Title: Overt Diabetes Mellitus among newly diagnosed Ugandan Tuberculosis patients: a cross sectional study.

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Author's response to reviews: see over
Responses to the reviewers comments for the manuscript “Overt Diabetes Mellitus among newly diagnosed Ugandan Tuberculosis patients: a cross sectional study”.

We would like to express our appreciation for the very constructive criticism and comments by the reviewers. Below is a point-for-point the responses to the reviewers’ concerns.

REVIEWER 1. Fiona Young.

1. A really interesting piece of research within the field of TB-DM. Title and abstract clearly convey papers key points. Appropriate, and well defined, methods have been used to address succinct research questions. Data collected are sound and reported appropriately. Discussions and conclusions are well balanced and adequately supported by the data provided with limitations clearly stated. Very thorough discussion of previous work completed in the area and appropriate reference given to the outcomes from the expert meeting paper.

We truly appreciate the reviewer’s positive compliments.

2. Please clarify the second sentence of the abstract methods section - were lab data collected by validated questionnaire?! Or as well as the data collected by validated questionnaire?

As noted by the reviewer, we have corrected this section as highlighted in paragraph three of the abstract to read “Laboratory findings as well as the socio-demographic and clinical data collected using a validated questionnaire was obtained.”

3. In paragraph two of the background it may be worth noting that the reason this is of great public health importance within SSA countries is due to the dual burden of communicable and non-communicable diseases.
We have accordingly revised the statement as follows “currently, both TB and DM are of great public health importance globally especially in Sub Saharan Africa (SSA) due to the converging epidemics of both communicable and non communicable diseases.

4. I'd argue recent evidence to support the association is good but not unequivocal - e.g. few studies have assessed the association amongst groups with high HIV rates or assessed co-linearity between the risk factors such as age. You may want to temper this statement. We agree with the reviewer and in response, we have changed the sentence on recent evidence to support the association between DM and TB to “There is plausible evidence to support the strong association between DM and TB” instead of using the word unequivocal.

5. There is a repetitive use of % in the statistical methods section. In Table 1, 2 and 3 please remove the dash before mean figures as it reads as if a minus symbol.
   We have deleted some %s in that section. We used % to offer a better descriptive presentation of the data. We have removed all the dashes in the tables.

6. Does Uganda truly have the highest prevalence or incidence of TB in SSA. Please refer to the WHO global TB incidence and prevalence figures.
   We have revised this to state Uganda is one of the high burden TB countries in SSA.

7. In discussion it is perhaps worth mentioning the dates of some of the other studies. Given the trends of DM incidence in SSA it wouldn't be too surprising to find higher rates of DM now than some of the older studies have.
   Thank you for this suggestion. The periods when the African studies on DM among TB patients has been included in the 2nd paragraph of the discussion section as 1980-2006.

8. In discussion upon hepatitis and its effects upon DM status you may wish to site a recent paper by E.Sobngwi and colleagues.
We agree with the reviewer’s suggestion and in response, we have written about studies supporting the possible etiological role of the hepatitis viruses and other viruses in the etiology of type 2 Diabetes Mellitus (references 37-41, paragraphs 9 and 10 of the discussion section). The literature by E. Sobnogwi and colleagues has been referenced (reference 41, paragraph 10, discussion section).

9. It is interesting to note the poor glucose control amongst individuals with DM, this warrants further discussion.

The cause of poor glycemic control among DM patients with TB infection has been briefly discussed in the text (6th paragraph of the discussion section).

REVIEWER 2: Christopher Czaja

1. It appears from the tables that HIV is inversely associated with DM (ie persons with glucose <200 are more likely to be HIV positive). This is not clearly stated in the results, and the discussion seems to argue how HIV may lead to higher glucose.

We agree with the reviewer’s observation. We reviewed our data and noted a coding error. This has been rectified and we have corrected this in the table and the results section (HIV correlation-OR 0.32 95% CI=0.13-0.79, p=0.016) for bivariate analysis and (OR 0.17 95% CI 0.06-0.51 p=0.002) on multivariate analysis. In addition we think that cotrimoxazole prophylaxis which is routinely given to patients with HIV-infection may explain the apparent protective effect of HIV infection on DM as it has been shown to have hypoglycemic effects. However, we have also acknowledged that the relationship of DM and HIV in our study needs interpretation with caution.

We have no apparent explanation as to why HIV appeared protective of DM in our study.
2. I am not familiar with the Kish-Leslie sample size calculation, but a calculation of sample size was done but the justification for the sample size is not clear. What is the minimum sample size needed to show?

The sample size calculation was done in order to enable our study to recruit the minimum number of patients to detect a statistically significant relationship between DM and TB. We used an 80% power, a two-sided critical level of 0.05 and a prevalence of 13.2% of DM among TB patients in Indonesia to calculate the minimum desired sample size.

3. In Tables 3 and 4, the OR's for continuous variables are hard to interpret. Is the OR odds of DM per unit increase in the covariate? Can you specify the unit increase (eg per 1 U increase in AST)? Also, some of the 95%CI's for these covariates don't include the point estimate.

We agree with the reviewer’s concern and in response we have categorised the continuous variables into the normal and abnormal variable cut off points and compared the association between these and the random blood sugar levels by use of the chi square test or Fischer's exact test where appropriate. Bivariate and multivariate analysis has then been done. The new odds ratios for the continuous variables on bivariate analysis reflect the odds of DM in those with abnormal variable values in comparison to those with normal variable values.

In the multivariate regression output, for every unit increase in the ALT level there is a corresponding increase of RBS by 2.4 units. This has been noted in the results section.

We have cross checked all the OR and 95% confidence intervals and we have had them revised.
4. As these are all patients admitted to the hospital, are you able to comment on the prevalence of DM among all or non-TB patients admitted to the hospital?

*Thanks for the suggestion. We have cross checked the medical records and noted that the background prevalence of DM in all the medical units in the hospital during the study period was 6.4%, lower than what we obtained among the TB patients.*

5. Results paragraph 1: indicates a 76% prevalence of EPTB which is the reverse of what is listed in Table 1. I suspect the Results are intended to indicate 76% prevalence of PTB.

*Thank you for pointing this out. The error in the sentence in paragraph 1 of the results section has been corrected.*

6. Table 2: can you list a normal range for some of the laboratory values (eg. ALT, ALP).

*Thank you again. The normal values of some laboratory parameters have been inserted into the table.*