Author’s response to reviews

Title: Distribution of Candida albicans and non-albicans Candida species isolated in different clinical samples and their in vitro antifungal susceptibility profile in Ethiopia

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Author’s response to reviews:

Point by point responses to comments of Reviewer 1.

First of all we thank you for your time and important comments that can improve our work. Point by point response to your comments are given below for your kind consideration.

1. Your comment on page 1 line 37.
   - Your comments are constructive and we have accepted your comment by changing prospective study to descriptive study.

2. Your comment on page 1, line 42 was corrected, i.e., sits was changed into sites.

3. Your comment on page 2, line 33 was modified as per your comment.

4. Your comment on page 3 lines 43 to 54 has been rewritten as per your comment.

5. Your comment on page 5, lines 7-12. The swabs used were cotton swabs. As far as blood sample is considered, it was not deliberate exclusion but patients with blood stream candida infection were not referred to Arsho Advanced Medical Laboratory.

6. Your comment on page 6, lines 33-38. It a rule. Collection of clinical samples without coding is never practiced in Arsho Advanced Medical Laboratory. However, we have removed double entered as it is not relevant.

7. Your comment on page 6, lines 15-17 has been elaborated as per your comment.

8. Your comment on page 4, line 4-7 has been modified as per your comment.
9. Your comment on Page 7, lines 12-28. Since the number of per infection site were not the same and are not large, reporting percentage of each sample category that was positive for yeasts appeared to as less meaning full as normative statistical analysis.

10. Your comment on Page 7, lines 28-33, was accepted and corrected

11. Your comment on page 7 lines 59 to page 8, line 4. There were some mistakes and they were corrected. As far as C. famata and C. ciferrii are considered, all isolates including C. famata and C. ciferrii were tested against the five antifungal drugs. However, MIC values to all drugs against C. famata and MIC values of capspofungin and micfungin against C. ciferrii were not provided by the machine. Please refer table 3. Possible explanations for the issue are given in the discussion section of the paper

12. Your comment on page 9, line 11, yes you are correct. The most dominant yeasts isolated various from one study to another as we have tried to show such various in table 3. As you said these difference could be affected by many factor

13. Your comment on page 9, lines 53, mistake in spelling was corrected

14. Your comment on page 10, lines 16-25. This is one of the limitation of phenotypic identification by VITEK. The problem is associated with only C. famata. Hence we recommended that all yeasts identified as C. famata should be confirmed by molecular methods

15. Your comment on page 10 line 43 we have accepted your comment and corrected the percentage

16. Your comment on page 8, line 4 was absolutely right. The mistake that we committed here is an extension of the mistake from page 8, lines 4-9 in the original paper. This has been corrected in page 8 in the revised document.

Response to your general comments

Yes, the study has a number of limitations, and these limitations were encountered for the following reasons

- As per your comment this study was not prospective but it was rather descriptive as the requisition form filled up by physicians was used as standard preformat for patient information. Unfortunately, clinical data of the study participant were not recorded in the request form. However, patients are referred to diagnostic laboratory by the physician is to confirm his clinical findings. We hope our study have some clinical importance

- Although we aware that candidemia is a life-threatening fungal infection, it was not included in our study. This is because no patient with candidemia was referred to Arsho Advanced Medical Laboratory.
Your comment regarding shift of C. albicans to non-albican candida species

- Candida albicans is the most common cause of candidiasis accounting for about 60-80% of infections. However, in our study the proportion of Candida albicans to non-albicans candida species is nearly equal i.e., 104 to 90 indicating a shift from a predominance of C. albicans to non-albicans candida species. Increased rate of detection of non-albicans candida species by VITEK or true prevalence could be possible reasons. This should be sorted out by doing more studies. In general, our work appears to be essential in country where diseases of fungal origin are considered as a neglected diseases like other tropical diseases in the sub-Saharan region. Therefore, our study could serve as baseline data for further comprehensive studies in the future even many limitations.

Comments regarding reference

- Attempts were made to up-to-date our references by including more recent literatures suggested by the reviewer.

Reviewer 2

First of all we would like to extend our thanks to you for appreciating our work as such type of work in African countries is lacking. Here are our point by point responses to your constructive comments for your kind consideration. we thank you for your time and important comments that can improve our work.

Response to your comment with regards to shifting of C. albicans to non-albican Candida species.

- Candida albicans is the most common cause of candidiasis accounting for about 60-80% of infections. However, in our study the proportion of Candida albicans to non-albicans candida species is nearly equal i.e., 104 to 90 indicating a shift from a predominance of C. albicans to non-albicans candida species. Increased rate of detection of non-albicans candida species by VITEK or true prevalence could be possible reasons. This should be sorted out by doing more studies. Our work appears to be essential in country where diseases of fungal origin are considered as neglected diseases like other tropical diseases in the sub-Saharan region. Therefore, our study could serve as baseline data for further comprehensive studies in the future.

Response to your comment regarding the shifting scenario in the discussion Page 9
• We have modified Table to by adding year of publication and hence the changes made in table 2 improves the shifting scenario in the discussion on page 9.

Response to your comment regarding the inclusion of Ethiopia in the tile of the manuscript has been well taken.

Response to your comment that our work appears to be partly a review and partly original research

The work is an original one. As you know the predominate yeast isolates vary from one study to another. This could be because of difference in study population, the type of clinical sample, immune status of patients, and/or geography. Inclusion of the results of previous similar studies in table 2 is merely for comparison purpose in a very short form. Inclusion of year of publication of previous works in table 2 could solve the problem your raised.

Comments regarding minor language problems, we have go through the manuscript ones more and we think the language has been better than the previous one

Comments regarding references

• We have up-dated our reference as per your suggestion.

Comments Regarding table 4

Break points of isolates against the five antifungal drugs tested varies from one strain to another within the same species. We think this have clinical significance and hence we preferred to keep as it is.

Your comment given as content corrections have been modified. We have also edited fond/ bold as per your comment