Author’s response to reviews

Title: Prevalence of Anemia and its associated factors in Human Immuno Deficiency Virus infected adult individuals in Ethiopia. A Systematic Review and Meta-Analysis

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Author’s response to reviews:

Date 21 Sep 2018
To: BMC Hematology Editorial
From: Ayenew Negesse
Subject:A letter Accompanying Revision in Response to Reviewers Comments

Dear Editors

I am happy to resubmit the revised version of “Prevalence of Anemia and its associated factors in Human Immuno Deficiency Virus infected adult individuals in Ethiopia. A Systematic Review and Meta-Analysis” for publication in BMC Hematology Journal. The comments of the Editors and the reviewers were highly insightful and enabled us to greatly improve the quality of our manuscript. In the following pages, we have addressed your concerns in a point by point format by highlighting (color change) the response and those points that addressed were highlighted throughout the manuscript using track changes.

We look forward to hearing from you at your earliest convenience.
With regards

AyenewNegesse

On the behalf of other authors

Reviewer 1 comments and authors justifications

1. However, I would have needed more specific information on why the 429 articles were excluded:

   • Thank you for your comment: As indicated in the PRISMA flow chart, the authors used two stages of Screening. Primarily, the authors screened the titles and abstracts based on the criteria set in the protocol. Secondly, the authors’ identified potentially relevant articles using titles and abstracts for further re-screening. Accordingly, after critical review and discussion, the authors decided to exclude these 429 articles from further re-screening based on the predefined inclusion criteria’s (Refer line 221 of the revised manuscript).

2. The authors should clarify what they meant by "publication bias" as a source of heterogeneity in Hemoglobin levels:

   • Thank you for this concern! This statement has been revised in the revised manuscript to be meaningful (Refer line 263 and 264 of the revised manuscript).

3. What was the hemoglobin cut-off in the cited European and South Indian studies?

   • We tried to revise the discussion section of the manuscript based on the comment. The hemoglobin cut off point for the cited European study was defined as: non-anemic if hemoglobin was defined as hemoglobin greater than 14 g/dl for men and 12 g/dl for women; anemic if it was less than or equal to 14 g/dl for men and less than or equal to 12 g/dl for women. The hemoglobin cut off point for cited south Indian study was defined as: Non-anemic if hemoglobin was defined as hemoglobin greater than or equal to 13 g/dl for men and 12 g/dl for women; anemic if it was less than 13 g/dl for men and less than 12 g/dl for women.
• So that under this section, the authors would like to explain that hemoglobin cut off point for both the cited European and south Indian studies may overestimate the prevalence of anemia as compared with the current systematic review and meta-analysis conducted in Ethiopia in which anemia was defined if hemoglobin level was less than 11g/dl for both men and women according to WHO definition criteria for anemia criteria. (Refer line 308-313 of the revised manuscript)

4. What in the geographic location will account for the differences in hemoglobin in the Tanzanian, Ethiopian and European studies?

• Thank you for this concern and the authors tried to revise the manuscript based on the given comment. In countries where study areas are located in different altitudes above sea level, this variable is critical and should always be taken into account when defining anemia. So that altitude difference across Ethiopia, Tanzania and European countries may change the level of hemoglobin concentration at different settings. (Refer line 314-316 of the revised manuscript).

Reviewer 2 comments and authors justification

1. This review considers articles published in English only. However, given the focus of the study (i.e., Ethiopia), I wonder why articles published in the languages of Ethiopia were excluded. I mean, this is not a review of articles published throughout the world. Studies with no accessible full text were excluded. This is not a good reason. There are other ways to get the articles (e.g., contacting the authors). Grey literature (e.g., health authorities’ reports) was not mentioned. This is a flaw.

• The comments are considered in the revised manuscript. In scientific researches, Ethiopia used only English language as a medium of instruction rather than an official Amharic language. So that every researchers and scientific investigators of public health issue at higher institution are enforced to use English language as a medium of instruction for the purpose of academic communication at the international level through publication at international reputable and peer reviewed journals. So, any scientific researches conducted in Ethiopia have English language ground across the country and none of the studies could be conducted in local Amharic language.

• Pertaining about the searching strategies, we tried to revise the manuscript based on the comments. We wrote in the final manuscript what was found at the final stage. As a
procedure, we have followed the systematic searching strategies to identify both published and unpublished articles throughout Ethiopia. We didn’t simply ignore articles that were not accessed with full articles rather we used websites which may access full text papers freely, contacted authors for those articles which requested full text access.

- Regarding grey literatures, we also tried to identify unpublished papers from shelf (health authorities reports and conference proceedings), google and google scolar. But papers we found in hardcopies were reports that didn’t follow the scientific flow of the research which was also disqualified after we used the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) adapted for cross sectional studies. (Refer lines 145-150 and lines 171 and 172 of the revised manuscript).

2. It is important to remember that, according to PRISMA-P, the inclusion or not of literature in multiple languages and unpublished data can influence the effect estimates in meta-analyses.

- Thank you the comment forwarded. We followed such guideline and we tried to explain based on the comments forwarded from reviewer.

3. Why were only studies conducted in rural households of Ethiopia considered?

- Thank you for this critical comment! We already revised the manuscript accordingly since it was an editorial error. We made a mistake when we write the protocol. At the beginning we wrote the protocol about “prevalence of food insecurity among female headed rural households and its association with gender preference on household head as systematic review and meta-analysis. The mistake was made when we change our intension from food insecurity to anemia among HIV positive adult individuals. For the current systematic review and meta-analysis, we tried to include studies conducted both at community and institutional level. (Refer line 169 of the revised manuscript)

4. In subgroup analysis and meta regression, the sampling method, sample size, and mean age should be taken into account. In addition, gender distribution was not considered among the characteristics of included studies, as well as subgroup analysis and Meta regression.

- Thank you for your comment! We have included all the aforementioned variables and revised the manuscript by incorporating the given comments. (Refer lines 234-281 of the revised manuscript)
5. The theoretical and practical implications of the study findings need to be discussed more deeply.

- We incorporated the comments and revised the manuscript as follows:

Theoretical and practical implications

HIV infected adult individuals are more prone to develop concomitant infections demanding comprehensive package of health services including ART. This evidence also indicated that those anemic HIV infected individuals deserve more attention where integrated service provision is critical to identify and manage underlying causes for anemia at early stages. Hence, specific considerations tailored to anemia screening and management needs to be taken into account during ART program design and implementation across the health system. Despite the vast investment of resources in tackling the occurrence of anemia in low and middle income countries few studies, are available to inform policy and decision making. Therefore, further studies are also recommended to generate pooled evidence at global level in general and in developing countries in particular. (Refer lines 336-346 of the revised manuscript)

6. What is the exact meaning of strengthening the system and procedures for the early diagnosis of opportunistic infection and screening of underlying problems like under nutrition?

The meaning is as follows:

- The findings of this review revealed that opportunistic infection and low level of BMI were found to be the predisposing factors for the development of anemia in HIV positive adult individuals. Hence, to reduce the occurrence of anemia in HIV infected adult individuals’ early detection and diagnosis of opportunistic infection and screening of under nutrition has paramount importance. Therefore, we recommend all stakeholders working in the health system to take part in this initiative.