Reviewer's report

Title: Utility of clinical parameters to identify HIV infection in infants below ten weeks of age in South Africa: a prospective cohort study

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Reviewer: Francois Rouet

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Major compulsory comments

Jaspan and collaborators developed a clinical algorithm to identify HIV infection in young infants (<10 weeks of age) enrolled in two clinical trials (CHER trial with baseline CD4 <25%; and additionally an observational cohort with CD4 <25%) conducted in South Africa. It’s a very important topic in resource-constrained settings where the early diagnosis of pediatric infection, by using molecular (HIV DNA or RNA) tools, is difficult to implement. The paper is well written, the study well designed, and the results are well expressed. The discussion is informative, including limitations.

I have two main comments about this work:

1/ First, the authors indicated that their findings need to be validated in other settings, due to lack of severe clinical disease amongst children with CD4 <25% enrolled in the CHER trial. I agree with this point. However, in the present study, 62 HIV-1-infected infants showed CD4 <25%. So, my question is: Do the authors investigate clinical spectrum specifically observed in this sub-population more immunocompromised? What about the frequency of clinical signs among these 62 children, compared to those enrolled in the CHER trial? Finally, when stratifying by CD4 (≥25% vs. <25%), what about the performance of the algorithms (better amongst children with CD4 <25%?)?

2/ Second, in methods, the authors explained that they performed quantitative HIV-1 RNA measurements among all HIV-1-infected children (initially identified with qualitative Roche Amplicor HIV-1 DNA assay). My question is: Do the authors assess relationship between the identified symptoms of acute HIV infection and infant viral load measurements? It could be a good plus to know that and report it in the paper.

Minor essential revisions

- Results

P.8: According to Table 1, a history of gastroenteritis was not significantly associated (p=0.17) with acute HIV infection in children.

- Bibliography

The authors claimed that this is the first study investigating clinical
symptoms/diagnostic algorithms in the VTP era. To my opinion, it’s not completely true. For instance, Rouet et al. described acute retroviral syndrome in children infected through breast-feeding in the DITRAME trial (Ivory Coast). Richardson and colleagues performed a similar work among Kenyan infants (including infection diagnosed at <2 months of age). Probably, the references need to be slightly updated.

**Level of interest:** An article of outstanding merit and interest 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 interest' below.