

Peer Review Response:

Reviewer# 00503255. No revisions needed

Reviewer# 00504024: No revisions needed:

Reviewer# 00138749:

Comments To Author:

Major points: - Prevention: They state it is one of the aims of the review. However I think this part could be improved. Authors should clarify in which conditions prophylaxis should be recommended. - For diagnosis: The authors state detection limit for DAT is 1:100. However, this should be reviewed) as the correct figure is 1:400, as stated by WHO documents: - Organization WH. Report of the Second Meeting of the Leptospirosis Burden Epidemiology Reference Group. 2011. - India WHOCof. Leptospirosis Laboratory Manual. 2007. Minor points: - While specific ventilatory management is controversial, a brief discussion concerning severe pulmonary impairment should be offered (I.e. In this setting HFOV may indeed be lifesaving in severe LPHS [Mat Nor MB Indian J Crit Care Med. 2016 Jun;20(6):342-8] - Page 3. Line 3. The sentence has been stated previously in the manuscript. -Some references seem to be a little bit old: Instead of reference 11 I would favour "Hartskeerl RA, Smythe LD. The role of leptospirosis reference laboratories. Curr Top Microbiol Immunol 2015; 387:273–288." Considering ref 13, additionally the reference: Mgode GF, Machang'u RS, Mhamphi GG, et al. Leptospira serovars for diagnosis of leptospirosis in humans and animals in Africa: common leptospira isolates and reservoir hosts. PLoS Negl Trop Dis 2015; 9:e0004251 could be of Interest to demonstrate specific living Leptospira strains are necessary. Ref 21 is an outdated one. I would replace it. One suggestion is any of this two: Waggoner JJ, Balassiano I, Mohamed-Hadley A, et al. Reverse-transcriptase PCR detection of leptospira: absence of agreement with single-specimen microscopic agglutination testing. PLoS One 2015; 10:e0132988. OR Backstedt BT, Buyuktanir O, Lindow J, et al. Efficient detection of pathogenic leptospires using 16S ribosomal RNA. PLoS One 2015; 10:e0128913.

By Point:

1. Prevention: They state it is one of the aims of the review. However I think this part could be improved. Authors should clarify in which conditions prophylaxis should be recommended

Author Response: We agree this section is minimal, but that is because the data is sparse. We feel it would be inappropriate to extrapolate general recommendations such as what conditions warrant prophylaxis from one small study. Further research in this area is needed.

2. For diagnosis: The authors state detection limit for DAT is 1:100. However, this should be reviewed) as the correct figure is 1:400, as stated by WHO documents:
- Organization WH. Report of the Second Meeting of the Leptospirosis Burden Epidemiology Reference Group. 2011. - India WHOCof. Leptospirosis Laboratory Manual. 2007

Authors Response: There is variability amongst the detection limit. Reviewing the 2011 WHO document, 1:400 is their reported detection limit though exploring the WHO's references, the detection limit ranged from 1:100 to 1:800. We found that the most common (and most sensitive) limit is 1:100. We provided 2 additional references that support our value. We did add a point that there is variability.

3. While specific ventilatory management is controversial, a brief discussion concerning severe pulmonary impairment should be offered (I.e. In this setting HFOV may indeed be lifesaving in severe LPHS [Mat Nor MB Indian J Crit Care Med. 2016 Jun;20(6):342-8]

Authors Response: The referenced paper is a case report of 5 patients with severe LPHS who were successfully treated with HFOV. We found no other published studies, case series or even reports that have even examined this question. While the case series is perhaps promising, we feel a single case series of 5 patients is insufficient quality of evidence to include in the review.

4. Page 3. Line 3. The sentence has been stated previously in the manuscript.

Authors Response: Uncertain of which sentence has been repeated.

5. Some references seem to be a little bit old: Instead of reference 11 I would favour "Hartskeerl RA, Smythe LD. The role of leptospirosis reference laboratories. Curr Top Microbiol Immunol 2015; 387:273–288." Considering ref 13, additionally the reference: Mgone GF, Machang'u RS, Mhamphi GG, et al. Leptospira serovars for diagnosis of leptospirosis in humans and animals in Africa: common leptospira isolates and reservoir hosts. PLoS Negl Trop Dis 2015; 9:e0004251 could be of Interest to demonstrate specific living Leptospira strains are necessary. Ref 21 is an outdated one. I would replace it. One suggestion is any of this two: Waggoner JJ, Balassiano I, Mohamed-Hadley A, et al. Reverse-transcriptase PCR detection of leptospira: absence of agreement with single-specimen microscopic agglutination testing. PLoS One 2015; 10:e0132988. OR Backstedt BT, Buyuktanir O, Lindow J, et al. Efficient detection of pathogenic leptospires using 16S ribosomal RNA. PLoS One 2015; 10:e0128913.

Authors Response: reference 11 and 13 are published in 2015. Reference 21 was published in 2011, but we feel it is an excellent paper.