Reviewer's report

Title: Nosocomial outbreak of the pandemic Influenza A (H1N1) 2009 in critical hematologic patients during seasonal influenza 2010-2011: relevance of oseltamivir resistant variant viruses.

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Reviewer: Sallene S Wong

Reviewer's report:

This report is important to add on the data related to emergence of oseltamivir resistant H1N1pdm09 in immunocompromised patients after prolong antiviral treatment. The evidence suggested that there was noscomial outbreak of H1N1pdm09 in this hospital setting but none of the patients acquired the oseltamivir resistant virus initially.

1. Is the question posed by the authors well defined? Yes
2. Are the methods appropriate and well described? Sufficient, full genome sequencing of the viruses will have the added benefit to address the nosocomial infection aspect.
3. Are the data sound? Fair
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Not quite, more clarity in Table1 and Figure1, as well as in the RESULTS description.
5. Are the discussion and conclusions well balanced and adequately supported by the data? Not sufficient, please refer to comments.
6. Are limitations of the work clearly stated? No
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? No, there is not sufficient data to support the oseltamivir resistance is the sole relevance to the nosocomial outbreak.
8. Do the title and abstract accurately convey what has been found? The authors should conclude on the relevance of oseltamivir resistant variant viruses based on the evidence.
9. Is the writing acceptable? There are English, spelling and grammar errors throughout the manuscript, more attention is required.

Minor Essential Revisions:

1. Should be consistency with the terminologies, and differentiate H1N1 and pandemic influenza A (H1N1) 2009, because H1N1 can be interpreted as seasonal H1N1 (pre-2009 seasons).
2. H1N1pdm09 is the correct name; please check spelling on (H1N1dpm09) throughout the manuscript.
3. Referring to Background, first paragraph; correct the spelling of neuramindase (NA) gene.

4. Referring to METHODS>Study population, last paragraph describing clinical samples was collected as nasopharyngeal swab. It is inconsistent stated that in Table1; diagnosis of Flu in lower respiratory tract infection was confirmed in patient 1 and 4, but not mentioned in the MEHTODS.

5. Referring to METHODS>RNA extraction, real-time RT-PCR, multiplex and one step RT-PCR; first paragraph, “DNA was automatically extracted” should be written as total nucleic acid was automatically extracted. Third paragraph; the first sentence is required clarification on “subtype H1N1” and “viral RNA was carried tested by Fast set H1N1v”.

6. Table1 is still very confusing; symbol is not clearly identified in the legend for “Inpatient ward without outbreak”. Under Clinical events, what is the double line arrow for “Other”? I cannot find the description in the RESULT section. The color and symbol for Flu A PCR- are not quite the same as in the legend.

7. Referring to RESULTS, there is no mention of viral clearance in patients 3, 5 and 6, but the symbol for Flu A PCR- was added to 3 and 5 in this new Figure1.

8. Referring to RESULTS, fourth paragraph; Patients 2,3,5,6 were subjected to oseltamivir therapy at various times; and patients 2, 4, 5 were infected by oseltamivir resistant H1N1dpm09. I suggest this sentence should be rewritten as: Patients 2,3,5,6 were subjected to oseltamivir therapy at various times; and oseltamivir resistant H1N1pdm09 with NA gene H275Y mutation was emerged in patients 2, 4 and 5.

9. Referring to RESULTS, the last paragraph indicated that 12 presented ILI symptoms of lower respiratory tract (LRT), was any LRT specimens collected and performed viral testing? Usually more different source of specimens will be collected for testing in ICU patients.

10. Spelling error in the first paragraph of DISCUSSION, “whether” should be “wheather”.

11. In the DISCUSSION, referring to this sentence: the 91% of nosocomial patients with Influenza A virus was H1N1dpm09 infected and 9% was infected by influenza A (H3N2). Was any resistance testing done on these 91% H1N1pdm09 samples? These samples can be used as control case study.

12. Second paragraph in the DISCUSSION: “The mortality rate in the patients subjected to H1N1dpm09 test in our Hospital was to 15%, while in Haematology ward was to 13.1%.” I do not understand the word “test” used in this sentence and the relevant to the objective of this study?

13. Clarify “H1N1” in the third paragraph of DISCUSSION.

Discretionary Revisions:

1. Referring to articles such as Baldanti et.al 2010, Chutinimitkul et.al 2010 JVI and Drews et.al 2010 on the subject of the relevance of D222N and D222G to influenza pathogenesis and transmissibility in H1N1pdm09; and expand on the
discussion related to fatality caused by H1N1pdm09 infection. Was any sequence performed to identify the D222 mutation in Hemagglutinin gene of H1N1pdm09 virus found in this group of patients?

2. There is alternative anti-viral therapy available for oseltamivir resistance should be included in the discussion.

3. Infection prevention and control in hospital setting is important to reduce nosocomial transmission in ILI patients, especially in hematologic/oncologic wards, and this subject should be included in the discussion.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

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.