Are HIV-positive presumptive tuberculosis patients without tuberculosis getting the care they need in Zimbabwe?

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Setting: Emakhandeni Clinic provides decentralised and integrated tuberculosis (TB) and human immunodeficiency virus (HIV) care in Bulawayo, Zimbabwe.

Objectives: To compare HIV care for presumptive TB patients with and without TB registered in 2013.

Design: Retrospective cohort study using routine programme data.

Results: Of 422 registered presumptive TB patients, 26% were already known to be HIV-positive. Among the remaining 315 patients, 255 (81%) were tested for HIV, of whom 190 (75%) tested HIV-positive. Of these, 26% were diagnosed with TB and 71% without TB (3% had no TB result recorded). For the 134 patients without TB, antiretroviral treatment (ART) eligibility data were recorded for 42 (31%); 95% of these were ART eligible. Initiation of cotrimoxazole preventive therapy (CPT) and ART was recorded for respectively 88% and 90% of HIV-positive patients with TB compared with respectively 40% and 38% of HIV-positive patients without TB (P < 0.001).

Conclusion: Presumptive TB patients without TB had a high HIV positivity rate and, for those with available data, most were ART eligible. Unlike HIV-positive patients diagnosed with TB, CPT and ART uptake for these patients was poor. A ‘test and treat’ approach and better service linkages could be life-saving for these patients, especially in southern Africa, where there are high burdens of HIV and TB.

Among persons seeking care for symptoms suggestive of tuberculosis (TB) in sub-Saharan Africa, human immunodeficiency virus (HIV) prevalence rates of as high as 63% have been reported.1-3 These findings support the importance of offering provider-initiated HIV testing and counselling (PITC) to patients with presumptive TB, an initiative that is now recommended in the international guidelines for collaborative TB-HIV activities; PITC was previously recommended only for patients diagnosed with TB.4

In high TB-HIV burden countries, among presumptive TB patients found to have TB, an increasing number undergo HIV testing. Of those found to be HIV-positive, a substantial proportion are started on antiretroviral therapy (ART),5 which is known to improve survival and TB treatment outcomes.6 In contrast, little is known about what happens to presumptive TB patients who are found not to have TB but who are diagnosed as HIV-positive. This could be compounded by the fact that internationally recommended indicators for monitoring collaborative TB-HIV activities focus primarily on HIV-positive patients with TB and not on HIV-positive patients without TB.7

Since the 1990s, Zimbabwe has experienced a devastating HIV-associated TB epidemic.8 While great strides have been made in the diagnosis and treatment of HIV-positive TB patients, with 91% of patients knowing their HIV status and 77% of HIV-positive TB patients accessing ART in 2013,9 less attention has been paid to whether HIV-positive presumptive TB patients without TB benefit from ART. A study from Zimbabwe that followed up this patient group suggested that they fare poorly, with limited ART access and a high 12-month mortality rate.9

The present study aimed to compare the HIV diagnostic and treatment cascade, including ART initiation, in presumptive TB patients with and without TB in a primary health care facility in Bulawayo, Zimbabwe. The study objective was to determine annual numbers and proportions of presumptive TB patients who were HIV tested and found to be positive between 2009 and 2013. Other objectives were to determine, among presumptive TB patients registered in 2013, 1) the number and proportion HIV tested and found to be HIV-positive, 2) the number and proportion newly diagnosed as HIV-positive without TB who were eligible for ART, and 3) the number and proportion newly diagnosed as HIV-positive who were started on ART and cotrimoxazole preventive therapy (CPT), based on their TB status.

METHODS

Study design
This was a retrospective cohort study using routine programme data.

Study setting
General
Zimbabwe, situated in southern Africa, is one of the countries hardest hit by the HIV epidemic, with an HIV prevalence of approximately 15% among persons aged 15–49 years.10 It also has a large TB epidemic, with 32 899 new and relapse TB cases reported in 2013, equating to a notification rate of 233 per 100 000 population.5

Management of presumptive TB patients and ART eligibility in Zimbabwe
In Zimbabwe, a presumptive TB patient is defined as a person presenting with a chronic cough of ≥2 weeks.11 A register for presumptive TB patients was introduced

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in 2007 to monitor TB detection. A year later, information on HIV test results was also included.

The diagnosis of TB is based mainly on sputum smear microscopy of acid-fast bacilli (AFB) using the Ziehl-Neelsen method and, more recently, on rapid molecular testing using Xpert® MTB/RIF (Cepheid Inc, Sunnyvale, CA, USA). A patient is defined as having bacteriologically confirmed TB if 1) at least one sputum microscopy result is AFB-positive, or 2) an Xpert result is positive for Mycobacterium tuberculosis, or 3) M. tuberculosis grows on culture. Presumptive TB patients whose sputum results are negative and who do not have a positive response to a course of antibiotics are evaluated by a medical officer who may make a clinical diagnosis, often based on chest radiographic findings.

HIV testing and counselling are offered to persons with presumptive TB who have not previously tested HIV-positive, in accordance with national guidelines.12 HIV test results usually become available during the first clinic visit and, if positive, the patient is started on CPT. World Health Organization (WHO) clinical staging for HIV infection, CD4 cell count measurement and other tests follow. These patients are supposed to be referred for pre-ART and ART care and recorded in the respective registers. Before December 2013, HIV-positive patients classified as WHO clinical stage 3 or 4 and/or with a CD4 cell count <350 cells/mm³ were considered eligible for ART initiation in Zimbabwe.13

Study site
Bulawayo is the second largest city in Zimbabwe, with an estimated population of 653 000 in 2012.14 Since the mid-1990s, decentralised TB diagnostic and treatment services have been provided through 19 primary health care clinics, one microscopy laboratory and one infectious diseases hospital. Since 2004, free-of-charge HIV treatment and care, including ART initiation and follow up, have gradually been decentralised and integrated into the general health services provided by the clinics. The national TB and HIV care recording and reporting tools are used. One of the city’s health facilities, Emakhandeni Clinic, which has a catchment population of 30 000, provides comprehensive curative and preventive services and manages on average 100 out-patients daily. It has no in-patient facilities. The staff consist of one visiting medical doctor, 10 nurses and seven auxiliary staff.

Study population
The study included all presumptive TB patients attending Emakhandeni Clinic between January 2009 and December 2013. HIV testing and test results were reported for all patients, and a more detailed assessment was undertaken for patients registered between 1 January and 31 December 2013.

Data variables, collection and source of data
For all presumptive TB patients registered between 2009 and 2013, information on HIV testing and results was collected. For those patients registered in 2013, additional data variables included: name, age, sex and TB status and, for HIV-positive presumptive TB patients, assessment for ART eligibility with clinical staging or

FIGURE 1 Number of presumptive TB patients by HIV testing status and result, Emakhandeni Clinic, Bulawayo, Zimbabwe, 2009–2013. TB = tuberculosis; HIV = human immunodeficiency virus.

CD4 cell count and ART and CPT initiation. Data were sourced from the presumptive TB, TB, pre-ART and ART registers and clinic-based patient ART folders. Patients in the various registers were linked by name, age and sex. The study data were collected from 1 March to 30 April 2015 and double-entered using EpiData Entry software (version 3.1, EpiData Association, Odense, Denmark).

Analysis and statistics
A descriptive analysis was performed using frequencies and proportions. Differences between groups were determined using the χ² test and the Wilcoxon rank sum test for continuous variables. Levels of significance were set at 5%. Data were analysed using EpiData Analysis software (version 2.2.182).

Ethics approval
Ethics approval for the study was obtained from the Health Services Department of the City of Bulawayo, Zimbabwe, and from the Ethics Advisory Group of the International Union Against Tuberculosis and Lung Disease, Paris, France. As the study was based on record review, informed patient consent was not required.

RESULTS

HIV testing and positivity rates among presumptive TB patients
Figure 1 shows the annual number of presumptive TB patients by HIV testing status and result from 2009 to 2013. The number of presumptive TB patients increased from 386 in 2009 to 565 in 2011, after which it stayed relatively constant; it was 422 in 2013. The proportion of patients tested for HIV increased from 56% in 2009 and plateaued from 2011 onwards, at 76–86%. Among patients tested for HIV, positivity rates decreased over consecutive years but remained high (77–88%).

Presumptive TB patients registered in 2013

Characteristics of newly diagnosed HIV-positive patients
Figure 2 shows the HIV and TB diagnostic cascade for presumptive TB patients registered in 2013. Of the 422

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Conflicts of interest: none declared.

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registered patients, 107 (26%) were already known to be HIV-positive, and of these, 30 (28%) were found to have TB and 103 (96%) had been started on ART (data not shown). Among the remaining 315 patients without a known HIV positive status, 255 (81%) were tested for HIV, of whom 190 (75%) were found to be HIV-positive. Of these HIV-positive patients, 26% were diagnosed with TB (15 by bacteriological confirmation and 35 by clinical diagnosis) and 71% without TB; 3% had no recorded TB test result. No differences in sex or age distribution were found between newly diagnosed HIV-positive presumptive TB cases with and without TB (data not shown).

**ART eligibility among newly diagnosed HIV-positive patients without TB**

Among the 134 newly diagnosed HIV-positive patients found not to have TB, data on ART eligibility were only recorded in 42 (31%) cases, of whom 40 (95%) were ART eligible (Table). Age and sex distribution was similar for those with and without ART eligibility data.

**CPT and ART initiation among newly diagnosed HIV-positive presumptive TB patients by TB status**

Among 184 newly diagnosed HIV-positive patients with a known TB test result, CPT and ART initiation was recorded for respectively 88 (48%) and 45 (90%) patients with TB vs. respectively 53 (40%) and 51 (38%) patients without TB ($P < 0.001$) (Figure 3).

<table>
<thead>
<tr>
<th>TABLE</th>
<th>Assessment of ART eligibility among newly diagnosed HIV-positive presumptive TB patients without TB, Emakhandeni Clinic, Bulawayo, Zimbabwe, 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Data on ART eligibility recorded</td>
<td>n (%)</td>
</tr>
<tr>
<td>Total</td>
<td>134</td>
</tr>
<tr>
<td>No*</td>
<td>92 (69)</td>
</tr>
<tr>
<td>Yes</td>
<td>42 (31)</td>
</tr>
<tr>
<td>Eligible for ART</td>
<td>40 (95)</td>
</tr>
<tr>
<td>WHO stage 3 or 4</td>
<td>23</td>
</tr>
<tr>
<td>WHO stage 1 or 2 &amp; CD4 &lt; 350 cells/mm$^3$</td>
<td>17</td>
</tr>
<tr>
<td>Not eligible for ART</td>
<td>2 (5)</td>
</tr>
</tbody>
</table>

*Includes any patient with 1) no WHO clinical stage or CD4 count recorded, or 2) WHO stage 1 or 2 recorded but no CD4 count recorded, or 3) no WHO clinical stage recorded and CD4 count $\geq$350 cells/mm$^3$ recorded.

**DISCUSSION**

This is the first study from Zimbabwe to report on how HIV-positive presumptive TB patients found not to have TB access HIV care at the primary health care level where decentralised and integrated TB and HIV services have been provided since 2008. Our study findings showed that of approximately 500 patients with presumptive TB registered annually, approximately 80% were newly tested for HIV, and that among those tested, HIV positivity was high. An assessment of patients registered in 2013 revealed that one in four patients was already known to be HIV-positive and undergoing ART. For newly tested patients, three quarters were found to be HIV-infected, and 70% of these were found not to have TB. Almost all HIV-positive patients without TB for whom data were available were eligible for ART. Nonetheless, HIV-positive non-TB patients were in general far less likely to be initiated on CPT or ART compared with HIV-positive TB patients.

The strengths of this study are that it involved a large number of presumptive TB patients and that it was conducted in a routine setting, thus likely reflecting the operational realities on the ground. In addition, the study adhered to the Strengthening the...
Reporting of Observational studies in Epidemiology (STROBE) guidelines.

Limitations included the use of routine register data, which were incomplete in certain areas and may have been inaccurate. We also assumed that the large numbers of newly diagnosed HIV-positive presumptive patients without TB and not recorded as having started ART or CPT were not initiated on these interventions. We do not know this for certain, however; it is possible that the patients received ART at the clinic without documentation or were initiated elsewhere without the information being communicated to Emakhandeni Clinic. Finally, it is possible that clinically diagnosed TB patients may have been misdiagnosed as having TB and, conversely, that in severely immunosuppressed patients, clinical TB may have been missed in view of the fact that up to one quarter of such patients with culture-positive M. tuberculosis disease can be sputum smear-negative and have a normal chest radiograph.

Previous studies reporting on the diagnosis and management of presumptive TB patients have found HIV testing uptake to range between 59% and 95%,17–22 which is comparable to our findings. In terms of ART enrolment, a study carried out in Harare, Zimbabwe, in the mid-2000s, a time when public health sector ART was largely unavailable, reported that only 15% of HIV-positive presumptive TB patients without TB were started on ART.3 We have demonstrated a better ART initiation rate among this patient group, although it is still much lower than among HIV-positive TB patients.

This study has several important programmatic implications. First, while the uptake of HIV testing among patients with presumptive TB was over 80%, attempts should be made to increase this to as close to 100% as possible, especially as the HIV positivity yield is high. This would not only be of benefit at the individual level, it would also assist Zimbabwe’s contribution towards the global goal of the joint United Nations Programme on HIV/AIDS (UNAIDS) to achieve its new 90–90–90 treatment targets for ending the AIDS epidemic.23 These targets specify that by 2020, 90% of individuals living with HIV will be diagnosed and know their HIV status, 90% of people with HIV infection will receive sustained ART and 90% of those on ART will be virally suppressed. Knowledge of HIV status for all patients is the gateway to this cascade.

Second, although data on ART eligibility for HIV-positive patients without TB were infrequent, most patients with available data were eligible. This suggests that this particular group of patients, similar to those with TB, could benefit from a ‘test and treat’ approach. Previous studies have already shown that HIV-positive presumptive TB patients without TB have high 12-month mortality,4 and as such, offering them ART regardless of CD4 cell count should improve survival and potentially reduce the risk of TB. Until then, the assessment of ART eligibility needs to improve, including all patients having a baseline CD4 cell count measured and recorded.

Third, national TB programmes need to invest in newer technology to improve TB diagnosis in HIV-positive patients. Sputum smear microscopy followed by chest radiography in those with negative sputum smears is currently the mainstay for TB diagnosis. This approach is time consuming, costly for patients who need to make multiple journeys to the clinic and diagnostically insensitive.24,25 The Xpert assay, which is more sensitive and enables a rapid TB diagnosis, needs to be scaled up.26

Fourth, more attention should be paid to follow-up and the monitoring of patients without TB. These patients enter the health system through the TB services, and it appears that once a diagnosis of TB has been excluded, their follow-up is weak. This is likely due to a lack of clear guidelines and monitoring of uptake of services. The situation must change: clear procedures are required to guide staff, and collaboration should be strengthened between personnel in TB and HIV services through mentorship and supervision to ensure effective referral of these patients for HIV care.

Fifth, and related to the point above, is the need for better recording and reporting of what happens to patients with presumptive TB, and especially those found to be HIV-positive. Registers for presumptive TB patients require additional columns explicitly for recording whether a newly diagnosed HIV-positive patient has been started on CPT and ART. Similarly, newly diagnosed HIV-infected patients, with or without TB, need to be recorded in the ART registers. The WHO should have a section in the annual global TB report on HIV testing and care for presumptive TB patients.

In conclusion, this study showed that in a primary health care setting in Zimbabwe, a high proportion of presumptive TB patients found not to have TB were HIV-positive and that of those with available data, most were eligible for ART. Unlike HIV-positive patients with TB, however, enrolment into HIV care for these non-TB patients was poor. A ‘test and treat’ approach and better TB-HIV service linkages could be life-saving for these patients, especially in southern Africa with high burdens of HIV and TB.

References
Contexte : Le centre de santé Emakhandeni, qui offre une prise en charge de la tuberculose (TB) et du virus de l’immunodéficience humaine (VIH) décentralisée et intégrée à Bulawayo, Zimbabwe.

Objectifs : Comparer la prise en charge du VIH pour les patients presumés tuberculeux, avec et sans TB, enregistrés en 2013.

Schéma : Etude rétrospective de cohorte basée sur les données de routine du programme.

Résultats : Sur 422 patients presumés tuberculeux enregistrés, 26% étaient connus comme VIH positifs. Parmi les 315 patients restants, 255 (81%) ont eu un test VIH, dont 190 (75%) se sont avérés positifs. Parmi eux, 26% ont eu un diagnostic de TB et 71% n’ont pas été confirmés positifs. Parmi les 315 patients restants, 255 (81%) ont eu un test VIH, dont 190 (75%) se sont avérés positifs. Parmi eux, 26% ont eu un diagnostic de TB et 71% n’ont pas été confirmés positifs. Parmi les 315 patients restants, 255 (81%) ont eu un test VIH, dont 190 (75%) se sont avérés positifs. Parmi eux, 26% ont eu un diagnostic de TB et 71% n’ont pas été confirmés positifs. Parmi les 315 patients restants, 255 (81%) ont eu un test VIH, dont 190 (75%) se sont avérés positifs.

Conclusions : Les patients présumés TB mais non confirmés avaient un taux élevé de positivité au VIH et pour ceux dont les données étaient disponibles, la majorité était éligible à l’ART. Par contre, pour les patients VIH positifs sans une TB confirmée, le taux de mise en œuvre du traitement préventif par cotrimoxazole (CPT) et l’ART a été médiocre. Une approche « tester et traiter » et de meilleurs liens entre les services pourraient sauver la vie de ces patients, surtout en Afrique australe où les taux de VIH et de TB sont très élevés.