Article: HIV Coinfection in Multidrug- and Extensively Drug-Resistant Tuberculosis Results in High Early Mortality

Reviewer’s Comments:

Overall this study did a good job of describing the burden of MDR and XDR TB in the Tugela Ferry region of South Africa, and identified some important barriers to addressing the epidemic of drug resistant tuberculosis in resource-limited settings with high prevalence of HIV. It was a retrospective descriptive study, and used appropriate methods and statistical analysis for its data. However, some of the following changes could improve the study:

1. More emphasis on the aspect HIV Co-infection: The paper is about the impact of HIV co-infection on MDR and XDR TB, but there is little reference to the statistics regarding HIV infection, other than to say that this study was carried out in a setting with high HIV prevalence. I think it would be very helpful to have statistics showing the differences (if any) between the HIV positive and negative groups. Specifically, although the rates of coinfection were high, did the patients without coinfection share the same mortality statistics? What was their average survival time? It does not seem that the survival curve figures differentiate patients that do not have an HIV infection from those that do. While this would be a significantly smaller sample size, considering 98% of XDR TB patients were HIV positive, this data should be reported somewhere, or if possible included in the survival curve figure for comparison. Also of interest would be whether those patients receiving antiretroviral therapy at the time of TB diagnosis have different mortality profiles than those who start ART after diagnosis and treatment of their TB.

2. If available, it would be good to present more information about the TB treatment provided in this region. One of the main conclusions in the discussions session is that TB treatment programs in the area need to be strengthened, but little is provided about how patients are given access to care. In the methods section, it references that patients were given standard first-line TB treatment while awaiting culture results. More specifics on what this standard of care involves should be included, especially description of the standard drug regimens, whether these drugs are the same or different for HIV positive patients, and what is their cost to the patient, how they are distributed or if there are other barriers to care that might be of importance in a poor/rural area. This would serve to get a better sense of TB care in the area, as well as whether patients are effectively receiving the treatment they’re prescribed with.

The paper’s description of drug resistant TB cases was sound and the analysis of mortality among patients with drug resistant strains provides a valuable snapshot of the burden of drug resistance in South Africa. The findings regarding the first 30 day window of high mortality, and the authors’ conclusions, that faster diagnosis and treatment referral could help reduce this mortality, are well argued. However, the conclusion that this is because of HIV co-infection seems tenuous. It seems like the region’s high HIV prevalence is just assumed to be the reason for the unusually high mortality statistics, although this was not really proven using the data. References to other studies showing lower mortality rates in low prevalence HIV regions were only included in the introduction, not as substantive...
analysis. As such, I would recommend changing the wording to indicate that the two epidemics are closely interrelated instead of necessarily causal.