Reviewer's report

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

Version: Date: 10 January 2015

Reviewer: Zahra Hasan

Reviewer's report:

The manuscript by Junaid et al describes a cohort of pulmonary TB patients from Pakistan in whom vitamin D levels were determined, sputum conversion times determined and genetic polymorphisms for vitamin D R, DBP and CYP2R1 were determined.

The manuscript is generally well written. The data is presented clearly. The size of the study is sufficiently large to draw conclusions from. The work is important as TB is prevalent in Pakistan and vitamin D levels are found to be reduced in a large proportion of individuals.

Major compulsory revisions

Methods
Were sputum specimens from all patients who should a positive result at 2 weeks cultured with DST? This is not clear from the write up – in total how many sputum specimens were subjected to culture DST? Of these, who many patients were diagnosed as having MDR-TB

Line 246. How was MDR-TB managed? Was the patient put on MDR-therapy? If there was a treatment change then how was the time to sputum smear conversion calculated??

Minor compulsory revisions

Introduction. Some sentences are unnecessarily long and should be re-written in a simpler manner such as those in ‘line 106-109’, ‘line 115-119’, line 298-304

Methods
Line 165, the definition for HPF with the acronym should be provided the first time it is used

Give details as to how MTB culture and DST was performed.

Figure 1 is alright but some labels on the right side of the flow chart are redundant. It is not necessary to say ‘0 died’ or ‘0 lost to follow up’ so these can be removed

Discussion

The data related to Table 4 regarding the multivariate analysis of the genetic
polymorphisms should be placed in the Results section rather than the Discussion section.

The study makes the observation that reduced vitamin D levels were coincident with bilateral TB and delayed sputum conversion. However, it is not clear what was done when the vitamin D levels in these patients were found to be deficient. Was vitamin D supplementation provided? Were patients informed regarding their vitamin D status and advised to receive vitamin D supplementation?

There are several reports of vitamin D levels in the Pakistan population, lowered vitamin D levels have been identified in patients with TB. Also, vitamin D levels are found to be reduced in women. If the general population already has reduced vitamin D levels then it is the trend of deficient and insufficient levels in TB patients the same as the general population or is to different? The authors should give their hypothesis as to what they believe could be the reason for low vitamin D levels in TB in this population.

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.