Reviewer's report

Title: Genotype-independent association between profound vitamin D deficiency and delayed sputum smear conversion in pulmonary tuberculosis

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Reviewer: Anna Ralph

Reviewer's report:

This is a well-conducted, interesting study which adds further to the literature on the association between vitamin D and TB. The questions are clear and methods are appropriate on the whole. Data analyses are sound.

Major compulsory revisions

1. Can the authors describe why they chose to categorise xray severity according to whether disease was unilateral or bilateral? There are better measures of radiological severity than this. Severe cavitary disease may be unilateral; mild disease with infiltrates which clear quickly may be bilateral. Robust severity scores correlate with time to sputum smear conversion but the x-ray severity categorisation here does not. Do the authors have records of cavitary status at least (still not the best severity measure on its own), or percentage of lung affected, and if so, can these measures be used in the uni- and multivariable models instead?

2. The crux of the results is time to smear negativity. According to Figure 3A, 80% of individuals with replete vitamin D concentration >25 converted to smear neg by 2 weeks, much faster than is usually expected. The majority of people at baseline had a low sputum smear grade, from what I can deduce (two thirds had <100 per 100 HPFs which I think is grade 1 or 2+). Can the authors elaborate on the quality of smear microscopy, specifically, any cross checking, whether the lab participates in QC processes, whether the follow up specimens were graded or classified as positive/negative only, and whether staff providing sputum smear readings were blinded to vitamin D status.

Minor essential revisions

3. Methods – page 5 line 133 – would be helpful to add in latitude here (mentioned in the discussion).

4. Line 147 – samples for vitamin D ELISA were stored at -20 degrees (a standard domestic freezer?)– can the author comment on stability at this temperature (instead of -70), average duration of storage, and any potential impact on results? also on accuracy/repeatability of the ELISA method used?

5. Participants were followed up for 8 weeks only yet figure 3 shows some were followed out to day 70. Please explain.
6. The comments in line 258 to 262 do not appear to relate to Table 4 (there is no mention of FF, ff or Ff in Table 4).

7. Line 275 – the authors express surprise that so many (54%) patients had vitamin D level <25, yet they had estimated (in the sample size calculation) that 79% would have vitamin D level <25. Can the authors address if there are social reasons for the low vitamin D levels, especially in women?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests