Author’s response to reviews

Title: Spoligotyping based genetic diversity of Mycobacterium tuberculosis in Ethiopia: A systematic review

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Point by point response:

- First of all, the reason why we focused only on Spoligotyping is there are limited published data on other techniques like MIRU-VNTR, RFLP and Genome Sequencing and as a result, we could not get a comprehensive genetic result representing the nine regions of Ethiopia. However, we found that Spoligotyping genetic results covers a wide range of geographical set up.

- The number of isolates and strains identified were 3071 and 3067 respectively. This is due to some isolates might have similar strains. As the number of isolates and strains varies in different study identified it was difficult for specifying the four strains.
- Introduction section:
  o Page 2, 2nd Paragraph: 30th changed to 30
  o Page 2, 2nd Paragraph: “TB is the leading causes” changed to “TB is one of the leading causes”

- Genomics of M. tuberculosis section:
  o Page 3, 2nd paragraph, 2nd line- “(MTBC) known by causing TB diseases” changed to “(MTBC) known to cause TB”
  o Page 3, 2nd paragraph: The sentence 'The outer membrane of M. tuberculosis possess a lipid bilayer of long fatty acids ... the two most effective anti-TB drugs" is deleted.
  o Page 4, 2nd paragraph: “On the other hand, others” changed to “On the other hand, other”
  o Page 4, 3rd paragraph: “is” is inserted after the word “spoligotyping” in the sentence “Although spoligotyping also…”.

- Materials and methods section:
  o Page 6, 1st paragraph: the word “Country” is replaced by “country”.

- Result section:
  o Page 7, 2nd paragraph: “In the understanding strain diversity”, “the” is deleted.
  o Page 7, 2nd paragraph: in the sentence “In lining with this, there were only few studies reported...““, the word “which” is added before the word “reported”.
  o Page 7, 2nd paragraph: in the phrase, “(missing spacers 4-24) were sequenced using...”, the phrase “were sequenced” is deleted.
  o Page 7, 4th paragraph: in the phrase “On the other hand, a highest number of strains”, “a” is deleted

- In Table 1, raw 1, the number of strains isolated by Agonafir et al., was corrected to 81.

Addional language edition made to the manuscript

- Abstract section:
  o Page 1, background subsection: “the” is deleted from the phrase, “paramount importance for the tuberculosis (TB) control program of that country”
Page 1, Methods subsection: space is removed between “key” and “words” and changed to “keywords”.

Page 1, result subsection: hyphen is inserted between “Twenty” and “one”.

- Introduction section:
  
  Page 2, paragraph 1, line 5: “were” changed to “was”.
  
  Page 2, paragraph 1, line 6: “,” removed after that.
  
  Page 2, paragraph 2, line 3: “were” changed to “was”.
  
  Page 2, paragraph 2, line 5 and 6: hyphen is inserted between “drug resistant” and “multidrug resistant” words.
  
  Page 3, paragraph 3, line 6: space removed between “extra pulmonary” and changed to “extrapulmonary”.
  
  Page 3, paragraph 4, line 4: “the” is added before the word “presence”.

- Genomics of Mycobacterium tuberculosis section:
  
  Page 3, paragraph 1, line 3: “,” is removed after the word “sequences”.
  
  Page 3, paragraph 1, line 6: “have” is changed to “has”.
  
  Page 4, paragraph 3, line 3: “a” is added before “great deal of information”
  
  Page 4, paragraph 3, line 6: space is removed between the “hyper virulence”
  
  Page 4, paragraph 3, line 6: hyphen is added between “human associated”
  
  Page 4, paragraph 4, line 7: “the” is added before the word “ chromosome”
  
  Page 4, paragraph 4, line 9: “provides” changed to “provide”
  
  Page 4, paragraph 5, line 1: “Spoligotyping” changed to “Spoligotyping”
  
  Page 4, paragraph 5, line 1: “are” is changed to “is”
  
  Page 5, paragraph 7, line 2: “the” is added before the word “majority”
  
  Page 5, paragraph 7, line 3: “;” is added after the word “result”
  
  Page 5, paragraph 7, line 5: “of” is removed.
  
  Page 5, paragraph 7, line 6: “a” after the word “reviewed” is removed
Page 5, paragraph 7, line 6: “the” is added before the phrase “genetic diversity”
Page 5, paragraph 7, line 7: the space between “extra” and pulmonary is deleted.

Methods and materials section:
Page 5, paragraph 1, line 2: “,” added after “2017”
Page 5, paragraph 2, line 3: a space removed between “in” and “to”
Page 6, paragraph 3, line 2: “the” added before the phrase “Ethiopian population”
Page 6, paragraph 3, line 5: “land locked” changed to “landlocked”
Page 6, paragraph 3, line 8: “ethno-linguistic” changed to “ethnolinguistic”
Page 6, paragraph 4, line 6: “,” added after the word “lineages”
Page 6, paragraph 5, line 1: “were” changed to “was”
Page 6, paragraph 5, line 2: “it among” changed to “it to”
Page 6, paragraph 5, line 2: a multi-marker

Result section:
Page 6, paragraph 1, line 2: “in-terms of” changed to “based on”
Page 7, paragraph 2, line 4: “lining” changed to “line”
Page 7, paragraph 2, line 5: “few” changed to “a few”
Page 7, paragraph 2, line 9: “the” is inserted before “Northern”
Page 7, paragraph 4, line 1: “the” is inserted before the word “highest”

Spoligotyping results of M. tuberculosis strains from Ethiopia subsection:
Page 8, paragraph 1, line 2: “,” is added after the word “review”
Page 8, paragraph 1, line 11: “was” replaced by “were”
Page 8, paragraph 1, line 12: “were” replaced by “was”
Page 8, paragraph 1, line 14: “were found orphan” changed to “was found to be orphan”
Page 8, paragraph 4, line 3: “make” changed to “makes”
- Discussion section:
  o Page 9, paragraph 1, line 2: “the” is added before “Indian Ocean”
  o Page 9, paragraph 1, line 7: “contributed in” changed to “contributed to”
  o Page 9, paragraph 1, line 9: “the” is added before the word “colonial”
  o Page 9, paragraph 2, line 2: “,” is added after the word “result”
  o Page 9, paragraph 2, line 5: “,” is added after the word “Oromia”
  o Page 10, paragraph 2, line 9: “investigation for” changed to “investigation to”
  o Page 10, paragraph 2, line 10: “,” added after the word “result”
  o Page 10, paragraph 2, line 11: “a” is added before the word “complex”
  o Page 10, paragraph 3, line 6: “a” is added before the word “high”
  o Page 10, paragraph 3, line 6: “data bases” changed to “databases”
  o Page 10, paragraph 3, line 6: “,” is removed after the word “lineage”
  o Page 10, paragraph 4, line 3: “,” is added after the word “Oromia”
- Strength and Limitations section:
  o Page 10, paragraph 1, line 1: “the” is added before the word “genotype”
  o Page 10, paragraph 1, line 5: “is removed before the word “primarily”
- Conclusion section:
  o Page 11, paragraph 1, line 5: “the” is added before the word “high”
  o Page 11, paragraph 1, line 10: “drug resistant” changed to “drug-resistant”