Author’s response to reviews

Title: Distribution and transmission of Mycobacterium tuberculosis complex lineages among children in peri-urban Kampala, Uganda

Authors:

- Eddie M Wampande (wamps@covab.mak.ac.ug)
- Ezekiel Mupere (mupez@yahoo.com)
- Devan Jaganath (djaganath@mednet.ucla.edu)
- Mary Nsereko (mnsereko@mucwru.or.ug)
- Harriet K Mayanja (hmk@chs.mak.ac.ug)
- Kathleen Eisenach (eisenackathleen@uams.edu)
- Henry W Boom (whb@case.edu)
- Sebastien Gagneux (sebastien.gagneux@unibas.ch)
- Moses L Joloba (mlj10@case.edu)

Version: 5 Date: 23 June 2015

Author’s response to reviews: see over
To the Journal Editorial office
BMC Pediatrics

Dear Sir/Madam
We write to thank you for accepting our manuscript for review, enclosed you will find our revisions with original title: “Severe disease in children a measure of tuberculosis transmission demonstrates that Mycobacterium tuberculosis lineages circulating in peri-urban Kampala transmit equally” and now the new title is “Distribution and transmission of Mycobacterium tuberculosis complex lineages among children in peri-urban Kampala, Uganda”. In the revised version 49 of 118 samples were excluded since they were not part of the approved study. We have re-analyzed the data and revised the manuscript using 69 patients, the outcome does not affect our conclusions and discussion.

We have also included in our submission a step by step response to the comments as highlighted by the reviewers.

Thank you,

Eddie M Wampande
On behalf of the co-authors
Response to reviewer 1

Dear Dr. Ehsan Aryan,

Thank you for accepting to review our manuscript that we submitted to BMC pediatrics and for the positive comments. We have looked at the comments and we have provided point by point responses as shown below.

A. Minor revisions

1. Page 2 line 37 and page 5 line 91: the period of the study has been mentioned 2002-2010 while in page 8 line 160 it has been mentioned 2000-2010.
   Response: We have corrected this anomaly in the manuscript; the study period is 2002-2010 (See line 41-42, 88-89 and 162-163).

2. Page 8 line 161: the number of children aged up to 5 years should be changed from 77% to 66% (78/118).

3. Page 8 line 162: the number of HIV positive children should be changed from 8.8% (10/114) to 10% (11/114) according to data presented in Table 1.

4. Page 8 line 165: the number of TST positive children should be corrected according to data presented in Table 1.
   Response for 2,3 & 4: We have accurately recomputed the proportions of children with the different TB risk factors (See table 1, page 20)

5. In figure 1, MIB genotype should be corrected to MTB genotypes.
   Response: We have deleted figure 1 as advised by reviewer 2
Response to reviewer 2

Dear Dr. Laura Rindi,

Thank you for accepting to review our manuscript that we submitted to BMC pediatrics and for the positive comments. We have looked at the comments and we have provided point by point responses as shown below.

**Major comments**

1. To better understand the transmissibility of the MTBC lineages, I strongly suggest authors to evaluate the genetic diversity among isolates by MIRU-VNTR analysis, a highly discriminative typing method that has been extensively used in molecular epidemiology surveys.

   **Response:** True we agree MIRU-VNTR has been used extensively in TB molecular epidemiology surveys; one of the limitation of our methodology is the inability of SNP typing assay to discriminate strains (See line 243-242), however they are robust markers in defining MTBC lineages unlike MIRU-VNTR that is prone to convergent evolution due to homoplasy, thus we think the information provided by SNP typing is more accurate than what MIRU-VNTR would give (Comas et al, 2010, Coscolla and Gagneux, 2014, Kato-Maeda et al, 2012).

2. The authors should make an effort to revise the discussion section.

3. The paper needs to be revised by an English-mother-language scientist

   **Response for 2 & 3:** We have revised the whole manuscript where necessary with the help of language experts; we were also advised to change the title to one that best suits the message in the manuscript.

**Minor comments**

1. Figure 1 is not really needed and should be deleted

   **Response:** We have deleted figure 1