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

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Reviewer: Kulkanya Chokephaibulkit

Reviewer's report:

Major compulsory revision:

1. The authors have made responses to the comments well. However, the response to the critical comments on the conclusion that prolonged viremia was associated with severe complications is not satisfied. The day of the blood drawn depended on the day that the patients hospitalized. It could be that all the milder case were admitted earlier by any reasons, then got the blood drawn earlier, while the sicker patients did not recovered by day 3 of illness showed up and hospitalized later, and therefore got the blood drawn later. But because the second blood drawn was not performed therefore the milder cases who may also have prolonged viremia will never be discovered. Although it is suggestive from Fig 1 that the chance of detecting the virus was less in later days, one may assume the milder case will not have a viremia in the subsequent blood drawn if it was done. But this has to be proven. It is likely because the sicker patients tended to be hospitalized after day 3 that led to the higher proportion of more severe cases in viremic population after day 3. The milder cases probably already recovered by day 3 while the grade 3-4 CNS symptoms usually presented after day 3. Therefore what found in Fig 3 may be just reflecting the proportion of sicker patients hospitalized before or after day 3. This figure may be misleading from selection bias (sicker hospitalized later), not the that the sicker had higher chance of viremia in the later days, and should not include in the manuscript. If Fig 3 is to be presented, it should present the proportion of viremia in patient with grade 1-2 vs grade 3-4 on before and after day 3 of illness.

In order to clarify this, I suggest that the proportion and number of patients with severe complications (grade 3-4) should be added at the bottom of Fig 1. If the proportion of viremia in patients with grade 3-4 when they get blood drawn after day 3 of illness was higher than the proportion of viremia in the patients with grade 1-2 on the similar days, then prolonged virmemia in grade 3-4 can be concluded.

The conclusion at this point can only say that the proportion of grade 3-4 patients was higher in viremic patients who presented after day 3. It cannot generalize that the grade 3-4 patients had a longer period of viremia.

2. The Method on page 6, as well as in Abstract are not quite similar. Please clarify this that the blood drawn for virologic test was performed on the first day of admission. If not, how delayed it is from the point of admission.
3. In Table 3 and 4, the authors added Fever in the variables. Please clarify the fever, eg. the peak temperature after hospitalization, or any fever T.37.8 degree celcius?

4. In the Results in the Abstract stated "2/3 of viremia occurred within the first 3 days of infection." This should be revised to "2/3 of viremic cases were detected in the first 3 days of illness.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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.