Reviewer’s report

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

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Reviewer: Tamilarasu Kadhiravan

Reviewer’s report:

General comments

The authors studied serum vitamin D levels in 551 participants from Zimbabwe, and make comparisons based on HIV status and the presence of pulmonary TB. Contrary to previous studies, vitamin D levels were higher in participants with PTB. The strengths of this study are — a fairly large sample was studied, and vitamin D levels were estimated by CLIA.

Major comments

1. Study design: This was a cross-sectional study, not a case-control design as reported.

2. Extrapulmonary TB is common among HIV-infected persons. It is unclear whether patients with isolated extrapulmonary TB were excluded from the HIV+PTB- group.

3. If one carefully looks at the distribution of vitamin D levels (Fig 1), it appears that a handful of higher values are possibly influencing the observed difference in medians. Hence, it is prudent to rule out bias and confounding as possible explanations.

4. One potential reason could be that HIV-negative and HIV-infected participants entered the study through different enrollment strategies. In particular, the HIV-infected patients were participants in a trial of POC urinary LAM testing strategy. Could this have introduced a systematic difference among the participants?

5. Second, were any of the participants taking multivitamin supplements before enrolment? Could this explain a few values in the higher range?

6. The authors offer two potential explanations for the higher levels of vitamin D seen in PTB - low body-mass index as a result of malnutrition, and 1α-hydroxylase activity of granulomas. Were data on BMI and disease severity (such as radiological scoring) collected in this study? If available, the authors may test these suppositions.

Minor comments
7. Was the vitamin D assay validated against the VDSP standards?

8. Table 3: "Co-variates of serum vitamin D levels" - Since a logistic regression was used it would be appropriate to call this as co-variates of vitamin D status, rather than levels.

9. The adjusted ORs may be reported in the Table 3.

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

No

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

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