Reviewer's report

Title: Dengue NS1 antigen as a marker of severe clinical disease

Version: 3 Date: 26 August 2014

Reviewer: Nguyen Phuoc Long

Reviewer's report:

In general, this version is better than the previous article. Nevertheless, the study is still confined and the writing quality needs some improvement.

Major comments:

1. The figure 1B was not included in the revised manuscript. Also, the correlative figure legend should be reconsider, how can we predict “shock” when there is no concrete evidence about the time that “shock” happened (line 504, page 21).

2. Figure 2 needs correction with a line demonstrating the median value.

3. A multivariable analysis should be performed to control confounder, if any.

4. There were only 25 cases in total which had Dengue Shock Syndrome (DSS). I wonder how many cases had DSS before being hospitalized and how many cases actually developed DSS later. Then the fact is the magnitude is possibly small, we have to avoid “over-interpret statistical significance”. Therefore, it would be better to put some limitations in the discussion sentence at line 328 to 330, page 14.

5. The discussion section: (1) Please add some more sentences discussing the results of NS1 from previous studies if any, and make a comparison (2) A limitation paragraph should be included. E.g.: Study design (no control group, not-blinded study, and different criteria for severe and non-severe dengue...).

Minor comments:

1. Because of the complication of the study, it would be better to have a workflow figure. Workflow figure can help readers follow the study better.

2. The introduction section:
   a. The sentence “Therefore, a simple test that can be done in a ward would be of utmost importance to determine the patients who are most likely to develop severe clinical disease” (line 91 to 93, page 4) should be deleted because it was written at line 116 to 117, page 5.
   b. The sentence from line 110 to 112, page 5 should have a reference.
   c. The sentence from line 110 to 114, page 5 should be deleted because it is identical to meaning of the next paragraph.

3. The result section:
a. Line 221-222, page 10, it would be better not to use the mean (average) day and (SD). It is better to use median and IQR.
b. The result section can be more concise:
i. The sentences from 223 to 229, page 10 and the sentence from line 300 to 303 can be moved to the discussion section.
ii. Please consider to delete the sentences from line 289 to 292, page 12 which started with “The NS1 antigen” and ended with “at the bedside”.

4. The discussion section:
a. The sentence from 330 to 332, page 14 should be moved to the next sentence, where the authors discussed the liver transaminase levels, platelet counts and other factors.
b. Line 351-352, page 15. The method section did not mention the correlation test but this sentence pointed out the result. In addition, to find out the relevant causality of this result, a regression analysis should be performed.

5. Line 376, page 16. Is it “The authors declare no competing financial interest.”?
6. The author’s reply comments did not contain the line and the page number of the correlative correction(s). Therefore, it takes time to find out the corresponding information.

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

**Declaration of competing interests:**
I declare that I have no competing interest.