Author’s response to reviews

Title: Impact and clinical profiles of Mycoplasma pneumoniae co-detection in childhood community-acquired pneumonia

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Replies to the reviewers’ comments:
Reviewer reports:

Kyung-Yil Lee (Reviewer 1): This reviewer re-reviewed the paper titled "Impact and clinical profiles of Mycoplasma pneumoniae co-infection in childhood community-acquired pneumonia".

The reviewer thanks the authors' agreement of my suggestions and revision of the manuscript. The revised one is improved over the previous version.

As this reviewer indicated in previous review, this study may have patient-selection bias; 1) patients collection might be done during post-MP epidemic year, and 2) study methods used in the both groups were not identical (maybe serologic test for MP infection, PCR method for viral infections, and blood culture method for bacterial infections). Thus, many patients with MP infection-only in this study might have pneumonia with unidentified pathogens and a history of recent past MP infection in recent MP epidemic.
Next MP epidemic would occur in coming 2019-2020 in China. Thus with a prospective and proper study design, the authors can obtain good results for the issues on this study.

Response: Thank you very much for re-reviewing this paper. Your suggestions are really helpful for our study, and we will further explore the issues on this study in the coming Mp epidemic.

Hong Kai Lee (Reviewer 2): Well done for the significant efforts in this study.

Line 147-8: It would be useful to know if there is statistical difference in age and gender between the 176 Mp CAP children and the 4148 population CAP children.

Response: We have now added the stats information in line 149-152.

Table 3: Please use median/IQR to describe ages and non-parametric stats test for inferential testing in all groups. In particular, the MP-Bac and Mp-Bac-Vir groups with only sample size of 8 do not qualify for a parametric description or testing.

Response: We have used median/IQR to describe ages and non-parametric stats test for inferential testing in all groups.

Table 4 & 5: Please use median/IQR to describe all the continuous data and non-parametric stats test for inferential testing in all groups. In particular, the MP-Bac and Mp-Bac-Vir groups with only sample size of 8 do not qualify for a parametric description or testing.

Response: We followed the suggestions.

Line 200-2: Please state the stats from the Wuhan study.

Response: We added the stats from the Wuhan study as suggested in line 208.

Summary Results and Discussion Line 224-5, 261-4: This study may have overly amplified the significance of Mp-HRV coinfection but inevitably underweighed the Mp-Vir coinfection group caused by other respiratory viruses. Such claims may pose a risk that underestimates the clinical impact of other potential viruses lacking of supporting sample sizes in this study. In fact, the significance of clinical manifestations including complications (0.057 vs 0.02) of Mp-Vir and
Mp-HRV appear to be quite similar when compared to the Mp monoinfection group. The significance of Mp-HRV coinfection over other MP-Vir coinfection by other resp viruses should be tested separately by comparing Mp-HRV group against Mp-Vir group separately.

Please note that HRV is a prevalent respiratory virus detected in many parts of the world. It is certainly appropriate to highlight the HRV prevalence in overall Mp-Virus infection as part of study observation and discussion.

Response: We are very appreciated with these important suggestions by the reviewer and totally agree with this. We have now investigated the differences in clinical outcomes between Mp-virus (excluding HRV) co-infection and Mp CAP children and the statistics results have added in Table 3, 4, 5. Meanwhile, we made some corresponding changes in the Methods (lines 95-98), Results (lines 155-156, 188-190) and Discussion section (lines 266-270).

Minor:

Proper formatting is required for the Table 2 footnote, i.e. all Genus should start with Capital Letter. If possible please split the Genus and Species properly, i.e. to allow a single spacing between Genus and sp, "S.epidermidis"

Response: The correction was made per your request.

Ching-Chi Lee, MD, MSc (Reviewer 3): This manuscript is, "Impact and clinical profiles of Mycoplasma pneumoniae co-infection in childhood community-acquired pneumonia" by Dr. Zhao and his colleagues. This is an interesting study that substantially addresses a comparison of clinical manifestation in pneumonia child caused by mycoplasma alone and coinfection with other pathogens. This work comprehensive collected various pathogens and analyze numerous clinical characteristics, such as patient demography, comorbidities, symptoms/signs, image presentations, lab data, pneumonia severity, and complication

My primary concerns are the following:

First, because of fewer patient number in mycoplasma group, such as Mp-Vir (47 patients), Mp-HRV (30), Mp-Bact(8), and Mp-Bcat-Vir (8). These small population size indeed diminish the
statistic power. You should collect more patients to diminish this type II error and calculate the power.

Response: Fewer patients with Mp infection were recruited due to a low Mp detection rate in this study. Although agree with this suggestion, we are very sorry that we can’t collect more patients now, because this study is prospective. Instead, we have now stated clearly the limitation of small sample size in lines 302-305. And we will validate the conclusions of this study by expanding the sample size in our further study.

Second, in Figure 5, several parameters was graded for pneumonia severity, but all were not suitable and standard. In my opinion, pneumonia severity, such as PSI, or sepsis severity, such as ASPS, APACH, and SOFA, was suggested.

Response: We are truly appreciated with these valuable suggestions by the reviewer. This suggestion is really helpful. Although the PSI, ASPS, APACH, or SOFA scores cannot be calculated, we added the incidence of severe CAP as one of the parameters for pneumonia severity in line 106, 195 and 260. The differences in the incidence of CAP among various etiological groups are presented in Table 5. The diagnosis criteria of severe CAP accords to the Chinese Medical Association Guidelines for the management of community-acquired pneumonia in children (revised 2013) (Chin J Pediatr. 2013; 51(11):856-62).

Third, numerous comorbidity types were analyzed in your work, but the comorbidity severity is necessary to compare between Mycoplasma mono-infection and its co-infections.

Response: First, following this suggestion, we have now evaluated the severity of the pleural effusion and pulmonary consolidation by the amount of pleural effusion and pulmonary consolidation scope. The results are showed in Table 5. Second, all cases of pulmonary atelectasis are single lobar and all cases of liver dysfunction, myocardial damage and abnormal blood gas are mild. We have added an explanation in Table 5. Unfortunately, we failed to assess the severity of central nervous system infection due to clinical data collection is not complete.

Fourth, in the Figure 3 and 4, continuous variables should be expressed as the mean values ± standard deviations and compared by the Student's t test. The address in the format of median (IQR) was not analyzed by Student's t test.

Response: Because continuous data in this study cannot meet the normality and homogeneity of variance, the Student's t test is not adopted. We have now used median/IQR to describe all
Continuous variables and two sets of independent continuous data were compared by the Mann-Whitney U test.