Author’s response to reviews

Title: Clinical and immunological failure among HIV positive adults taking first line Antiretroviral therapy in Dire Dawa, Eastern Ethiopia

Authors:

Getinet Lenjiso (aberagetinet@yahoo.com)
Birhanu Endale (seyoumbe07@gmail.com)
Yadeta Bacha (yad_de2005@yahoo.com)

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Author’s response to reviews:

Reviewer #1

1. List of patients in each health institutions are Sampling frames not sampling procedures, so the statement on page 5 line number 15 (sampling procedure) shall be replaced by sampling frame.

   - Response: Corrected as recommended; Highlighted in yellow on page 6, line 29

2. Since, Binary logistic regression model is one among others, the statement binary logistic regression models on page7, line number 10, shall be “binary logistic regression model was used”

   - Response: Corrected as recommended; Highlighted in yellow on page 7, line 24

3. The statement “Only 33 (15%) of the study subjects with failure were” seems incomplete, so it might be better to say “Only 33 (15%) of the study subjects with failure status were”

   - Response: Corrected as recommended; Highlighted in yellow on page 11, line 7

4. Usually, data are plural, but the author expressed data as singular (example, in the methods section, page 5, line number5.)
- Response: Editorial work has been done throughout the manuscript as much as possible including the example mentioned in here.

5. Table3, page 12, line number 37 needs careful edition.
- Response: A missing bracket identified and corrected as highlighted in yellow

6. Page 13, line number 45 (Among patient identified as failure ) this also needs revision since this statement should be written as “Among patients identified as failure”
- Response: Corrected as recommended; Highlighted in yellow on page 14, line 11

7. Generally the manuscript needs series language edition by language expertise?
- Response: I couldn’t find a fluent language expert but a thorough language review is made and edited accordingly

Questions/ concerns raised in the manuscript

1. Since the study was cross sectional, why adherence level (poor adherent and good adherent percentage) at the time of survey not included in the descriptive part of Table2 in the investigation like other clinical characteristics?
- Response: As indicated in the multivariate analysis, adherence is one of the variables included as clinical characteristics. Adherence at different follow up times was looked at but the significant association was found when adherence is evaluated at the time of least CD4 record during on ART follow up. This is unknowingly missed from the descriptive part but now I have included it both in the narrative and in Table 2. (page 9, line 39-42 & page 10, table 2, line 28-31)

2. Why the author used oldest version of the SPSS software (version 16)? Now days we have SPSS software version 23 and more recent version. If the data were analyzed using latest versions, there may be results different from existed in the paper. Therefore, I recommended using latest version of the software.
- Response: I was able to access SPSS version 16 by the time I did the analysis. But now, I couldn’t find the time to re-analyze the data because of personal reasons. I hope the differences as the result of the SPSS versions difference are not significant once.

3. Why pre-testing was conducted outside the study area? As far as my knowledge is concerned, it should be tested within the study area (Data collection sub-section).

- Response: This was done just to avoid the introduction of any new changes in the recording system by healthcare workers during pre-testing the questionnaire and before the actual data collection started; there by minimizing any kind of biases introduction.

Reviewer #2

1. Title....... Remove the repeated phrase "Antiretroviral therapy". You may modify the title as "clinical and immunologic failure among HIV positive adults taking first line antiretroviral therapy Dire Dawa, Eastern Ethiopia"

- Response: Revised as recommended (the changes in the title are highlighted in yellow)

2. Abstract, objective.... Remove the date

- Response: Corrected by deleting the date (page 2, line 19)

3. Introduction ....... Introduction should be well organized and have a meaning full flow that contains ideas related to HIV, benefits from ART, the challenges of treatment failure, brief review of studies done on the topic in Ethiopia justification for the current study and finally the objective of this study.

- Response: As per the recommendation, the introduction section is revised by including relevant information and editions

4. Material and methods, design...... Add the total number of RVI patients served at the health facilities of Dire Dawa

Add separate "study area" sub section
5. Material and methods, measurements. Definition of treatment failure should be connected to virologic failure. Clinical and immunologic failure may not necessarily be true failures. Modify the title as clinical and immunologic failure rather than treatment failure.

- Response: Modified as per the recommendation both at the title, objective, methods, result and discussion sections as appropriate (it is highlighted in yellow in all the revised sections).

6. Material and methods, Data collection. Mention how the data collection tool was developed. Cite relevant literatures reviewed or previously used tools.

- Response: The source of the data collection tool development is included (page 6, line 51–53).

7. Result, table 1. What is your standard for age classification eg old is >65 while you put >55 as the highest class. Mention "others" under the table.

- Response: The age group is classified based on the reviewed articles which I believe is relevant for the purpose of comparison (for example the study done in Ethiopia (study 13) uses the same age classification); Others – included (page 9, under table 1, line 19-20).

8. Table 2. Why you take cut point for CD4 as 100, why not 200 or 350.

- Response: Similar reason as the above, for comparison purpose; (e.g. study 13).

9. Page 9 line 34. Not clear, Rewrite the sentence.

- Response: Revised as recommended: Page 9, line 34-37.

10. Factors associated with first line ART failure. How can death be a factor for treatment failure? It is a result of failure but not a reason for it.
- Response: It is re-stated as “clinical characteristics associated with clinical and immunological failure” (page 11, line 19)

11. Discussion line 43-45........ clinical failures =19.3%, immunological failure= 2% both= 1.4% did patients with both failure counted in the immunologic failure or clinical failure? if so the overall failure rate should be 20.3%. If not add the word 'only' with immunologic and clinical failures.

- Response: The overall failure is 22.7%. So the word “only” is added as recommended (page 13, line 2 – 4)


- Response: The sentence is rephrased, page 13, line 14-17

13. Page 13 Line 12-15...... "It also shows a gradual decline in the magnitude of treatment failure overtime"….. did you do cohort study to see this. Your study is cross sectional which cannot give you such information.

- Response: The sentence is deleted as commented, it doesn't give sense

14. Page 13, Line 34-41............ 'enrolled to care with severe immune suppression'….show the mean baseline CD4 in your study and study in reference 20 to support this claim. Is the adherence in study 20 better than your sample patients.

- Response: Revised as recommended (for the CD4) page 14, line 4-7; For the adherence, only the finding from the study is mentioned as there is no reported finding from study 20

15. Page 13, Line 49-53........... "This shows that patients who are failing on first line regimen are not or not timely switched to second line regimen"……..do you think that all patients with clinical or immunological failure should be switched to second line regimen without confirming for viral load?

- Response: No, I don't think they should be, hence, the sentence is rephrased as “This might show that ….” Page 14, line 15-18. With the current availability of viral load testing, switching is
recommended after doing viral load test and following a management protocol. But before &
even now in areas where viral load testing is inaccessible, clients with clinical and
immunological failure may be switched after addressing barriers to adherence & treating OIs

16. Conclusion, line 7-10....... Did all patients with 'ambulatory or bedridden functional status'
have treatment failure. Line 7-10 has that message.

- Response: Rephrased, page 16 Conclusion line 41-46

17. Conclusion ..........Your recommendations should be based on your research result.

- Response: The recommendations are revised by deleting those beyond the scope of this
research finding


- Response: I couldn’t find a fluent language expert but a thorough language review is made and
edited accordingly

19. References............. Put date of access for references taken from web pages, Use consistent
referencing (e.g. journal name abbreviated or full, style of referencing- Harvard, Vancouver…),
put the volume, issue,and page numbers for journal articles

- Response: As per the recommendations, the whole references are edited, with 3 additional
references and I tried to follow a consistent “Vancouver” reference listing style