Reviewer’s report

Title: Pandemic influenza A/H1N1 virus infection and TNF, LTA, IL1B, IL6, IL8, and CCL polymorphisms in Mexican population: a case-control study

Version: 3 Date: 31 August 2012

Reviewer: Chung Yan Cheung

Reviewer’s report:

The revised manuscript by Morales-García et al. has addressed most of my points, however a major exists concerning the validity of the AHC group in the MS (as described below).

Major Compulsory Revisions

1. The authors presented a group of patients as “Asymptomatic Healthy Controls (AHC)” or Healthy Controls in table 3 which the authors described as persons who had personal contact with A(H1N1)pdm09 patients and confirmed exposure with the presence of anti-influenza A(H1N1)pdm09 antibodies. However, the presence of antibody does not confirm infection with A(H1N1)pdm09 as there is the likelihood of cross-reactivity (Hancock et al. NEJM 2009) especially in an older age group which seems to be the case in this patient group. Therefore several issues have to be addressed as this group consists of a large sample size of 176 patients and seems to play a major role in subsequent analysis. The result of which is featured in Table 4,5, and maybe 6 (as non-fatal group? See below) where the authors appear to include this group of patients as being infected with A(H1N1)pdm09:

   a. the authors should describe the methods used in determining the presence of antibody (micro-neutralization assays?) and the data should be shown,

   b. can sero-conversion or rising titer for these patients be demonstrated?

   c. were antibodies for A(H1N1)pdm09 tested for in the ILI patients (they could been previously infected as well).

   d. Was the AHC group included into the non-lethal cases of A(H1N1)pdm09 infection for analysis to give the results in Table 6 ie. what are the inclusion criteria to compare with mortality group?

2. The timing and dosage of anti-viral drug administration could impact outcome significantly, although the authors stated that all patients were treated “upon admittance to at hospital” (please note grammatical mistake!), further information is needed:

   a. the days after symptom onset in which the patients were admitted into the hospital (ie. sample collection) should be shown, for without this data it is difficult
to determine whether the timing of treatment will confound the results?

b. Did all the patients receive the same dosage of anti-viral drug?

3. One of the most common complications of influenza infection is secondary bacterial infection. In the serious cases, did the authors investigated whether these patients have bacterial infection as this may have confounded the analysis?

Minor Essential Revisions

4. in background (line 6): “In Mexico, the global lethal rate was estimated to be 1.2% ……….” Does the authors mean globally, in Mexico or both?

5. On page 7 line 3 (Method) : “These samples were analyzed for direct antigen detection of influenza specific RNA by using real-time reverse-transcriptase (rtRT)-PCR (RespiFinder)” does not make sense. Maybe the direct antigen detection bit should not be there.

Discretionary Revisions

none

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: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests