV era. J Infect Dis. 2007; 196(Suppl 1):S15–S27. [PubMed: 17624822]
17. Lawn SD, Edwards SD, Kranzer K, Vogt M, Bekker L- G, Wood R. Urine lipoarabinomannan assay for tuberculosis screening prior to ART: diagnostic yield and association with immune reconstitution disease. AIDS. 2009; 23:1875–1880. [PubMed: 20108382]
18. Bassett, I.; Chetty, S.; Wang, B.; Giddy, J.; Losina, E.; Mazibuko, M., et al. Intensive TB screening for HIV-infected patients ready to start ART in Durban, South Africa: limitations of WHO guidelines; Program and Abstracts of the 16th Conference on Retroviruses and Opportunistic Infections; Montreal, Canada. Feb. 2009 abstract #779
19. Dawson R, Masuka P, Edwards DJ, Bekker L-G, Bateman E, Wood R, et al. Chest radiograph reading and reporting system: evaluation for TB screening in patients with advanced HIV. Int J Tuberc Lung Dis. 2010; 14:52–58. [PubMed: 20003695]
20. Lawn SD, Myer L, Orrell C, Bekker LG, Wood R. Early mortality among adults accessing a community-based antiretroviral service in South Africa: implications for programme design. AIDS. 2005; 19:2141–2148. [PubMed: 16284464]
21. Lawn SD, Myer L, Bekker LG, Wood R. Tuberculosis-associated immune reconstitution disease: incidence, risk factors and impact in an antiretroviral treatment service in South Africa. AIDS. 2007; 21:335–341. [PubMed: 17255740]
22. Barnard M, Albert H, Coetzee G, O'Brien R, Bosman ME. Rapid molecular screening for multidrug-resistant tuberculosis in a high-volume public health laboratory in South Africa. Am J Respir Crit Care Med. 2008; 177:787–792. [PubMed: 18202343]
23. Getahun, H. Meta-analysis to inform the development of a standardised approach for TB screening in HIV-infected patients; 40th Union World Conference on Lung Health; Cancun, Mexico. Dec. 2009
24. World Health Organization. The use of liquid TB culture and drug susceptibility testing (DST) in low and medium income settings. Geneva; World Health Organization; 2007. http://www.who.int/tb/dots/laboratory/Use%20of%20Liquid%20TB%20Culture_Summary%20Report.pdf. [Accessed 5 January 2010]
25. Lawn SD, Harries AD, Anglaret X, Myer L, Wood R. Early mortality among adults accessing antiretroviral treatment programmes in sub-Saharan Africa. AIDS. 2009; 22:1897–1908. [PubMed: 18784453]
26. Jarvis JN, Lawn SD, Vogt M, Bangani N, Wood R, Harrison TS. Screening for cryptococcal antigenemia in patients accessing an antiretroviral treatment program in South Africa. Clin Infect Dis. 2009; 48:856–862. [PubMed: 19222372]
27. Lucas SB, Hounnou A, Peacock C, Beaumel A, Djomand G, N'Gbichi JM, et al. The mortality and pathology of HIV infection in a west African city. AIDS. 1993; 7:1569–1579. [PubMed: 7904450]
28. Rana FS, Hawken MP, Mwachari C, Bhatt SM, Abdullah F, Ng'ang'a LW, et al. Autopsy study of HIV-1-positive and HIV-1-negative adult medical patients in Nairobi, Kenya. J Acquir Immune Defic Syndr. 2000; 24:23–29. [PubMed: 10877491]
29. Brittle W, Marais BJ, Hesseling AC, Schaaf HS, Kidd M, Wasserman E, et al. Improvement in mycobacterial yield and reduced time to detection in pediatric samples by use of a nutrient broth growth supplement. J Clin Microbiol. 2009; 47:1287–1289. [PubMed: 19279173]
30. Shah M, Variava E, Holmes CB, Coppin A, Golub JE, McCallum J, et al. Diagnostic Accuracy of a Urine Lipoarabinomannan Test for Tuberculosis in Hospitalized Patients in a High HIV Prevalence Setting. J Acquir Immune Defic Syndr. 2009; 52:145–151. [PubMed: 19692904]

31. Lawn SD, Wilkinson RJ, Lipman MC, Wood R. Immune reconstitution and ‘unmasking’ of tuberculosis during antiretroviral therapy. Am J Respir Crit Care Med. 2008; 177:680–685. [PubMed: 18202347]

32. Goldsack NR, Allen S, Lipman MC. Adult respiratory distress syndrome as a severe immune reconstitution disease following the commencement of highly active antiretroviral therapy. Sex Transm Infect. 2003; 79:337–338. [PubMed: 12902592]

33. Lawn SD, Wainwright H, Orrell C. Fatal unmasking tuberculosis immune reconstitution disease with bronchiolitis obliterans organizing pneumonia: the role of macrophages. AIDS. 2009; 23:143–145. [PubMed: 19050399]

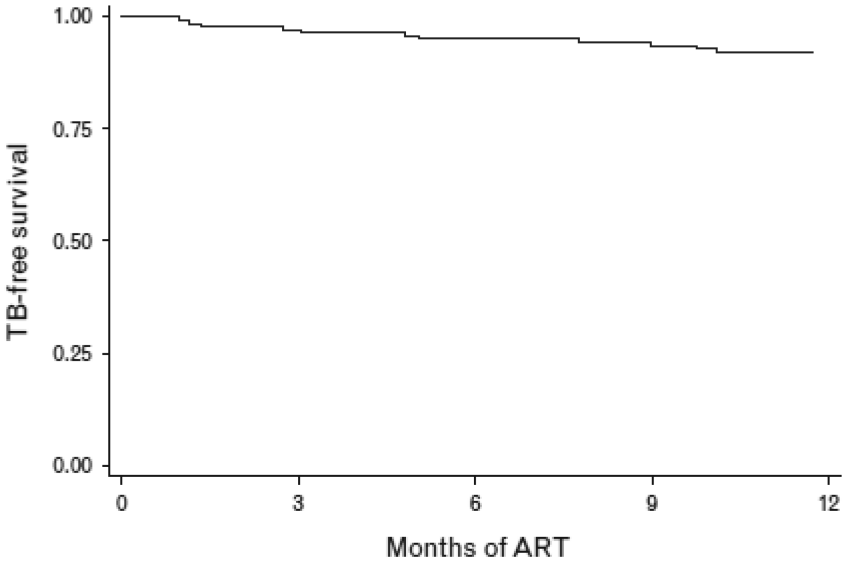

Fig. 1.

A Kaplan–Meier plot showing incident tuberculosis free survival from the time of initiating antiretroviral therapy up to the end of the first year of treatment. The timing of tuberculosis (TB) episodes denoted the time of symptom onset rather than the date of diagnosis. ART, Antiretroviral therapy.

Table 1

Characteristics and outcomes of patients who remained tuberculosis-free throughout the study period or who were diagnosed as having either tuberculosis at baseline (prevalent tuberculosis) or tuberculosis presenting during antiretroviral therapy (incident tuberculosis).

	TB-free, *N*=1.54 (63.9%)	**Prevalent TB, *N* = 76 (31.5%)**	**Incident TB, *N*= 11 (4.6%)**
Baseline characteristics			
Age [median (IQR)]	33 (28−40)	33 (29−39)	34 (30−39)
Female	109 (71)	58 (76)	6 (55)
Pregnant women (%)	16 (15)	8 (14)	0 (0)
WHO stage			
1 and 2	82 (53)	25 (33)	4 (36)
3	62 (40)	40 (53)	6 (55)
4	10 (6)	11 (15)	1 (9)
CD4 cell count [median (IQR)]	149 (91−191)	85 (41−168)	115 (24−196)
CD4 cell count <100 cells/μl	44 (30)	40 (53)	4 (36)
Log viral load >10^5 copies/ml[a]	55 (37)	39 (53)	1 (9)
Past history of TB	37 (24)	14 (18)	5 (45)
Patient outcomes			
Pre-AKT outcomes			
Did not start ART	23 (15)	18 (24)	0
Pre-ART death	2 (1)	6 (8)	0
Pre-ART loss to follow-up	9 (6)	9 (12)	0
Pre-ART transfer-out	7 (5)	3 (4)	
Ineligible for ART	5 (3)	0 (0)	0
ART outcomes			
Started ART	131 (85)	58 (76)	11 (100)
Death on ART	3 (2)	6 (8)	0
Lost to follow-up on ART	10 (6)	7 (9)	1 (9)
Transfer-out on ART	6 (4)	0	0
Alive on ART	112 (73)	45 (59)	10 (91)
TB characteristics			
Proportion of all TB cases	-	87 (79−93)	13 (7−21)
PTB		70 (92)	7 (64)
Smear + PTB cases		10 (13)	1 (9)
Culture + PTB cases		59 (78)	4 (36)
EPTB exclusively		6 (8)	4 (36)

Data are shown in n (%) except where stated otherwise. ART, antiretroviral therapy; EPTB, extra pulmonary TB; IQR, interquartile range; PTB, pulmonary TB; TB, tuberculosis.

[a]Data available for 232 patients.