Reviewer's report

Title: Adherence to antiretroviral therapy and associated factors among HIV infected children in Ethiopia: unannounced home-based pill count versus caregivers' report

Version: 1 Date: 2 June 2013

Reviewer: Mogomotsi Matshaba

Reviewer's report:

See below for numbers

- Major Compulsory Revisions
  Number of comments: 6, 8, 17, 18, 19, 21, 25

- Minor Essential Revisions
  2, 4, 5, 9, 11, 12, 14, 22, 23

- Discretionary Revisions
  1, 3, 7, 10, 13, 15, 16, 20, 24

Abbreviations: Discretionary Revisions (DR), Minor Essential Revisions(MER), Major Compulsory Revisions.(MCR)

Background:
1. Background paragraph 2, choice of word, replace curve with curb(DR)

Materials and Methods
2. Study area: Well written paragraph but the backgrounds needs to be more clear: Actual drug regimen available: first line, second line. The state of the supply chain management needs to be clear especially for paediatric formulations. Liquid formulations tend to be more difficult to administer and monitor. It is not clear if all were pills or liquids. Cultural issues and stigma could have been stated here as they all ultimately affect adherence. Routine labs followed can also be used to triangulate these data.(MER)

Study Design and study participants:
3. Timing: This is one of the busiest time in the Ethiopian calendar with several celebrations and festivities: Christmas Genna, January 7th, Timkat, Kullubi. It is well known that during festive season, adherence becomes poor where stigma is still an issue. Impact should be discussed.(DR)

4. Define the inclusion/exclusion criteria well, what was the lower age cut off.(MER)

Methods of Data Collection
5. Timing of the laboratory data should be clarified, ie up 6 months prior to study entry. (MER)

6. Pill counts were conducted a week after interview, did the parents know that? (MCR)

Operational Definitions

7. Period assessed for adherence was too short, will under estimate true adherence especially for once daily dosed efavirenz. (DR)

Data management and analysis

8. Appropriate tests, Chi square tests and multivariate logistic regression were chosen for these data. See my comment on results below. (MCR)

Ethics

Well covered

Results

Paragraph one: Socio Economic

9. Age breakdown of the children not very useful; We know adherence becomes a problem with teenagers. It is not clear how many are strictly supervised, just reminded or take medications independently. (MER)

Social and Disclosure variable of children,

10. Did not assess the child’s understanding of disclosure. It would be a much more objective way of assessing this important factor. (DR)

11. Define what 4c/4d mean for the drug regimen. (MER)

12. Define what other regimens the rest of the patients were on. (MER)

Clinical Marker of children on ART

13. Include mean time from initiation (DR)

Adherence;

14. Paragraph 1: It is difficult to compare pill counts to parent reports. Level of adherence is different ie, for self report it is 100% meaning no missed doses while it is 95% for the home pill counts. (MER)

15. Paragraph 2, could have compared those with extra pills vs those with out after correcting for other factors. (DR)

16. Paragraph 3 reason for children refusing medications and their ages would make this more useful information. Younger children might be taste or smell while older children reason might be pill fatigue, pill burden or stigma related. (DR)

17. Paragraph 4: I am not a statistician but seems to me that the logistic regression model was not interrogated fully. Some conclusions cannot be made with the information as presented. Variables need to be included and excluded multiple times or corrected for before some conclusion can be made. (MCR)

18. Example one is not clear whether the marital status conclusion was based on
other variables like age, educational level, income status factored in. Same applies to the disclosure conclusion, was age, sex, and level of disclosure corrected for? (MCR)

19. Paragraph 5 Given the short duration of assessment of adherence, one week, the difference in the denominator for calculating adherence become critical. One missed dose of EFV results in poorer adherence than one missed dose of NVP given that there are once daily and twice daily dosing respectively. (MCR)

Discussion

20. Paragraph 2 line 3, change finding to findings-grammar (DR)

21. Paragraph 4 see my comments on results above paragraph 4. It is not clear if age and other variables are included and corrected for in the model. If done this might actually be an age or experience factor rather than marital status. (MCR)

22. Paragraph 5: same argument as above. In other settings, controlled early disclosure leads to favourable outcomes. (MER)

23. Paragraph 6 see argument for results paragraph 5. This is not a fair comparison. (MER)

24. Paragraph 7 Weaknesses acknowledged well. Others include comparing different adherence monitoring modalities, recall bias, selection bias and the holiday season impact. (DR)

Conclusion

Based on the results and discussion.

With more interrogation of the data, different conclusions may be drawn.

Overall Assessment

25. The results of the logistic regression need to be interrogated more rigorously by a statistician or epidemiologist. This study cannot be published until all major issues raised (MCR) are corrected. It is difficult at this point to firmly make most of these conclusions.

26. No signs of misconduct were picked up

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

'I declare that I have no competing interests'