Reviewer’s report

Title: Characterisation of acute respiratory infections at a UK paediatric teaching hospital following the H1N1 pandemic (Observational study assessing the impact of H1N1 on predominant viral pathogens)

Version: 2  
Date: 7 February 2014

Reviewer: Rodolfo E Begue

Reviewer’s report:

General Comment
The paper presented is an evaluation of 645 patients seen over a year period with ARI and evaluated for respiratory viruses. The authors found that RSV was more common but influenza A(H1N1) was more severe than others. The paper is a nice description of the present status in the UK and provides some important information on diagnostic yield of collection methods and the importance of co-morbidities for different age-groups. Some aspects need clarification, though.

Major Compulsory Revisions
Materials and Methods, Ethics Statement: please clarify whether the protocol was reviewed by an IRB and determined not to require IRB oversight, or whether the determination was made by the researchers and the protocol not submitted to the IRB for review?

Materials and Methods, Pathogen Detection, RSV testing: it seems by the description that RSV was tested by 2 methods, while other viruses were tested by one (is that correct?) which may account for the higher detection of RSV. Furthermore, it seems that if the rapid RSV test was positive, then no further testing was done (lowering the chances of detecting other organisms); and, if rapid RSV negative, then multiplex PCR was performed to detect other viruses (and again, detect RSV). If that is true, it should be mentioned as a limitation.

Discussion: the opening statement, while correct, is too strong and may be misinterpreted; many children with influenza A(H1N1) did not have a severe illness or died and some with other viral infections (or PCR-negative) could also experience severe illness and death. Besides, this is a select group of hospitalized patients and not necessarily representative of all children with influenza A(H1N1). Since this is the opening sentence of Discussion, I suggest elaborate more.

The Discussion should have a comprehensive paragraph on limitations of the study.

Minor Essential Revisions
Throughout the paper: The appropriate term should be “influenza A(H1N1)pdm09” or at least “flu A(H1N1) when referring to that specific strain, and not just “H1N1”
Materials and Methods: please clarify how participating cases were selected. Was it by finding those with ARI or by finding those who had a respiratory specimen submitted for viral testing? If by ARI, was it by coded diagnosis (ie, using administrative datasets with either admission or discharge diagnosis) or by review of charts and identification of patients who met pre-established definition of ARI? If so, what was the definition of ARI? If done by patients tested, were they identified by review of laboratory records? And, once identified, were charts reviewed to confirm they indeed met pre-established criteria for ARI?

Materials and Methods: it is unclear to this reviewer why the authors specifically single out patients admitted for surgery as an additional group (as opposed to patients admitted for any other non-ARI reason). Is it that patients are only admitted to either medical or surgical services and they are trying to include both (ie, all) groups? If so, please clarify.

Results, paragraph 1: to avoid confusion please spell out dates since nomenclature may be different in different parts of the world (ie, day/month order).

Results: in cases of co-infections it is unclear which one (if any) was a real pathogen and which one represented asymptomatic shedding (that point should be mentioned in Discussion). If there was any quantification of “viral load” by qPCR please provide that information; that may help sort out the relative importance of each of the co-infecting viruses.

Results: was there any information in bacterial culture? If not, please state that clearly and mention as a limitation in Discussion. At least theoretically, in some cases detected viruses may represent asymptomatic shedding and an unidentified bacterial infection may be the actual cause of hospitalization. That may explain why the “negative” cases tended to be more severe.

The designation of “non-H1N1” seems to be different in Figure 2 than in Table 1, which creates confusion. Better description terms should be used, such as “other viruses” for Figure 2 and “non-H1N1 influenza A virus” for Table 1 (or similar terms).

Discussion, paragraph 1: the sentence “the prevalence of co-morbidities increased as children aged” needs to be re-phrased. I guess, what the authors mean is that “the presence of co-morbidities was detected more frequently in older cohorts” (or something similar).

Results, 2 paragraphs before Conclusions: the point about cohorting is poorly developed and more confusing than useful. While potentially useful, the authors must either clarify their point or leave it out (since it seems to represent mostly implications of their work more than discussion of their findings).

Conclusion, last paragraph: I suggest modifying first sentence slightly to read something like “This study confirms influenza A(H1N1) infection as an ongoing cause of occasionally severe disease affecting both healthy children and children with co-morbidities”. I think the last sentence (“Continued preventative measures …”) can be omitted since I don’t believe anyone is disputing continue use of vaccination and other preventative measures (same comment for end of
Abstract.

Figure 1: please describe (in a legend) the abbreviations used at the bottom of the figure.

Table 1: also describe (or avoid) abbreviations.

Discretionary Revisions

Being standard, description of BinaxNOW RSV method is unnecessary.

Were p values calculated with Microsoft Excel 2010? Other more standard statistical packages would be more appropriate.

Please be consistent in how data is presented throughout the paper. I suggest the use of median (range; IQR) and not mean. When indicating p value, as much as possible, please indicate exact value and not simply p <0.05 (or similar). Because of multiple tests, some p values may be marginal and of questionable significance.

Page 12-13: another cause of variability in PICU admissions may be local practices for indication for PICU admission (did they all require intubation?).

Title (and Text): in my opinion too much emphasis is put in A(H1N1) making the paper look biased towards that specific virus. A more general title and description in the paper with a conclusion of the importance of A(H1N1) would be more appropriate. For starters, I suggest taking the last part of the title (“following the H1N1 pandemic”) out.

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

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