Reviewer’s report

Title: Association of high serum vitamin D concentrations with active pulmonary TB in an HIV co-endemic setting, Harare, Zimbabwe

Version: 0 Date: 04 Oct 2016

Reviewer: Peter Daley

Reviewer’s report:

Thanks for allowing me to review this manuscript reporting vitamin D levels among HIV infected and non-infected and pulmonary TB infected and non-infected patients in Zimbabwe. There is equipoise on the association between serum vitamin D and risk of infection or reactivation of tuberculosis. The paper is well written in good English, and contains a thoughtful discussion section. There are design problems which limit the conclusions that can be made on the data collected, some of which are acknowledged by the authors.

The populations are not matched, with the specimens for the HIV negative cohort coming from health care workers and HIV testing volunteers, and the specimens for the HIV positive cohort coming from a previous clinical trial. There were significant differences seen between groups with regard to age and gender, so comparisons made between these different populations cannot be completely valid. This is the primary design limitation and needs to be strongly included in the discussion and conclusions.

Patient recruitment is not clearly described in the manuscript. A Figure 1 outlining recruitment success should be added (how many patients were approached for consent, how many gave consent, how many were excluded for any reason). Furthermore, timing of measurement of vitamin D may have been at different stages of HIV or TB disease (prior to or during HIV treatment, early after TB infection or reactivation, paucibacillary or multibacillary TB, low CD4 or high CD4, cavitary or non-cavitary). These variables may affect vitamin D levels at the time of measurement. These data may not be available to the authors.

A few small additional improvements would be describing mycobacterial culture/smear/Xpert lab methods, "Mann-Whitney" instead of "Manney-Whitney", and don't reverse the order of "HIV/PTB" throughout the report.

A high threshold for retaining variables in the multivariable regression was used (p<0.25), but with the few variables included, this is not inappropriate.

Overall I think the conclusions are too strong for the design weaknesses, and the paper should acknowledge that it would be difficult to make a conclusion about this association with the data collected. Still, I think the paper should be revised and published.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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