Author's response to reviews

Title: Clinical and Laboratory Findings Associated with Severe Scrub Typhus

Authors:

Dong-Min Kim (drongkim@chosun.ac.kr)
Seok Won Kim (chosunns@hanmail.net)
Seong-Hyung Choi (penta15@hanmail.net)
Na Ra Yun (shine-0222@hanmail.net)

Version: 4 Date: 17 March 2010

Author's response to reviews: see over
To the Editor,

Re: MS: 2812462873128525  (Revision #2)
“Clinical and Laboratory Findings Associated with Severe Scrub Typhus”

Dear Editor

Thank you for your review and helpful comments regarding our paper.

We have made great efforts to revise our paper. Please see the attached one main text file. We believe that we have addressed all the questions and comments, but we would be happy to provide further information or revision if necessary. Thank you for your consideration and please feel free to contact us if we can help you in any way.

Dong-Min Kim, M.D.
Department of Internal Medicine
Chosun University College of Medicine

Following is our response to your questions and comments.

Reviewer’s report
Title: Clinical and Laboratory Findings Associated with Severe Scrub Typhus
Version: 3 Date: 15 February 2010
Reviewer: Si-Shiun Lin
Reviewer’s report:
Although the author responds to my previous comments, many important
changes mentioned in the response letter were not actually made in the revised manuscript! Several minor essential revisions are necessary for acceptance of this manuscript.

Minor Essential Revisions#

Abstract:
1. Result section. The words in revised manuscript is “(2) the presence of eschar (OR=0.15, P=0.03, CI=0.03-0.82)” rather than the correct one “(2) the absence of eschar (OR=6.62, P=0.03, CI=1.22-35.8)” mentioned in response letter! The author should check the whole manuscript carefully and use “absence of eschar” in text with correct statistic values in text as well as in Table 4.

Responds: We apologize for our carelessness. We corrected “present of eschar” to “absence of eschar” in result section and Table 4.

2. Conclusion section. The last sentence “Close observation and intensive care for scrub typhus patients with the potential for complications can prevent serious complications with subsequent reduction in its mortality rate.” This study only identified the potential characteristics of severe scrub typhus by statistic methods, not investigated whether identification of these characteristics “can prevent” serious complications with subsequent reduction in its mortality rate. It would be better change the word “can” to “may”, or re-write this sentence.

Responds: We totally agree with the review’s view.
As the reviewer’s comment, we have changed it.

Methods.
1. Page 4, line 5. The reviewer 3 suggests “increased titer” is enough, however, “increased four times or more in titer” is universally used gold-standard. The author also used “failure to demonstrate a fourfold or greater rise” in 5th line in Result and Discussion section.

Responds: As the reviewer’s suggestion, we have changed it

Result and Discussion
1. Page 8, the last line. Again, “transient cranial nerve palsy” is not one of the 7 conditions of severe scrub typhus defined by the author. The same problem for Table 1.

Responds: We are sorry for our carelessness. We have changed it as your recommendation.

2. Page 6, line 12-18 “There were no significant differences in...between the two groups” are redundant sentences. Only significant or important issues should be mentioned in text.

Responds: As the reviewer’s comment, we changed deleted the redundant sentence.
3. Page 7, line 8. The author use “the absence of eschar (OR=6.62, P=0.03, CI=1.22-35.8) here, but the referral Table 4 is “presence of eschar (OR=0.15, P=0.03,CI=0.03-0.82”. The Table 4 should be corrected because the title of table is for severe scrub typhus.

**Responds:** As your suggestion, we revised our Table 4.

4. Page 7, line 19. “predictive valuables” or “predictive variables”?

**Responds:** Right! Thank you so much for your correction. As the reviewer’s comment, we changed it.

5. Page 8, line 6. Add “(data not shown)” following “(P=0.011)”.

**Responds:** As the reviewer’s comment, we add it.

6. Page 9, line 2. The author did not respond well to our previous comment: Citation of references and more clear description is needed for the statement of “Despite the fact that this study included older patients than other studies, the mortality rate was lower.”

Most of the reader may not know the general age distribution or mortality rate of scrub typhus! The author neither provide information nor cite relevant references to support the statement about the patients included in their study are older than other studies. Only one report from India was used to support that their mortality rate is low, but the author did not mention about the age of the report. The authors explained many in the response letter and stated that they have changed and added the references, however, I did not see any description or cited references for this sentence in the revised manuscript! In one study from Japan (Ogawa M, et al. Am J Trop Med Hyg. 2002 Aug;67:162-5, among the 462 cases, 63% are aged 51-75 and 14% aged >75. Are patients included in this study older than cases from Japan? or just older than cases from southeast Asia?

**Responds:** According to your suggestion, we added some more information and relevant references.

Varghese et al [8] reported that median age of scrub typhus patients in the southern part of India was 36.5 (range: 12–75 years), and the mortality rate was 14%. In one study from Taiwan, Lai CH et al [14] reported that mean age of scrub typhus patients was around 43. Watt G et al [17] reported the case fatality rate of 15% ~30% in scrub typhus patients from Thailand.


However, in our study, only one patient died of scrub typhus and there was no one who needed ventilation support or renal replacement therapy. In Korea the population of the farming villages in rural areas is getting old just like one study from Japan [11, 18], the greatest number of scrub typhus patients in Korea was in the age group 50–69 years.

7. Page 10, line 2. Add “(data not shown)” following “severe scrub typhus group”.

**Responds:** As the reviewer’s comment, we add it.

8. Page 10, line 10. Why “these three parameter”? There are four characteristics identified in this study.

**Responds:** I’m so sorry for many mistakes. As the reviewer’s comment, we changed it.

Table 2 and 3
Previous comments: Important underlying disease should be included such as DM, liver cirrhosis, COPD,… etc, especially older patients were included in this study. Liver cirrhosis had been identified to be associated with mortality in recent publication (Kim et al. Scrub typhus in patients with liver cirrhosis: a preliminary study. Clin Microbiol Infect. 2009 Jul 14. [Epub ahead of print]).

Responds: As your recommendation, we assessed the underlying diseases such as diabetes, liver cirrhosis, COPD, except hypertension. But in our study there was no statistic significance. We added the results in our tables. However, I did not see any variables about underlying diseases such as diabetes, liver cirrhosis, COPD,…etc were added in Table 2 and 3.

**Responds:** As the reviewer’s comment, we added “underlying disease(diabetes, COPD, liver cirrhosis)” in Table 2 and Table 3.

Table 4.
Change the “Presence of eschar” to “Absence of eschar” as well as the statistic values.

**Responds:** As the reviewer’s comment, we changed it.

Reviewer’s report
Title: Clinical and Laboratory Findings Associated with Severe Scrub Typhus
Version: 3 Date: 8 February 2010
Reviewer: Ramakrishnan Ramachandran
Reviewer's report:
Authors have taken care of all the comments. They have admitted that they did
not consider the sample size for this study, which was responsible for wide CIs.

Level of interest: An article of importance in its field

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'

Responds: As I said before, we did not consider the sample size when we designed this study.

We understand the importance of evaluation of the sample size for the cases and controls.

We are thankful for your good comment. We will consider the statistics method before we start to design a new study.