Author’s response to reviews

Title: Molecular detection of fluoroquinolone-resistance in multi-drug resistant tuberculosis in Cambodia suggests low association with XDR phenotypes.

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Author’s response to reviews:

Dear Editor,

We thank you very much for your feedback concerning our manuscript. We have taken into account all comments of the reviewer Angel Cataldi. There was no comment from the other reviewer. We have slightly modified the wording of the title and of several paragraphs after including modifications required by the reviewer.

Here are our responses to the questions and comments of the reviewer:

Question:

All recent papers about FQ resistance presenting results of molecular detection compare it to phenotypic-gold standard test. It is not clear why it was not possible to do that in this work. Moreover, the authors state that the percentage of FQ resistant isolates that carry gyrB mutations was found to be highly variable by other authors.

Answer:

As indicated in our manuscript, there is no available second line DST in many developing countries including Cambodia. This is why the aim of this paper was to test the usefulness of molecular DST for second line drugs. The vast majority of FQ-R phenotypes are associated with known gyrA mutations. A few gyrB mutations are associated with FQ-R, however, the number of such cases is low.
and very variable as shown by the different studies we have gathered on our WEB site (moleculartb.org).

Comment:
Page 2, Introduction: a reference is needed after “Indeed, only nine of the 22 high burden countries (HBCs), who account for 80% of incident TB cases, had access to second-line DST” (reference).

Answer:
The reference has been added.

Comment:
Page 3 Methods: the inclusion and exclusion criteria of simples are not explained. Were all strains isolated during the collection period included?

Answer:
We have modified the paragraph to indicate the criteria for selecting strains included in our study.

Comment:
Page 4, Results: data of spoligotyping 53 full susceptible trains are not presented. This omission of information makes difficult to perform a full genotypic analysis.

Answer:
The non MDR strains have been spoligotyped. Results are presented in table 3 together with antibiotic resistance information.

Comment:
Page 5, Results: a reference is needed after “This polymorphism is not associated with resistance”.

Answer:
The reference has been added.
Page 7: I suggest to rephrase the following paragraph “The percentage of FQ-R M. tuberculosis clinical isolates with gyr mutations ha been found to vary markedly. Some studies have reported between 2 and 50% whereas others have found almost 100% [7]. Because we have no access to FQ-R phenotypic tests, our analysis may have missed a few cases.” The point is that much (and not few) cases will be missed if the percentage of strains with gyrB mutations are close to 2%.

Answer:
The modification suggested has been introduced.