Title:

High Tuberculosis Burden among People living with HIV in Southern Mozambique

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Summary

High burden of TB, in terms of incident cases and case fatality, in people living with HIV in a rural district in Mozambique.
To the editors:

Tuberculosis (TB) remains an important public health concern and a leading cause of disease and death worldwide. Mozambique is one of the few TB high-burden countries where TB figures have not improved in recent years, with an estimated TB incidence for 2013 of 552 cases per 100,000 [1]. With 58% of all notified TB cases being HIV positive it also has one of the highest TB/HIV co-infection rates. Published data on the burden of TB or HIV disease in the country are scarce, and improving epidemiological surveillance has been identified as an urgent step to improve TB control [2].

People living with HIV (PLHIV) are at a higher risk of developing active TB, which is the main cause of death among this population, accounting for 26% of AIDS related deaths [3, 4]. It has been estimated that in the African Region, 31% of new TB cases in adults were attributable to HIV infection [5]. Most TB incidence measurements among HIV patients come from HIV cohorts [6, 7], clinical trials or from mathematical modelling using different strategies described elsewhere [1]. Very few settings, especially in Sub-Saharan Africa provide population level estimates of TB risk among PLHIV [8, 9]. We determined the incidence rate of TB among HIV positive and negative individuals during 2011 in a high HIV burden setting in Southern Mozambique.

The study was conducted at the Manhiça Health Research Centre (CISM from its acronym in Portuguese), located in the rural district of Manhiça, Southern Mozambique [10]. This retrospective population-based epidemiological analysis used three data sources. TB notification data were obtained from the 2011 registries of the National TB Control
Program for the District of Manhiça, based on passive surveillance. Population at risk was calculated from the latest official census data (2007) for the District of Manhiça obtained through the Mozambican National Statistics Institute and the estimated population growth for 2007-2011 using annual data from CISM’s Demographic Surveillance System (DSS). HIV prevalence in the district population was estimated using community-based HIV seroprevalence data from a survey conducted in 2010 [11], which only includes adults aged 18-47.

TB laboratory diagnosis in 2011 was made through conventional smear microscopy using Ziehl-Neelsen staining. Culture was only done in TB previously treated patients at diagnosis. Samples were processed at CISM’s laboratory which is subject to an External Quality Assurance assessment. TB case definitions followed WHO guidelines [1]. TB incidence rate estimates are described with an uncertainty variability range (VR) based on the confidence intervals of the HIV seroprevalence study. In order to avoid bias by false-positive empirical diagnoses, the primary analysis of TB incidence rate among PLHIV, incidence rate ratio (IRR) calculations and population-attributable fraction (PAF) was based on bacteriologically confirmed TB cases. The PAF to HIV was calculated using the formulae: \( \frac{P \times (I - 1)}{(P \times I - 1) + 1} \) where P is the prevalence of HIV in the population.

A total of 637 TB cases aged 18-47 were diagnosed in the district of Manhiça in 2011, of which 53.4% were male and 278 (43.6%) were confirmed by sputum smear.

Bacteriological confirmation was higher among HIV-negative compared to HIV-positive TB cases (62.2% vs 39.4% respectively, p<0.001). The prevalence of HIV among TB confirmed cases aged 18-47 was 77.2% (206/267). Only 15.0% of patients were reported to be on antiretroviral therapy (ARVs) at TB diagnosis or during TB treatment. Among
PLHIV, 14.6% of TB confirmed cases died during TB treatment, compared to none among HIV uninfected adults.

The estimated TB incidence rate among adults aged 18-47 was 456 per 100,000 population. The incidence rate of confirmed TB among PLHIV aged 18-47 was 847 per 100,000 (VR 772-941), compared to 168 per 100,000 (VR: 158-180) among HIV negative population.

**Figure 1** shows age and sex-specific TB incidence rates. Among HIV positive male and female adults, the highest TB incidence rate was observed in those aged 38-47 with 1884 and 861 cases per 100,000 males and females respectively.

The IRR of confirmed TB among HIV-infected compared to HIV-uninfected adults was 5.04 (95% CI: 3.77-6.82). The IRR of TB was highest in the age group of 38-47 (**Figure 1b**). The proportional reduction on TB risk that would be achieved if we eliminated HIV from our adult population (PAF) aged 18-47 would be 61.7%.

To our knowledge this study is the first study in Mozambique providing estimates of TB incidence among HIV infected population and one of the few studies assessing TB incidence among PLHIV in a general population in Sub-Saharan Africa [8]. The high TB morbidity and mortality associated with HIV infection found in this analysis underscore the urgent need for improved and integrated control efforts for both diseases [12].

We found an extremely high incidence of laboratory-confirmed TB (847/100,000) among HIV-infected adults aged 18-47, varying with age and sex although persistently higher in males. These figures, which depend to a great extent on the country TB prevalence and ARV coverage, are in line with those found in African high burden countries [6, 8, 13], although some of these studies included active case finding, high risk populations (e.g.
mine) or different age groups. Given the passive nature of TB notification and the presumably low case detection rate for our district (which could be as low as 34% according to WHO country estimates for Mozambique [1]), the lack of more sensitive diagnostic techniques at that time (e.g. culture, Xpert) and the inherent difficulties in diagnosing TB among PLHIV (often smear-negative and presenting with non-specific symptoms), our estimate is a minimum and the true TB incidence among PLHIV is likely to be much higher.

Our findings showing a low IRR of TB among HIV infected population (5.04) compared with HIV uninfected population go in line with previous published data [13, 14], which suggest that the higher the HIV prevalence is in the community, the lower the IRR [3]. However, we are almost certain that the true IRR among HIV infected vs uninfected populations was higher due to the higher underreporting of TB among PLHIV. The main explanation for this is the difficulty to diagnose TB among PLHIV who more frequently have extrapulmonary/disseminated forms of TB or paucibacillary forms of pulmonary TB, both of which are not detectable through smear examination[15]. The PAF of tuberculosis due to HIV (61.5%) is probably one of the highest ever published in Africa.

The use of sputum smear as a diagnostic method for tuberculosis diagnosis is a serious limitation, since both culture and newer molecular methods have higher sensitivity and specificity, especially in PLHIV. Moreover, taking into account that almost 50% of the population of the country is younger than 15, we cannot extend our conclusions to this important age group. We could neither assess the impact of other potential factors which could help to stratify the risk among HIV infected population, such as ARV coverage, the level of immunosuppression or the time from HIV infection to TB diagnosis. The low
number of TB patients on ARVs needs further evaluation to assess whether this data reflects poor ART coverage or poor reporting due to absence of an integrated TB-HIV management at that time.

In conclusion, this study shows an enormous burden of tuberculosis, in terms of incident cases and case fatality among PLHIV in a rural district of Southern Mozambique. Acknowledging there is a high underdiagnosis, the true burden of TB among PLHIV could be enormous. These findings call for urgent public health interventions to reverse current TB / HIV epidemic.

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References


Figure 1. a) Incidence rate of confirmed TB among HIV infected and uninfected population in the district of Manhiça (year 2011); b) Incidence Rate Ratio of Tuberculosis among HIV infected population compared to HIV uninfected population by age group in the district of Manhiça (year 2011)