Author's response to reviews

Title: Determination of Hematological and Immunological parameters among HIV positive patients taking highly active antiretroviral treatment and treatment naive in the antiretroviral therapy clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study

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Version: 4  Date: 11 February 2014

Author's response to reviews: see over
Author’s Response to Reviews

Determination of Hematological parameters among HIV positive patients taking HAART and HAART naïve in ART clinic of Gondar University Hospital, Gondar, North West Ethiopia: Comparative cross-sectional study

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Version: 4 Date: 11 February 2014

Author’s Response to Reviews: See over
Dear BMC Hematology editorials,

All the comments and suggestions given by each reviewer’s to our manuscript entitled “Determination of Hematological and Immunological parameters among HIV positive patients taking HAART and HAART naïve in the ART clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study” are very important and valuable to make the paper scientifically sound. We the authors tried to correct and include all the comments given by each reviewer’s point-by-point. For the convenience purpose, we attached/uploaded the point-by-point reply to each reviewers and the revised manuscript.

With regards
Author’s Response to Ivan Gentile

Determination of Hematological parameters among HIV positive patients taking HAART and HAART naïve in ART clinic of Gondar University Hospital, Gondar, North West Ethiopia: Comparative cross-sectional study

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Version: 4 Date: 27 January 2014

Author’s Response to Reviews: See over
Reviewer's report

Title: Determination of Hematological and Immunological parameters among HIV positive patients taking HAART and HAART naive in the ART clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study

Version: 3 Date: 13 January 2014

Reviewer: Ivan Gentile

Reviewer's report:

The authors have improved the manuscript significantly, but some points still needs to be improved according to my previous comments. Herein I list the issues that still remain open.

Major Compulsory Revisions still needed

1) Concerning the point one of the previous review, the authors gave a complete answer to me, but they should include this answer in the method and in the abstract of the manuscript.
   - The variables compared here are Hematological parameters (Total and differential WBC, RBC, Hgb, HCT, MCV, MCH, MCHC, RDW, PLT, MPV, and CD4).
   - The groups are HIV positive treatment naïve and those on HAART
     It is done as per the given comment

2) Concerning the point 2 (statistical analysis) the authors did not improve in a satisfactory way the manuscript. In fact, nevertheless comparisons on qualitative variables (%) are present in the manuscript, it is not reported the statistical test used to perform such comparisons. Finally, logistic regression analysis must be performed in order to find the independent predictors of hematological abnormalities.
   - The Biostatistician was consulted and they suggest independent T-test because the objective of the study is comparison of hematological and immunological parameters between HAART naïve and those on HAART HIV positive patients. Also the parameters are normally distributed therefore independent T-test is sufficient to describe the comparisons.
3) Concerning the point 3, the authors included a table (table 1) with demographic data. However they did not perform a separate analysis for AZT and non-AZT-based HAART as I suggested. At-least they should give details on which drug is used in HAART in table 1.

- Done as the following

  From HIV patients on HAART 58.8% were on Zidovudine (AZT) based therapy and all had macrocytosis. The remaining 41.2% were non AZT based therapy and 42.8% of them had normocytic normochromic anemia.

Minor essential revision

1) Concerning the point 5 of previous minor essential revision, the authors included only some of the references indicated. All of them should be included and their content should be discussed thoroughly

- The authors gave great thanks to the reviewer and related references are included.

Discretionary

Statistical analysis details are usually not reported in the abstract

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report

Declaration of competing interests:

I declare that I have no competing interests
Author’s Response to William Kwame Boakye Ansah Owiredu

Determination of Hematological parameters among HIV positive patients taking HAART and HAART naïve in ART clinic of Gondar University Hospital, Gondar, North West Ethiopia: Comparative cross-sectional study

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Version: 4 Date: 27 January 2014

Author’s Response to Reviews: See over
Reviewer's report

Title: Determination of Hematological and Immunological parameters among HIV positive patients taking HAART and HAART naive in the ART clinic of Gondar University Hospital, Gondar, Northwest Ethiopia: a comparative cross-sectional study

Version: 3 Date: 20 January 2014

Reviewer: William Kwame Boakye Ansah Owiredu

Reviewer's report:

The manuscript is acceptable, however there are recommended minor essential revisions which the editors can be trusted to oversee

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I have no competing interests whatsoever

Title: Okay

Authors Affiliation: Okay

Minor Essential Revisions

Corresponding Author: Should include name of corresponding author.

- Done as per the given comment
Abstract:

Background: Lines 3-5 should read: Thus a specific diagnosis and a determination of hematological and immunological parameters are required for initiating and monitoring early treatment to avert disease progression.

- Done as per the given comment

Methods: Line 1 should read: A comparative cross-sectional study was conducted on a total of 290 HIV …… Done as per the given comment

Line 5 should read: Hematological and immunological parameters were collected and processed ……… Done as per the given comment

Results: Line 1 should read: Prevalence of anemia, leucopenia, thrombocytopenia, neutropenia and lymphopenia were ….. Done as per the given comment

Line 3 should read; There was a significant difference in total WBC, ……. Done as per the given comment

Conclusion and Recommendation: Line 3 should read: ………prevalence increased as the CD4 count decreased.

- Done as per the given comment

INTRODUCTION

Paragraph 1 line 1 should read: Hematological abnormalities are common complications of ……… Done as per the given comment

Paragraph 2 line 6 should read: …..the prevalence and severity of anemia also increases (6,8).

- Done as per the given comment
Parahraph 3 line 2 should read: ….. infection which is found in 3-40% of individuals with HIV infection and could occur at any …….. Done as per the given comment

Paragraph 4 line 3 should read: ………and leads to decreased levels of granulocyte colony-stimulating factor, …. Done as per the given comment

Paragraph 4 line 5 should read:…….. Also myelosuppressive drugs or

- Done as per the given comment

Paragraph 6 line 3 should read: This study, therefore, assessed hematological parameters in HIV positive …… Done as per the given comment

METHODS

Study Setting and Study Population: Line 2 should read, During the study period there were about ……. Done as per the given comment

Line 5 should read, ….treatment naïve and 145 individuals on HAART for a period of 6 months or more were chosen.

- Done as per the given comment

Data collection: Line 2 should read, …….collected using a pre-tested structured questionnaire by …… Done as per the given comment

RESULTS

Hematological Abnormalities: Paragraph 1 Line 1 should read, Out of the total number of study participants, ……. Done as per the given comment

Paragraph 2 line 3 should read, …..patients on HAART, 58.8% had macrocytic normochromic anemia while from HAART-naïve ……… Done as per the given comment
**CD4 count and pancytopenia:** Lines 1-4 should read, The overall minimum CD4 count was 13 cell/µl and the maximum was 1336 cells/µl with a median CD4 count of 350 cells/µl and inter-quartile range of 218 – 518 cells/µl. Twenty percent of the study population had CD4 counts of < 200 cells and 15.5% of them had CD4 counts < 100 cells.

- Done as per the given comment

**DISCUSSION**

Paragraph 1 lines 6-8 should read, This may be due to the difference in study population, sociodemographic characteristics of study subjects and study design methods.

- Done as per the given comment

Paragraph 2 lines 4-5 should read, The findings of this study affirms that hematological disorders are corrected by combination antiretroviral therapy which also decreases the viral load (19).

- Done as per the given comment

Paragraph 3 line 2 should read, ……is supported by different studies in which normocytic-normochromic anemia is the commonest type …….. Done as per the given comment

Paragraph 4 line 2-3 should read, ……while about 58.8% patients developed macrocytic-normochromic anemia (p < 0.001). This is probably due to the effect of ……..

- Done as per the given comment

Paragraph 6 line 1 should read, Leucopenia prevalence in this study was 26.6% which was higher than the prevalence in studies done in ………. Done as per the given comment

Paragraph 6 lines 4-6 should read, In the present study, prevalence of neutropenia and lymphopenia was 21.4% and 2.1% respectively, which is lower than is reported in a study done in Nigeria between 1995 and 2000 in which 64.4% and 40% presented with lymphopenia and neutropenia respectively(21).

- Done as per the given comment
Paragraph 7 lines 1-3 should read, Patients on HAART showed statistically significant increase in leucopenia and neutropenia compared to their HAART-naïve counterparts (p < 0.01). Similarly when patients CD4 count decreases, prevalence of leucopenia and lymphopenia increases (p < 0.05). This may be due to suppression of bone marrow and …..

- **Done as per the given comment**

Paragraph 8 lines 2-4 should read, ….done in New Delhi (3.74%) (12) but lower than reports from a study done in Lagos (16%) (4) and Nigeria between 2002 and 203 (10%) (16). There was no significant difference in the prevalence of thrombocytopenia between study participants on HAART and those who are HAART-naïve.

- **Done as per the given comment**

Paraphr 8 lines 4-7 should read, Thrombocytopenia, however, increases as CD4 decreases (p = 0.007). Thus thrombocytopenia probably increases as immunological incompetence worsens thus leading to increased risk of excessive bleeding (22,23).

- **Done as per the given comment**

**Limitations of the Study**: The second bullet should read, the study focused only on comparisons of hematological and immunological parameters but does not address risk factors.

Note: This section should be a new paragraph under the discussion rather than being a new section entirely.

- **Done as per the given comment**

**CONCLUSION**:

Line 1 should read, The commonest hematological abnormalities in this cohort of study participants were anemia and leucopenia, especially neutropenia.

- **Done as per the given comment**
Lines 3-4 should read, Anemia, leucopenia, thrombocytopenia and lymphopenia were increased as CD4 count decreases

-  **Done as per the given comment**

Note: Conclusion should be on issues covered in the manuscript.

-  **Done as the comment**