Reviewer’s report

Title: Utility of Total lymphocyte Count as a Surrogate Marker for CD4 counts in HIV-1 infected Children in Kenya

Version: 2 Date: 1 June 2011

Reviewer: Anand Reddi

Reviewer’s report:

The authors have superbly addressed my concerns and great improved the quality of this interesting and well-written manuscript. This manuscript compromises a opus of excellent work from the University of Nairobi, Department of Pediatrics and Child Health that has eloquently documented the success of pediatric HIV outcomes in the resource limited settings of Kenya. The authors’ work on pediatric HIV is truly inspiration in the spirit of the Lazarus effect.

Synopsis of Manuscript:
Githinji et al. explored the use of total lymphocyte count (TLC) as an alternative to CD4 count and CD4% to monitor antiretroviral-naïve children in three HIV clinical sites in Kenya. The subject matter is interesting given that in many resource limited settings in Africa access to CD4 FACS machines is limited therefore making the ability to track HIV clinical progression with TLC an extremely useful and less expansive alternative to CD4. The manuscript reports that increasing established World Health Organization TLC results in greater sensitivity but reduced specificity. The authors demonstrate that current WHO TLC thresholds would have missed 67-75% of children below the age of 5 in their cohort. The authors proposed higher TLC thresholds and provided a detailed and thoughtful analysis. Additionally, the authors demonstrated that TLC was positively correlated with CD4 count, with stronger correlation among children who are severely immunocompromised. This finding is consistent with a recent manuscript by Napoli et al in Academic Emergency Medicine 2011. The manuscript, despite some limitations, is an important contribution to the literature and will provided increased evidence for the WHO to consider revising their age-specific TLC thresholds.

I attach are a few minor essential revisions to further improve this manuscript.

Minor Essential Revisions

Abstract

1. Correct sentence to read: In resource-limited settings, such as Kenya, access to CD4 testing is limited. Therefore, evaluation of less expensive laboratory diagnostics is urgently needed to diagnose immunosuppression in children.

2. Please include PPV and NPV calculations/values in the results section of the abstract.
Introduction
1. Please add a citation for the PEPFAR II goals to the first line of the last paragraph of the introduction.

2. Please correct the sentence in the last paragraph of the introduction to read: “Hence it is pertinent” not “Hence is it pertinent”.

3. Please correct the second to last sentence in the introduction to read: “Pre-HAART”

Methods
1. Please include by, before documentation: The sentence should read: “Evidence of HIV status was sought, specifically, by documentation of a…”

2. Delete (DNA or RNA) and just state PCR.

3. Delete additional word “one.” The sentence should read: “We excluded children under the age of one month due to uncertainty of HIV diagnosis in this group.”

Results/Discussion
Excellent

References
Ref 27: Correct journal to BMC Pediatr not BMC Paediatrics

Figures:
Make sure that in Figure 1 the y-axis is clear to read. Perhaps this will be easier to read when the manuscript is typeset.

Anand Reddi
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Level of interest: An exceptional article

Quality of written English: Acceptable

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' below.