Reviewer’s report

**Title:** C-reactive protein serum levels as an early predictor of outcome in patients with pandemic H1N1 influenza A virus infection

**Version:** 2  **Date:** 10 June 2010

**Reviewer:** Charles-Edouard Luyt

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In the present study, Dr Zimmerman and colleagues evaluated the usefulness of C-reactive protein (CRP) as a prognostic marker in patients with an influenza A (H1N1) infection. The authors retrospectively included 191 patients with a confirmed diagnosis of influenza A (H1N1) infection. They showed that mean CRP serum level was higher in patients admitted to ICU and who required mechanical ventilation than in patients who did not need ICU or mechanical ventilation. Moreover, they found that CRP, obtained on ED admission was the best predictor of whether a patient would need ICU care and mechanical ventilation.

I have the following reservations regarding the manuscript:

**Major compulsory revisions:**

1. The main limitation of this study, as for every study on a diagnostic or a prognostic marker, is the meaning at the patient level. The authors found that mean CRP level was higher in patients with subsequent ICU admission or mechanical ventilation than in patients with uncomplicated course. However, there is an overlap in the values (Figures 1 and 2). Thus, for a given patient, a value of CRP does not mean something.

2. The best way to express the results for a diagnostic test is probably to give the positive and negative likelihood ratios. If I am correct, the corresponding values for CRP to predict ICU admission are 2.6 and 0.5, respectively. These values are not typical of a good test.

3. As underlined by the authors, this study is retrospective, and 40% of the 315 patients were not evaluated. Thus, it is difficult to draw definite conclusions and I suggest them to be more cautious in the interpretation of their results. As an example, in the conclusion of the abstract, the authors should specify that these results are true for their population.

4. The authors should discuss their limitations more extensively. For example, it is not sure that the results can be extrapolated to another population.

5. The authors chose a model to show that CRP was an independent factor associated with ICU admission and mechanical ventilation. However, these parameters were obtained on the emergency department. Since most patients first stayed in the ED and were secondly referred to the ICU or the ward, it would have been more interesting to look at the kinetic of those parameters. As stated
above (comment 1 and 2), CRP does not seem to be a good test to predict ICU transfer.

6. The authors stated that CRP was the best predictor of whether a patient would need ICU care and mechanical ventilation. Again, this is true only when looking at the parameters obtained on ED admission, with the model the authors chose. The authors have to underline this point because it can be confusing for the reader.

7. More interesting for a clinician is the course of the disease. Do the authors have any data? How was the clinical course? And the evolution of blood gazes?

8. If I correctly understand what the authors did in there model was a stepwise forward analysis (this is not underlined in the methods. Please add the methodology in the corresponding section). What are the results if the authors enter first the results of the blood gazes (PaO2), then chest X-Ray and then abnormal auscultatory findings? Does CRP level entered into the model?

Level of interest: An article of limited interest

Quality of written English: Acceptable

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