Reviewer’s report

Title: Clinical and Temporal Patterns of Severe Pneumonia Causing Critical Illness during Hajj

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Reviewer: Shevin Jacob

Reviewer’s report:

In their manuscript entitled “Clinical and Temporal Patterns of Severe Pneumonia Causing Critical Illness during Hajj,” Mandourah and colleagues provide a description of patients diagnosed with pneumonia after being admitted to the ICU of 15 hospitals (7 temporary, 8 permanent) over 2 consecutive Hajj years. The paper is an important contribution to the body of literature on Hajj medicine given the important public health implications of respiratory infection during an annual pilgrimage involving several million people who travel to and from over 40 countries around the world. Although the manuscript is not ready for publication in its current form, major and minor revisions (as detailed below) should be sufficient to move the status of this manuscript to ready for publication.

Major Compulsory Revisions:

1. In the title and methods (para 1), the authors state that the primary outcome is “incidence rate and temporal onset for severe pneumonia.” An incidence rate (with person-time in the denominator), however, is not provided anywhere in the results. Either an incidence rate should be included or the title and methods should be revised to reflect that only point estimates are provided.

2. More background information about pilgrim density is needed for readers to understand the temporal onset of pneumonia during both consecutive periods of Hajj. The last sentence in the first paragraph of the Results section states “temporally, the vast majority of pneumonia occurred in the period following heaviest pilgrim density…” but there is no information in the background or results to let the reader know when the heaviest pilgrim density occurred during Hajj in the two consecutive years sampled. Accordingly, para 1, sentence 2 in the Discussion is not supported by evidence about temporal relation to spatial crowding.

   a. It is unclear from Figure 2 whether the incident cases for each day are a combined total from both Hajj years.

   b. The significance of the labels for Hajj sites on the x-axis needs clarification. Do all Hajj pilgrims migrate to the same site together so that, for example, all pilgrims are in Makkah for the first 7 days, in Mina on Day 8, in Arafat on Day 9, in Mina from Days 10-13, etc.? Or, is a proportion of pilgrims spread across all sites at any given time? How does this correspond to access to the temporary and permanent hospitals available? Can you include the denominator for each day (i.e., combined number of ICU hospitalizations for each day)?
3. Are the hospitals described in the Methods a representative sampling of a larger group of hospitals for Hajj or do they represent all hospitals available to Hajj pilgrims? Please provide a sentence describing this description of the hospitals sampled.

4. If all pneumonia is thought to be a result of some level of aspiration, what is the case definition for aspiration pneumonia in comparison to community-acquired or nosocomial pneumonia? Is this witnessed aspiration? Please clarify the case definition in the methods section.

5. Include antibiotic susceptibility results from bacterial isolates in Table 2. How many patients with pneumonia have multi-drug resistant bacteria? Could outcome be associated with antibiotic resistance?

Minor Essential Revisions:

1. Pre-abstract (answer 1 to what is the implication, what should change now?): last part of sentence is awkward. Consider rewording to “improvements in living conditions should be considered for Mina…to help lessen the potential risk of transmissible illness…”

2. Abstract (Background, sentence 1): maybe should be may be

3. Discussion (para 2, sentence 3): internationally should be international

4. Table 2: Acinobacter should be Acinetobacter

Discretionary Revisions:

1. In Table 1, can you provide information about the other (non-pneumonia) causes of ICU admissions?

2. Under Results>Clinical Outcomes (para 1, sentence 1), is the difference in 3-week mortality between all critically ill patients (16.2%) and patients with pneumonia (19.5%) significant?

3. What was the source of cultures for bacterial etiologic diagnosis of pneumonia [e.g., sputum (expectorated? induced?), BAL, etc]? Please include this detail in the Methods section.

4. Can logistic regression be performed to evaluate independent clinical correlates of poor outcome for ICU patients hospitalized with pneumonia?

5. Given considerable difference in MTB frequency reported in this manuscript compared to that reported in the Malaysian sub-population reported by Wilder-Smith, et al (ref #22), include methods used to diagnosis M. tuberculosis (e.g. clinical suspicion, AFB smear, culture, or PCR)? Perhaps methods used are poorly sensitive and actual frequency is underestimated. If this is the case, include this detail as a limitation in the Discussion section.

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.