Reviewer's report

Title: The correlation between the presence of viremia and clinical severity in patients with enterovirus 71 infection: a multi-center cohort study

Version: 3 Date: 11 June 2014

Reviewer: H Rogier van Doorn

Reviewer's report:

The authors have made some effort to address the reviewer's comments, but I'm afraid that this is not sufficient. The new figure 1 is very informative, and taken together if more analyses are done and results and discussion are rewritten accordingly, these data are new and interesting. However, many questions are still unanswered and several issues raised by the reviewers persist.

Specifically (all essential revisions, only referring to my own initial comments)

- Day of illness on sampling was not taken into account in the multivariate analysis, while this was my main concern. The authors suggest that patients who have viremia after day four are more likely to have severe disease, but they fail to mention whether patients who present at day four in general are more likely to have severe disease. For a reader to make sense of their data, it is crucial for the authors to present data on severity of illness per day of illness at sampling time. Without this we cannot give any value to potential associations the authors describe.

- Similar for children under one having a higher risk of viremia... did they present to hospital earlier and were they thus sampled earlier?

- There are still a lot of language and grammatical errors and the manuscript may benefit from additional review for this particular purpose.

- The authors should also carefully review their wording: the authors still discuss the viremia as if they have kinetic data (multiple timepoints per patients), this should be avoided. E.g. they should not that viremia rapidly decrease after day four, but that viremia was lower in patients sampled after day four etc. The authors have also not addressed my comments re the phrasing of their results, e.g. in the abstract section the sentence “Two-thirds 48 (68%) of viremia occurred within the first three days of infection” is still there. This sentence should read: e.g. xx% of patients samples before day 3 of illness, vs yy% of patients sampled after day 3.

- The revision of the background section was minimal. As said, the background section should be to the point and be less vague, describe well what we know, and what assessment of viremia may add.

- In the results section, classify patients by grade first and then discuss their symptoms. x patients were grade 1, y patients were grade 2 etc...
Level of interest: An article of importance in its field

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

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

Declaration of competing interests:
I declare that I have no competing interests