Author's response to reviews

Title: Evaluation of surveillance case definition in the diagnosis of leptospirosis, using the Microscopic Agglutination Test

Authors:

Dinesh Dassanayake (dlbdassanayake@hotmail.com)
Harith Wimalarathna (harithlc@slt.net.lk)
Suneth B Agampodi (sunethagampodi@yahoo.com)
Veranja C Liyanapathirana (veranjacl@yahoo.com)
Thibbotumunuwe A C L Piyarathna (taclthibbotumunuwa@yahoo.com)
Bimba L Goonapienuwala (Lakmi_g@yahoo.com)

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Author's response to reviews: see over
Dr D.L.B. Dassanayake,
Registrar in medicine,
Teaching Hospital,
Kandy,
Sri Lanka.
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The Editor,
BMC Infectious Disease

Dear Sir

\textbf{Submitting the revised manuscript - Evaluation of surveillance case definition in the diagnosis of leptospirosis, using the Microscopic Agglutination Test}

Many thanks for reviewing our manuscript. We have gone through the reviews made by all 3 reviewers. We are submitting the revised manuscript with this letter. We would be much appreciated if you could go through our responses to each reviewer.

Major compulsory revisions.

1. As pointed out by the 2\textsuperscript{nd} and 3\textsuperscript{rd} refries, we have clarified the objectives to state “This study was aimed \textit{at validating the leptospirosis surveillance case definition, using the Microscopic Agglutination Test (MAT)}”. Accordingly we have changed the last sentence in the methods section of the abstract to say “Leptospirosis case definition was evaluated with regard to sensitivity, specificity and predictive values, \textit{using a MAT titre of \geq 1:800 for confirming leptospirosis}”. These changes were made in page 2. Similar changes were
made in the conclusions sections on pages 3 and 10, also in the last sentence of introduction and materials & methods section on page 4, and in the first sentence of discussion on page 7.

2. The phrase “screening test” was also dropped as the 2nd author felt it was inappropriate. So the title was changed to “Evaluation of surveillance case definition in the diagnosis of leptospirosis, using the Microscopic Agglutination Test: a validation study.” This change was made on pages 1& 2. Similarly the term “screening test” was removed in pages 3,4,5,7,9,10 and 12. Accordingly heading of table 3 was changed to “4x4 table showing number of patients meeting clinical criteria of case definition and MAT results” on page 17 and heading of table 4 was changed to “Parameter estimates of leptospirosis surveillance case definition” on page 18.

3. As pointed out by the 2nd referee we have corrected the inconsistencies in the results section of abstract on page 2 as well as the main results section on page 6. Corrected sentence is “Total number of MAT positive cases was 62, therefore 5 were false negatives.”

4. Third referee disagrees on the use of a MAT titre of ≥ 1:800 in acute phase sera as the gold standard. This was used due to the practical difficulties in the use of rising titre as mentioned in the limitations of the study section. Although the use of a single titre of ≥ 1:800 had not been validated in local setting there is evidence to support its use from other countries [9, 10]. This is the titre specified by the Medical Research Institute (National reference laboratory) for diagnosis of leptospirosis when acute phase serum is
used. In this regard we have edited the sentences in methods section to state “MAT which is the only available method of confirming the disease in the government sector was used for confirming leptospirosis cases.” We have also inserted a sentence in limitation of study section on page 10 which states “This is the MAT titre specified by the MRI to diagnose leptospirosis if acute phase serum is used.” And we have dropped the term “gold standard”. We have also inserted a reference for the MAT [8].

Similar change was made in the procedure section on page 6 to justify the use of a MAT titre of \( \geq 1:800 \) in acute phase sera.

5. Use of Leptospira Patoc strain as the MAT antigen is a problem as we have already discussed in the limitations section. But this is the only available method of confirming leptospirosis in Medical research institute which is the national reference laboratory. Same method has been used in the study by Brato in 1995. Considering this, the statement “Same method had been used by Brato and colleagues in 1995 for their study but with a different titre [5]” was inserted on page 10 of limitations section.

Minor essential revisions:

1. As pointed out by the 2\(^{nd}\) reviewer acronym MAT and its full term was used in several places. This was corrected using the full term only in its first use, on page 2 and in other pages (2, 3, 4, 6, 10) it was replaced by the acronym.
2 The phrase MAT > 1:800 was corrected to state MAT ≥ 1:800 as suggested by the 2nd author.

3 Although the 3rd referee suggested removing table 2 and 3 we thought that the results section would be self explanatory with the two tables. But we have reorganized table 2 in descending order of percentages to improve the clarity, as proposed by the 2nd and 3rd referees.

4 Page numbers were inserted and the sub sections in the materials & methods section was minimized as pointed out by the 3rd referee.

5 Clinical details of cases were reorganized in table 2 and presentation of data analysis was improved in page 7 & 8 as suggested by the 3rd referee. The article was copy edited to improve the language. We hope the article would be published in your journal following the necessary revisions.

Thank You
Dr D L B Dassanayake
Registrar in Medicine
Teaching Hospital, Kandy
Sri Lanka.