Reviewer’s report

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

Version: 2
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Reviewer: Nguyen Phuoc Long

Reviewer’s report:

In general, this article tried to improve the outcome prediction of Dengue patients. The research question is interesting. Nevertheless, the study is confined and the writing needs some improvement.

Major comments

1. There are some limit of the study design:
   a. Was it a case control study?
   b. Year of sampling?
   c. The name of the hospital, City and the number of beds?
   d. Details of inclusion and exclusion criteria?
   e. Descriptive statistics: Characteristic of patients?
   f. What is “bleeding manifestations”?

2. In the method section, why did the authors choose those parameters as criteria for severity? According to WHO criteria or what else?

3. The manuscript did not mention the blindness of the method. Who did analyze the NS1 ELISA and measured bedside test? The outcome might be affected because doctors/researchers might be aware of NS1 results. So it is important to make it clear and reconsider one more limitation if the study design was not blind.

4. The statistical usage of results, it is not a normal distribution for all data (as mentioned in line 180-181, page 8), then non-parameter method should be used, not “difference in means”. Therefore, it is better to use median (and range or IQR) instead of mean (and SD).

5. The authors should consider revising the table 1, because:
   a. It is better to use footnotes to explain statistically significant differences and statistical test.
   b. It is better to use the unique decimal number in the result columns (Eg. 170.4 ± 196.9 or 170 ± 197).
   c. Word should not be exist in the result columns but in the headings (eg. Mean ± SD).
d. Publishers prefer to use three horizontal lines: One above the column headings, one below the column headings, and one below the data. The grid line between columns should not be included.

e. It is better to clarify the experimental details or abbreviations at footnote.

f. In case of the Non-normal distributed data, it is better to use Median ± range (or IQR).

6. Figure 1: N total = ? for each day? It is better to use "**" for significant difference and the day nomenclature should be “Day -3, -2, -1, 0 (defervescence day), +1, +2 (for prediction).

7. There was no figure for ROC curves.

8. When did the researcher perform platelet count? Why did the author use the lowest lymphocyte count instead of the value at admission day (line 253, page 11)? The lowest lymphocyte count would be useless for prediction.

9. Line 226-230, page 10, the sentence should be reconsider.

10. The purpose of this study is to prove that whether bedside quick test is reliable and good agreement with standard ELISA test. Therefore, the authors should show the correlation between two methods before stating the role of NS1 in the prediction of severity.

11. Bedside tests are mainly used for early detection, the author did not mention the time at the day NS1 test were performed (day 0).

Minor comments:

12. Line 58, page 3, which “levels” were mentioned and what are detailed numbers? How much is it “higher”?

13. Line 60, page 3, the author wrote that “Serum NS1 antigen levels inversely correlated with the total white cell counts and lymphocyte counts”. Is it statistically significant or not?

14. Line 61, page 3, please provide the detailed number of sensitivity and specificity.

15. Line 65, page 3, the conclusion of abstract is not clear. What is the overall benefit or/and advantage?

16. Line 71, page 4, what does “it” prefers to? Why not “they”?

17. Line 73, page 4; line 77, page 4; and line 84, page 4, need reference(s).

18. Line 91 and 92, page 4 and line 111-113, page 5, the sentence(s) should not be there, please consider moving it to the final paragraph of introduction.

19. Line 188, page 8, the authors did not write about positive predictive values and negative predictive values calculation. But in the line 217-219 they were
calculated.

20. Line 201, page 9, it is better to present OR or P-value here.

21. Line 249 and 250, page 11, the authors wrote that “our previous studies and others have shown that leucopenia and especially lymphopenia was associated with severe dengue” but just put one reference.

22. Line 256, need reference(s).

23. Line 297 and 298, page 13, I think the sentence “our previous studies and others have shown that leucopenia and especially lymphopenia was associated with severe dengue” is an overstate statement.

24. Line 297-301, page 13 need reference(s).

25. Line 311, page 13, it was said that “some have suggested that”, but there is just one reference.

26. Line 352-354, page 15, is it necessary to reconsider the order of authors?

27. The writing and presentation could be improved. For example:
   b. Line 147, page 7, it should be “informed consent”.
   c. Line 209, page 9; line 251, page 11, it is better to use “NS1 antigen”.
   d. Line 221-222, page 10, it is better to be “having the difference between systolic and diastolic pressure less than or equal to 20mmHg”.
   e. Line 238-241, page 10, it is better to be “The NS1 antigen levels did not have a significant correlation with the development of severe dengue”.
   f. Line 475-482, it is better to use full stop at the end of the sentence.

**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 interests.