Reviewer's report

Title: Risk factors for the development of severe typhoid fever in Vietnam

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Reviewer: Eric D Mintz

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This paper explores the risk factors for severe diseases among 581 patients with confirmed typhoid fever over two 3-year periods in Vietnam. It is fairly well-written and requires minor revisions only. There are some limitations in that the definition of "severe disease" encompassed nine individual outcomes, and relatively few patients met the criteria for any of those nine outcomes of interest.

Major Compulsory Revisions: None are required.

Minor Essential Revisions:

1) Abstract, Page 3; second sentence: the noun "sex" does not need to be modified by the adjective "female" as the pre-existing evidence goes both ways (per remarks on pages 5 and 13).

2) Results, Page 10; line 192: As there are two groups of children (those under 5 years old and those under 16 years old) to avoid confusion, I suggest the authors specify here "Children under 16 years old were more likely than adults...". I suggest that this be done again on line 196 on the following page.

3) Page 11; line 202: Table 3 lists 96 patients with severe or fatal disease, but here we are presented with only 90.

4) Page 11; lines 204 and 208: On line 204 (and elsewhere in the manuscript), we are told of six patients with intestinal perforation; on line 208 this has been reduced to just five patients.

5) Discussion; page 12; Lines 232-234: The sentence in question does not seem to make sense - a few changes in the wording or punctuation would likely help.

6) In Table 4, the footnote regarding the acronym "FLQ" appears to be unnecessary.

Discretionary Revisions:

1) While some things, such as extremes of age or malnutrition, can be risk factors for a plethora of different outcomes that represent severe disease, other things (such as gender) may be risk factors only for one particular severe outcome. The authors could consider looking at individual categories of severe disease and reporting specific risk factors for that outcome. For example, male gender has been reported as a risk factor for intestinal perforation in reference 4 and in other references; to my knowledge, female gender has never been reported as a risk factor for intestinal perforation. Although only 6 patients in this series developed intestinal perforation, it would be interesting to know whether
the association was validated among that small sub-group.

2) Do the authors have any data on risk factors for relapse? I know that was not considered an indication of severe disease, and that data were only collected on the initial admission, but it might be of interest to readers to know whether relapse was associated with a particular antimicrobial treatment or resistance pattern among isolates or to other factors.

3) It is unfortunate that no information is provided on antimicrobial treatment received in hospital, as it relates to the susceptibility of the infecting strain and the outcomes of interest. I understand that data on treatment prior to hospitalization were not available, but a comment on in-hospital treatment might be warranted.

4) Would the authors consider commenting on the striking association between a low hematocrit and severe disease as noted in Table 3? While perhaps not a risk factor per se for severe disease, it appears to be a marker for it.

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

**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 interests.