Author’s response to reviews

Title: Etiologic spectrum and occurrence of coinfections in children hospitalized with community acquired pneumonia

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Version: 1 Date: 26 Nov 2017

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Reviewer's comments:

Benoît Visseaux (Reviewer 1):

Major comment:

1- Is it possible to add a quick word or a simple figure to depict the number of included case over time as well as the epidemiology of the pathogens across the study period? This can be useful to discuss the importance of respiratory testing outside the winter period.

Response: we have added a figure to depict the number of included case over time as well as the epidemiology of the pathogens across the study period
2- A short word should be added about coronaviruses epidemiology in China. They are not detected by the authors but seems not so frequent in children in some previous work outside of China.

Response: our virus tests did not cover all the common viruses, such as coronaviruses, which had positive rate of 17.5% in patients with acute respiratory infections in a recent Chinese study. We have added this in our limitation.

3- The PCR primers are not given in the methods section. They should be added, or the reference of the paper describing them, as the primers' choice can greatly influence the sensitivity of the test.

Response: The PCR primers have been added in the methods section.

Minor comment:

1- Page 5, line 42. Regarding the nasopharyngeal samples, a word should be added regarding the maximum tolerated delay between the sampling and the reception in the lab.

Response: A total of 2 ml nasopharyngeal aspirates was obtained and sent for analysis within 30min.

2- Page 9, line 34. The first sentence of the paragraph need to be rephrased.

Response: we have done this.

3- A word can be added in the limitation of the study about the heterogeneity of the tests used for virus detection as some are detected by immune-fluorescence and some other by in-house PCR.

Response: we have added this in the limitation.
4- I am curious about the sentence on traditional Chinese hospitals (page 4, line 42) which present lower levels of mix infection rates. Is this because of the severity of the patients that is different or because of testing practice?

Response: in China, the severe patients were usually treated in the western medicine hospitals. Most of the traditional Chinese hospitals only serve the mild patients. These patients received the same testing practice.

Diego Viasus (Reviewer 2): I appreciate the invitation to review the manuscript. The authors describe the etiology of CAP in children and the factors associated with coinfection.

1. The authors should indicate the characteristics of the hospital and the population covered by it
Response: we have added the characteristics of our hospital and the population covered by it in the Method section.

2. How were the variables included in multivariate analysis chosen?. Information about results of the Hosmer-Lemeshow test and AUROC should be provided.
Response: “Only variables from the univariate analyses that were significant at the .05 level were entered into the multivariate logistic-regression analyses.” We have added this in the Method section. Results of the Hosmer-Lemeshow test and AUROC has been provided.

3. Did the patients have comorbidities?
Response: No, patients have comorbidities (history of a diagnosis of chronic lung disease, congenital heart disease, or immunodeficiency) were excluded from the study.
4. Why were urinary antigens not made for the detection of respiratory pathogens?

Response: According to the clinical practice guidelines for the management of community-acquired pneumonia in infants and children by IDSA1, urinary antigen detection tests are not recommended for the diagnosis of pneumococcal pneumonia in children, false-positive results are common. So urinary antigen detection was not made in our study.


5. What is the clinical value of identifying three or four pathogens in respiratory samples? This topic should be described in the discussion.

Response: we have added this topic in the discussion.

6. Which were the isolated causative pathogens in samples such as blood, pleural fluid and bronchoalveolar lavage (BAL)?

Response: as we said in the Bacterial detection section, a bacterial pathogen was defined as detection of H. influenza, M.catarrhalis and other Gram-negative bacteria, S. aureus, S. anginosus/mitis, S. pneumoniae, or S. pyogenes in blood, BAL specimen, or pleural fluid by culture2.