Reviewer's report

**Title:** Multiple micronutrient supplementation improves vitamin B12 and folate concentrations of HIV infected children in Uganda: a randomized controlled trial

**Version:** 1  **Date:** 20 January 2011

**Reviewer:** Angel F. F Remacha

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This is an interesting article studying vitamin B12/folate supplementation in African Children. Prevalence of low vitamin B12 and low serum folate is similar to pre-HAART era. Some comments should be addressed.

**Major Compulsory Revisions**

Low vitamin B12 is not synonymous of vitamin B12 deficiency. In fact, in previous works, most cases with low vitamin B12 serum levels in HIV patients this vitamin deficiency was not demonstrated using tests distinguishing low levels from real vitamin B12 deficiency, such as homocysteine or d-Uridine suppression test. This work does not use these tests, therefore it is impossible to assess this aspect. However, as Hb does not change in cases with low vit b12 after supplementation, this finding supports that there is not a real vitamin B12.

Low vitamin B12 could be related to folate deficiency or, more probably, to low vitamin B12-binding proteins (cobalophilin, transcobalamin I or R-Binders) as a consequence of neutropenia.

On the other hand, Hb increases in low folate children after supplementation, suggesting that the folate deficiency is present and is inducing anemia. In previous studies, Folate deficiency was common in HIV patients in pre-HAART era and this deficiency was demonstrated using the above mentioned tests. After folate treatment, for instance, hyperhomocysteinemia was normalized in adults.

With the design of this work is impossible to differentiate whether anemia is caused by folate or vitamin supplementation.

A study of vitamin B12/folate metabolites (homocysteine, methyl malonic acid) could help to solve this point.

HAART group is small and, therefore, it is difficult to obtain conclusions, curiously the prevalence of low vitamin B12 and low folate is similar to HIV children not in HAART therapy. In adults, this was not the case. CD4 levels in Haart and no-Haart patients could help to understand this discrepancy.

To evaluate better evaluate folate metabolism, red cell folate should have been determined.

**Minor Essential Revisions**

Tables using mean logs are difficult to follow, this tables should be rebuilt using
mean or not included.

Figures have not been received.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

'I declare that I have no competing interests'