Reviewer's report

Title: Clinical and Laboratory Findings Associated with Severe Scrub Typhus

Version: 1 Date: 19 November 2009

Reviewer: Si-Shiun Lin

Reviewer's report:

This is a study attempting to identify the predictors for clinical severe scrub typhus. However, several important minor essential revisions that the authors need to correct and clarify as listed below.

Minor Essential Revisions:

A. Abstract:
1. Page 2, line 12. “absence or presence of eschar” should be “absence of eschar”.
2. There are no denotations for abbreviations such as WBC, CRP, OR, and CI.
3. OR>1 indicate the results favor to the variable and OR<1 indicate the reverse results. The reversed OR and CI should be used for “absence of eschar”, and “albumin # 3.0 g/dl”.

B. Methods:
1. Page 4, line 7. A reference should be cited for the Cockcoft-Gault formula used for definition of renal failure.
2. Definition for “shock” is needed.
3. Page 4, line 12. The “effective antirickettsial antibiotic therapy” is not clear, tetracyclines, macrolides, fluoroquinolones? Did all patients not receive antibiotics effective for scrub typhus before assessment? Because this is a study about clinical characteristics and diseases severity, it is important to make sure that patients did not receive therapy before they were enrolled, or those who had received effective antibiotic treatment should be excluded. Why the author used “5 days” as therapeutic delay, was there any reference? or please explain briefly in one sentence here. For more objective comparison, I would suggest the author provide the data of “duration from disease onset to effective antirickettsial antibiotic therapy (days)” rather than “therapeutic delay” only in table 1.
4. Page 4, line 17. This is a prospective study and many blood tests are performed. Were signed informed consents obtained before the patients included in study? Please declare about this.

C. Result and Discussion:
1. Page 5, 1st line of this section. Please provide the number of possible cases and excluded cases according to the exclusive criteria.
2. 5th line of this section. Why rhabdomyolysis is presented here? It is not the
severe form defined by the author.

3. 8th line of this section. 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]).

4. Please denote the abbreviations in texts.

5. Where are the table 2 and 3 cited in text?

6. Page 6, line 5. The “absence or presence of eschar” should be “absence of eschar”.

7. Page 6, line 15. The sentence “Scrub typhus…its incidence being highest in Korea.” needs citation of reference.

8. Page 6, last line to page 7, line 5. I could not understand the association between presence of eschar and the length of time from onset of symptoms to hospital visit that the author discussed. Patients visit hospital mainly due to fever or other discomforts rather than eschar found by themselves. According to the result in this study, therapeutic delay is not different between the two groups (severe and non-severe cases). However, the duration (days) from disease onset to effective antirickettsial antibiotic therapy or therapeutic delay might be different between patients with and without eschar. That indicates the time of effective treatment rather than presence or absence of eschar is associated with severe scrub typhus. The author must clarify this. A recent publication comes from Korea also mentioned about absence of eschar is associated with mortality (Lee CS et al. Risk factors leading to fatal outcome in scrub typhus patients. Am J Trop Med Hyg. 2009 Sep;81:484-8.).

9. Page 7, line 7. The references cited by the author for the statement about frequency of presence of eschar “ but rare in Thailand and Taiwan [8,12]” are not appropriate. Ref. 8 is about 50 patients in south India and ref. 12 is about “pediatric” patients in Thailand. None of the references represent the adult scrub typhus in Thailand or Taiwan. In the study of Lai et al.(Int J Infect Dis. 2009 May;13:387-93), they reviewed literature about scrub typhus in Taiwan and stated that eschar could be found in 23-67% of patients with scrub typhus. The author should re-cite relevant references for this statement.

10. Page 7, line 10. 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.”.

11. Page 7, line 18. Because hypoalbuminemia is also a complication of liver cirrhosis and cirrhosis is associated with disease mortality, the author should provide evidence about there is no different frequency of diseases (particularly liver cirrhosis) associated with hypoalbuminemia between the two groups.

D. Table 1.
1. Add variables of important underlying disease (DM, COPD, liver cirrhosis, …etc.) and duration from disease onset to effective antirickettsial antibiotic therapy.

Table 3.
The title is for severe scrub typhus. So, the values of OR and CI are wrong for albumnin#3 g/dl. They should be reverse values.