

08/12/2017
Vellore

To,
Xiang Li, Assistant Editor, Editorial Office
Baishideng Publishing Group Inc

From,
Dr. Thomas Sudarsan
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Subject: Response to the peer review report related to manuscript “Spectrum of cardiac manifestations and its relationship to outcomes in patients admitted with scrub typhus infection” – manuscript no – 36486/ID - 02525367

Dear Sir /Madam,

Kindly find the response to the peer review report to the manuscript submitted for publication in your esteemed journal.

Step 1: Verify the accuracy of general information for your manuscript

Name of journal: World Journal of Critical Care Medicine

Manuscript NO.: 36486

Column: **Prospective Cohort Study**

Title: Spectrum of cardiac manifestations and its relationship to outcomes in patients admitted with scrub typhus infection.

Authors: Karthik Gunasekaran, Thomas Sudarsan, John Victor Peter, Thambu Sudarsanam, George Varghese, Paul Kundavaram, Sowmya Sathyendra, Ramya Iyyadurai and Kishore Pichamuthu

Correspondence to: Thomas Sudarsan, MD, Assistant Professor, Division of Critical Care, **Ida Scudder Road**, Christian Medical College, Vellore 632004, India.

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Reviewer code: 00502743, 02446706, and 00505382

First decision: 2017-11-30

Science editor: Fang-Fang Ji.

The above mentioned information is correct.

2. Response to the peer reviewer

Reviewer 1, code: 00505382

COMMENTS TO AUTHORS

Article is well written and covers an interesting topic. However, few issues should be considered before publication. - English Language can be revised to improve fluency.- Diagnostic tests for multivariable logistic regression should be presented to validate results (c-statistic, Hosmer-Lemeshow test); a backward stepwise approach might be used to reduce the number of variables in the multivariable model; a reduced duration of symptoms (associated with myocarditis) might imply a greater severity of symptoms, and therefore symptoms should be evaluated in the regression; the same reasoning applies to other variables obtained at hospital admission, in order to produce a regression model that is both statistically and clinically significant. For example, I would include in the regression analysis: diabetes, cough, myalgia, hemoglobin. Also, it is important to produce a multivariable model with a small number of variables, considering the limited sample size of the study

Author's response:

We thank you for your valuable comments, and for endorsing the value of our work. We have made several corrections to ensure fluency of English language and improve grammar.

We agree that "Goodness of fit statistic" is important for validation of data. Following consultation with a senior biostatistician, we have used the Hosmer-Lemeshow test and provided this statistic in the footnote in Table 4.

As regards incorporating other "significant variables" in baseline characteristics in the multivariate logistic regression analysis, we observed that the number of variables were very high and that would have limited the robustness of our model. Hence only clinically relevant variables were incorporated. This approach is clarified in the statistical methods section.

Reviewer 2, code: 00502743

COMMENTS TO AUTHORS

We know that scrub typhus is a current pathological condition in India and the Asian Pacific region. With respect to the epidemiological validity of scrub typhus in our region (South America), there have been re-emerging outbreaks in Peru, reporting up to 50% of the world's statistics. Likewise, outbreaks of scrub typhus have been recorded by *Rickettsia prowazekii* between 2006-2008 in Colombia, with recrudescence confirmed towards 2012. During the same period, cases of *Orientia tutsugameshi* in Chile were reported. The referred incidences leads us to reactualize both the clinical figure as well as the complications derived from this disease, in the face of possible developments of lethal epidemics in the region. Although the prevalent infectious agents in India are not clearly indicated in the work, I believe that the updating of the potential cardiac complications presented by Indian colleagues is very valid, especially the myocarditis that leads to heart failure (systolic dysfunction) and its early appearance - at 48 hs. After hospital admission

Author's response:

Thank you for pointing out the importance of reporting the prevalence of the problem. This would have been of importance. However this was not within the scope of our work.

Reviewer 3, code: 02446706

COMMENTS TO AUTHORS

The authors made a great effort describing the manifestations of cardiac involvement in scrub typhus. Minor error: page 6: line 3: reference 9 should be between brackets.

Author's response:

Thank you for your comment and for endorsing the importance of our work. We have corrected the minor error that you pointed out in page 6.

Thanking you,

Dr. Thomas Sudarsan