Reviewer’s report

Title: Factors associated with first-line antiretroviral treatment failure in adult HIV-positive patients: a case-control study from Ethiopia

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Reviewer: Nang Thu Thu Kyaw

Reviewer's report:

Summary
The study conducted by Bezabih et al aimed to identify risk factors associated with first-line ART failure among patients receiving care at an ART clinic of a hospital in Ethiopia. There are some risk factors associated with first-line ART failure already being identified in the global literature including in studies from Ethiopia, but there had been no study from Ethiopia that identified risk factor for first-line ART failure diagnosed using viral load. Hence, this study has potential to contribute to identify risk factors associated with first-line treatment failure in HIV population in Ethiopia. However, there are major concern on the methods, the results of the study and the presentation of the results in the manuscript.

Major comments
The author should follow one of the guidelines for reporting observational studies, for example, STROBE guideline.

Background
The author mentioned that the main contribution from this study was that the first-line ART was diagnosed in this study using viral load. The author should explain the potential weakness of using clinical or CD4 to diagnosed first-line ART failure in identifying the risk factors associated with it or the potential advantage on using viral load in this study to present a convincing rationale of this study.

Methods
The variables used in the study were not clearly defined. There was no detail on the measurements of the variables which made reader difficult to interpret the results and assess the internal validity of the study.
For example, the author mentioned that the controls were matched by age, sex and treatment duration. Is the treatment duration the duration on first-line ART? Was the ART interruption/discontinuation time during follow-up excluded from this duration?
In addition, it is not clear that whether the "TB co-infection" factor which is related to the main finding, was the patient having active TB disease during follow-up or active TB disease at the time of ART failure or patients having TB infection. Using the term" TB infection" can give wrong impression as
people might interpret as having latent TB infection.
The author needs to be explicit on which variables were measured at baseline and which ones were measured at the time of ART failure or during the follow-up.
There is no description on how the missing data was handled, whether no missing data or the patients with missing data were excluded.
I would suggest including the matching factor in the adjusted analysis because matching does not always remove the confounding of the matched factors. In addition, matching process in a case-control study can introduce bias by changing the association between the matching factor and the outcome and can create an association even if there were none before the matching was conducted.
Did the author check multicollinearity of factors that were included in the adjusted analysis? Patients who missed ART follow-up might be similar to those who discontinuation of ART.

Results
The author could mention the factors/variables consistently to make the reader easy to follow. The data in the table are not completed. Some of the rows did not have total for each category and percent should be row or column percent and they need to be consistent.
Some factors included in the bivariate analysis (table-2) were not presented in the descriptive table-1. The tables, their titles and legends should be stand alone. The author used some abbreviation which were not defined.

Discussion
The author should identify limitations of studies regarding internal validity and generalizability of the study.
The estimate for TB coinfection was very large compared to other studies that author mentioned, and author should comment on potential bias that might contribute to overestimation of the results. For example, imbalance distribution of patients with TB between case and control. The same suggestion for other factors that the study may overestimate or underestimate.

Conclusion
I would suggest rephrasing the conclusion based on the results presented and the discussion section and being cautious on the limitation of the study. The author correctly pointed out, the factors that were associated with first-line ART failure can be the consequences of the ART failure.
The conclusion on hygiene conditions to prevent diarrheal disease is not based on the results or was not discussed in the discussion.

Minor comments
Page 1, Line 57-58: History of TB treatment or current TB treatment or had active TB?
Page 4, Line 6-7: Was failure diagnosed with one-time viral load testing? If that the case, patient might have low adherence or not take ART at the time of VL test and it might not necessarily failure on first-line ART.
Page 4, Line 27-28: Does discontinuation of ART mean patients stopped ART for certain duration and retook again or completely stopped ART?
Page 6, Line 34-35: Column title should be properly named.
Page 6, Line 38-39: The second column should be number of total males. Or add another column for total for each category.
Page 6, Line 41-42: For age and ART duration variables, the distribution should be assessed and presented accordingly instead of presenting mean. I believe age might not normally distributed.

Page 6, line 50-54: Why there are no %?
The variables in the table-1 should be consistent in term of name, presentation (as continuous or categorical variables) and grouping.

Page 9, Line 20-21: "lead to first-line ART regimen"? It must be typo.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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