Peer Review File

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Reviewer A

The study is important; however, the paper needs to be revised. My suggestions are:

Comment 1 Line 39: Please include the age range.

Reply 1: We appreciate the reviewer's comment. We have modified our text as advised (see Page 3, line 55-56).

Changes in the text: "9,837 hospitalized children (≤ 14 years old) with CAP in our hospital from January 2010 to December 2019 were reviewed."

Comment 2 Line 41: Please add: oropharyngeal swab.

Reply 2: We appreciate the reviewer's comment. We have modified our text as advised (see Page 3, line 57-58).

Changes in the text: "the oropharyngeal swab specimens were collected and tested for RSV"

Comment 3 Line 47-52: Please add the numbers as well (not only %).

Reply 3: We appreciate the reviewer's comment. We have modified our text as advised (see Page 3-4, line 62-73).

Changes in the text: "The detection rate of RSV was 15.3% (1,507/9,837). From 2010 to 2019, the RSV detection rate showed a wavy change ($\chi2$=166.982, P<0.001), with the highest detection rate in 2011 (158/636, 24.8%), followed by 2015 (171/828, 20.7%) and 2017 (145/716, 20.3%). RSV can be detected throughout the year, with the highest detection rate in February (123/482, 25.5%). Children younger than 0.5 years old had the highest detection rate (410/1,671,24.5%). The detection rate of RSV in male children (1,024/6,226, 16.4%) was higher than that in female children (483/3,611, 13.4%) (P < 0.001). 17.7% (266/1,507) of RSV positive cases were also co-infected with other viruses. Multiple co-infection (85/266, 32.0%) was the most common infection type. INFA (41/266, 15.4%) was the most common co-infection virus. The incidence of severe pneumonia in RSV positive children (180/1, 507,11.9%) was higher than that in RSV-negative children (757/8330, 9.1%) ($\chi2$=11.754, P<0.001)."

Comment 4 Line 51: Please add: 17.7% (a/b) OF RSV positive cases were also positive with other viruses.....

Reply 4: We appreciate the reviewer's suggestion. We have modified our text as advised (see Page 3-4, line 69-71).

Changes in the text: "17.7% (266/1,507) of RSV positive cases were also co-infected with other viruses. Multiple co-infection (85/266, 32.0%) was the most common infection type. INFA (41/266, 15.4%) was the most common co-infection virus."

Comment 5 Line 53-54: severe pneumonia (is there any death case?)

Reply 5: We appreciate the reviewer's suggestion. There were 3 (0.2%) RSV-positive and 43 (0.5%) RSV-negative hospitalized CAP children died in our study, but the difference is not statistically significant (P = 0.10). We have added the information of death in the results section. We have modified our text as advised (see Page 9, line 179-181).

Changes in the text: "There were 3 (3/1507, 0.2%) RSV-positive and 43 (43/8330, 0.5%) RSV-negative hospitalized CAP children died in our study, but the difference is not statistically significant (P = 0.10)."

Comment 6 Line 55: p value?

Reply 6: We appreciate the reviewer's comment, we have added the p value in the revised manuscript as advised (see Page 4, line 71-73).

Changes in the text: "The incidence of severe pneumonia in RSV positive children (180/1, 507,11.9%) was higher than that in RSV-negative children (757/8330, 9.1%) ($\chi 2$=11.754, P<0.001)."

Comment 7 What's about the severity of co-infections vs single RSV infections?

Reply 7: We appreciate the reviewer's comment. Patients with co-infection (14.29%, 38/266) tended to have higher incidence of severe pneumonia than those without co-infection (11.44%, 142/1,241), but the difference was not statistically significant ($\chi 2$=1.684, P = 0.194). We have modified our text as advised (see Page 4, line 73-76).

Changes in the text: "In addition, patients with co-infection (38/266, 14.3%) tended to have higher incidence of severe pneumonia than those without co-infection (142/1,241, 11.4%), but the difference was not statistically significant (P = 0.194)."

Comment 8 Line 67: Please check whether CAP is the leading cause of death in children, OR is it diarrhea?

Reply 8: We apologize for making this confusion. Estimated by the World Health Organization (WHO), globally, pneumonia and diarrhea are the leading causes of infection in children under 5 years of age [1]. According to a systematic analysis of causes of under-5 mortality in 2000–15 in multiple countries and regions, pneumonia is the first cause of death in children under 5 years old, which accounts for 12.8% of all deaths. Diarrhea is the second cause of death in children under 5 years old, which accounts for 8.6% of all deaths [2]. We have modified our text as advised (see Page 5, line 86-87).

References:

[1] Yu Y, Fei A. Atypical pathogen infection in community-acquired pneumonia. Biosci Trends. 2016;10(1):7-13. doi:10.5582/bst.2016.01021

[2] Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, Lawn JE, Cousens S, Mathers C, Black RE. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet. 2016 Dec 17;388(10063):3027-3035. doi: 10.1016/S0140-6736(16)31593-8. Epub 2016 Nov 11. Erratum in: Lancet. 2017 May 13;389(10082):1884. PMCID: PMC5161777.

Changes in the text: "one of the leading causes of death in children younger than 5 years (1)."

Comment 9 Line 68: I do not understand why it is compared with AIDS, malaria and measles, not other infectious diseases such as diarrhea, dengue, or influenza?

Reply 9: We appreciate the reviewer's comment. In fact, not only AIDS, malaria and measles, pneumonia is the leading infectious cause of death in small children, which causes more death in small children than any other single infectious disease [1]. We have modified our text as advised (see Page 5, line 87-89).

Reference

[1] Swedberg E, Shah R, Sadruddin S, Soeripto J. Saving young children from forgotten killer: pneumonia. Am J Physiol Lung Cell Mol Physiol. 2020 Nov 1;319(5):L861-L862. doi: 10.1152/ajplung.00471.2020. Epub 2020 Oct 14.

Changes in the text: "According to previous study, pneumonia kills over 2 million children every year in the world, which causes more death in small children than any other single infectious disease and even exceeds the sum of AIDS, malaria, and measles (2)."

Comment 10 Line 74-76: needs revising.

Reply 10: We appreciate the reviewer's comment. We have modified our text as advised (see Page 5, line 94-96).

Changes in the text: "However, there are few reports on the epidemiology of RSV infection in hospitalized children with CAP in large samples."

Comment 11 Line 88: The conjunction Moreover here is not appropriate. Why based on previous studies if the criteria of severe CAP is used for this study? Unless, the criteria for this study used the same criteria as previous studies. If so, then the sentence needs revising.

Reply 11: Thank you for your suggestion. The criteria of severe CAP are based on the Child Community-Acquired Pneumonia Guidelines (I, II). We have modified our text as advised (see Page 6, line 113-116).

Changes in the text: "The severe CAP was defined as followed: (1) fever (≥38.5℃); (2) respiratory rate of greater than 70 breaths per minute in infant and 50 breaths per minute in children (except from cry); (3) cyanosis or intermittent apnea; (4) dehydration or confusion (5,6)."

Comment 12 Line 91: Please add citation

Reply 12: We appreciate the reviewer's comment. We have added citation as advised.

Changes in the text: Please see the revised manuscript.

Comment 13 Line 94: Please be consistent: oropharyngeal swab?

Reply 13: We appreciate the reviewer's comment. We have changed "throat swab" into "oropharyngeal swab". We have modified our text as advised (see Page 6, line 119-120).

Changes in the text: "Oropharyngeal swab samples were collected on the day of admission or in the early morning of the second day."

Comment 14 Line 106: Please briefly add the lab testing.

Reply 14: We appreciate the reviewer's comment. We have modified our text as advised (see Page 6-7, line 127-138).

Changes in the text: "In brief, DNA or RNA from oropharyngeal swab samples was extracted using QIAamp DNA Mini Kit or QIAamp Viral RNA Mini Kit (Qiagen Co. Ltd., Shanghai, China) in accordance with the manufacturer's protocols. For RSV detection, the primers and TaqMan probes were designed to detect RSV subgroups A (RSVA) and B (RSVB) by amplifying the RSV G gene. Multiplex real-time RT–PCR was conducted using our optimized reaction buffer and cycling conditions. The cycling conditions were 48°C for 10 min, 94°C for 2 min, and then 40 cycles of 94°C for 10 s and 55°C for 35 s. The amplified nucleic acids were detected with the Applied Biosystems 7500 Real-Time PCR System (Life Technologies, Singapore). RSV-positive samples were tested simultaneously for the following 9 respiratory tract pathogens: INFA, INFB, PIV, EV, CoV, HMPV, HBoV, HRV and ADV, using kits from Guangzhou HuYanSuo Medical Technology Co., Ltd."

Comment 15 Line 109: Please add the rule of citation software.

Reply 15: We appreciate the reviewer's comment. We have added the detailed description of statistical software as advised as advised (see Page 7, line 142-144).

Changes in the text: "SPSS 25.0 statistical software (IBM Corp. Released in 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) was used for the analysis."

Comment 16 Please add a flow chart explaining the methods of this study and a table describe the base line characteristics.

Reply 16: We appreciate the reviewer's comment. We have added the flowchart and table as advised.

Changes in the text: Please see Table 1 and Figure 1.

Comment 17 Line 157: Need a citation. This statement needs further discussion: whether other viruses have similar pattern, or it is just specific for RSV.

Reply 17: We appreciate the reviewer's comment. We have added the citation in the revised manuscript. In addition, infants are susceptible to various respiratory virus infection because of immature immune system. We have modified our text as advised

(see Page 10, line 200-201).

Changes in the text: "Thus, infants are susceptible to a variety of respiratory viruses, such as RSV (10), influenza virus (12) and measles (13)."

Comment 18 Line 160: p value?

Reply 18: Thank you for your suggestion. We have modified our text as advised (see Page 10, line 201-203).

Changes in the text: "we found that the detection rate of RSV in male children was significantly higher than that in female children ($P < 0.001$)"

Comment 19 Line 163: Needs further literature research and discussion. Why it is associated with the difference in growth and development between boys and girls?

Reply 19: Thank you for your suggestion. We have added detailed discussion about the correlation between sex difference and development of immune system in the revised manuscript. We have modified our text as advised (see Page 10, line 204-209).

Changes in the text: "Uekert et al also found that sex difference was correlated to either the frequency or severity of viral respiratory tract infections during the first few years of life (14). Sex differences in corticosteroid secretion and activity could theoretically explain variations in susceptibility to RSV infection, and there is conclusive evidence that sex hormones can influence the development of specific lymphocyte populations and cytokine production (15,16)."

Comment 20 Line 170: From the chart: high prevalence from January to April. November is the lowest?

Reply 20: Thank you for your question. Liu et al [1] investigated the relationship between month and RAV infection rate in Guangzhou, northern of China, and found that the highest detection rate was from January to March, which is consistent with our studies. However, Cui et al [2] investigated the correlation between season and the detection rate of RSV in Beijing, northern of China, and found that the winter season from November to February increased the RSV infection rate. Guangzhou locates in the subtropical and has lower latitude than Beijing, so winter comes later in Guangzhou than in Beijing. Study population in our study comes from Guangzhou city, which may explain why the month with the highest RSV detection rate in our study arrived later than that in Cui et al. We have modified our text as advised (see

Page 10-11, line 213-219).

Changes in the text: "In addition, the detection rates of RSV peaked in February, January and March in our study, which was consistent with the results in previous study (19). Cui et al.(20) found that the RSV infection rate in Beijing was highest from November to February. Guangzhou locates in the subtropical and has lower latitude than Beijing, so winter comes later in Guangzhou than in Beijing, which may explain why the month with the highest RSV detection rate in our study were later than that in Cui et al."

Comment 21 Line 173: One of the reasons may be gathering in the house during winter.

Reply 21: Thank you for your suggestion. We have added this important explanation in the revised manuscript as advised. We have modified our text as advised (see Page 11, line 221-222).

Changes in the text: "In addition, gathering in the house during winter may also increase the risk of virus spreading."

Comment 22 Line 176-195: The discussion is too lengthy. Please shorten it to address that this is related to the various circulating genotypes and the immunity (but unfortunately cannot be confirmed in this study).

Reply 22: Thank you for your suggestion. We have modified our text as advised (see Page 11, line 225-235).

Changes in the text: "The possible reason is the increased immunity for prevalent RSV subgroup in children after a period of time, which may lead to alternating prevalence between RSVA and RSVB (17,22). Song et al. (22) found that RSVB predominated between 2008 and 2010 in China, whereas RSVA predominated between 2010 and 2012. Previous studies also suggest that new mutant genotypes have been produced continuously since the BA genotype strain of RSVB was discovered in 2003. Until 2018, 15 genotypes deriving from BA has been identified, which can break through the previous established immunity for BA genotype (23,24). However, more studies are needed to confirm about the correlation between infection rate of RSV in different years and various circulating genotypes."

Comment 23 Line 198: Is it significant? I think it is not that simple, as we have to

consider co-infection with bacteria, which is not studied here. The non RSV group includes negative cases, Influenza and other respiratory viruses that may bias the interpretation.

Reply 23: Thank you for your question. Indeed, this is an important shortcoming of our research, because potential co-infection with bacteria or other virus in the non-RSV group may bias the results. Restricted by the sample collection protocol, we were unable to acquire the detailed information of co-infection in RSV-negative children. However, according to previous studies, co-infection is associated with increased risk of severe CAP, which is consistent with our results. We have added this important bias in the section of Limitation. We have modified our text as advised (see Page 13, line 259-261).

Changes in the text: "Second, limitded by the sample collection protocol, we were unable to acquire the detailed information of co-infection in RSV-negative children, and potential co-infection with bacteria or other virus in the non-RSV group may bias the results."

Comment 24 Line 206: how much higher? Authors need to have a table showing these 266 cases, describing each co-infection and the clinical outcomes.

Reply 24: Thank you for your suggestion. Patients with co-infection (38/266, 14.3%) tended to have higher incidence of severe pneumonia than those without co-infection (142/1,241, 11.4%), but the difference was not statistically significant ($\chi2$=1.684, P = 0.194). A detailed description of 266 co-infection cases has been added in Table 2. We have modified our text as advised (see Page 12, line 247-250).

Changes in the text: "Moreover, patients with co-infection (38/266, 14.3%) tended to have higher incidence of severe pneumonia than those without co-infection (142/1,241, 11.4%), but the difference was not statistically significant ($\chi2$=1.684, P = 0.194)." Please also see the Table 2.

Comment 25 Other limitations that should be mentioned: no sputum or induced sputum were collected or tested, no bacterial pathogens were detected, the detected pathogens may not be the causes of pneumonia (innocent bystanders, Mardian et al, Frontiers in Ped, 2021), and no data on clinical outcomes. Therefore the correlation between RSV or non-RSV cannot confidently said, as non-tested bacteria may cause the CAP.

Reply 25: Thank you for your suggestion. We have added these limitations in the revised manuscript as advised. We have modified our text as advised (see Page 13, line 259-267).

Changes in the text: "Second, restricted by the sample collection protocol, we were unable to acquire the detailed information of co-infection in RSV-negative children, and potential co-infection with bacteria or other virus in the non-RSV group may bias the results. In addition, we did not test the sputum, and possible pathogens in sputum were not available in our study. Although previous studies have demonstrated the sensitivity and specificity of oropharyngeal swabs is relatively high (30), the detected pathogens may not be the causes of pneumonia (31). Thus, the correlation between RSV and severe CAP cannot be confidently said, as our study did not analyze other pathogens such as bacteria that cause pneumonia."

Comment 26 Figure: need the numbers to be listed in all figs. Figs should be self-explanatory.

Reply 26: Thank you for your suggestion. We have revised all figures as advised.

Changes in the text: Please see the figures.

Reviewer A re-review comments:

Comment 1 Authors have not completely responded to Reviewer A's comment regarding comparing the number of deaths of pneumonia with AIDS, malaria, and measles. It may be more relevant if they compare it with diarrhea or dengue?

Reply 1: We appreciate the reviewer's comment. Diarrhea and dengue are both important infectious diseases among children. Previous study suggests that CAP is the most common causes of death in children under 5 years old and diarrhea is the leading cause of death among older children (5-9 years)[1]. There has been no study counted the global death of dengue among children, but global estimates of dengue virus infections based on an assumed constant annual infection rate among a crude approximation of the population at risk have yielded figures of 50-100 million infections per year[2]. In addition, nearly 95% of dengue infections are children less than 15 years[2]. We have revised the manuscript and compared the CAP with diarrhea and dengue, instead of AIDS, malaria, and measles. Per the editor's comment, we have modified our text as advised (see Page 5, line 90-93).

References:

[1] GBD 2017 Child and Adolescent Health Collaborators. Diseases, Injuries, and Risk Factors in Child and Adolescent Health, 1990 to 2017: Findings From the Global Burden of Diseases, Injuries, and Risk Factors 2017 Study. JAMA Pediatr. 2019 Jun 1;173(6):e190337.

[2] Verhagen LM, de Groot R. Dengue in children. J Infect. 2014 Nov;69 Suppl 1:S77-86.

Changes in the text: "According to a previous study, pneumonia kills over 2 million children worldwide every year, which accounts for more deaths of young children than any other single infectious disease, such as malaria, diarrhea and dengue (2)."

Comment 2 The incidence of severe pneumonia is significantly higher in RSV positive children vs RSV negative children (11.9% vs. 9.1%) and in patients with dual RSV and another virus infection compared to RSV alone (14.3% vs. 11.4%). Have the authors conducted multi-variate analysis to determine which one is correlated with severe illness to ensure that the conclusion is accurate?

Reply 2: Thank you for your important question. The difference of severe pneumonia rates between dual RSV and another virus infection compared to RSV alone was not significant which have been described in the manuscript, so no further analysis was done to investigate the correlation between coinfection and severe pneumonia. In addition, a multi-variate regression model which adjusted for sex, age, month and coinfection was used to assess the association of severe pneumonia with RSV infection, and we found the RSV positive children had higher incidence of severe pneumonia than RSV negative children ($p < 0.001$). However, we did not make further analysis, because the aim of our study was mainly to describe the epidemiology characteristics of RSV in children with CAP instead of identifying the risk factor of severe pneumonia. Per the editor's comment, we have modified our text as advised (see Page 7-8, line 149-151).

Changes in the text: "A multi-variate regression model which adjusted for sex, age, month and coinfection was used to assess the association of severe pneumonia with RSV infection."

Reviewer B

The manuscript "Epidemiology of Respiratory Syncytial Virus in hospitalized Children with Community Acquired Pneumonia in Guangzhou: A Ten-Year Study" conducted a retrospective study of RSV detection in children hospitalized with CAP from 2010 to 2019. The research has certain significance, but the manuscript has the following main defects:

Comment 1 In the methodology of sample selection, the author did not specify the criteria for inclusion and exclusion.

Reply 1: We appreciate the reviewer's comment. We have clarified the criteria for inclusion and exclusion in the revised article. In addition, a flowchart of analysis has been added (figure 1). We have modified our text as advised (see Page 6, line 108-113).

Changes in the text: "Total 10,216 hospitalized children (≤14 years old) who were diagnosed with CAP according to the criteria of the Child Community-Acquired Pneumonia Guidelines (I, II) (5,6) in our hospital from January 2010 to December 2019 were included in our study. The exclusion criteria were as follows: 1. Children with missing demographic data; 2. Children without RSV test results."

Please also see the flowchart of analysis in Figure 1.

Comment 2 It was difficult to understand whether the RT-PCR results came from clinical laboratory reports or from retrospective testing by the researcher. If it was a retrospective examination of preserved samples, the details of screening were not available

Reply 2: We apologize for making this confusion. All our results came from clinical laboratory reports, and we just retrospectively reviewed the clinical reports from the hospital database. We briefly described our institutional protocol for RSV test in the revised manuscript, and the details of screening can be found in our previously published articles (PMID: 23343342, 22168387). We have modified our text as advised (see Page 6-7, line 127-139).

Changes in the text: "In brief, DNA or RNA from oropharyngeal swab samples was extracted using QIAamp DNA Mini Kit or QIAamp Viral RNA Mini Kit (Qiagen Co. Ltd., Shanghai, China) in accordance with the manufacturer's protocols. For RSV detection, the primers and TaqMan probes were designed to detect RSV subgroups A (RSVA) and B (RSVB) by amplifying the RSV G gene. Multiplex real-time RT–PCR

was conducted using our optimized reaction buffer and cycling conditions. The cycling conditions were 48°C for 10 min, 94°C for 2 min, and then 40 cycles of 94°C for 10 s and 55°C for 35 s. The amplified nucleic acids were detected with the Applied Biosystems 7500 Real-Time PCR System (Life Technologies, Singapore). RSV-positive samples were tested simultaneously for the following 9 respiratory tract pathogens: INFA, INFB, PIV, EV, CoV, HMPV, HBoV, HRV and ADV, using kits from Guangzhou HuYanSuo Medical Technology Co., Ltd. The detailed testing procedure has been provided in previous reports (7,8).”

Comment 3 There might be some risks in using the etiology of throat swab samples to reflect the etiology of pneumonia, which were not discussed in the paper.

Reply 3: Thank you for your suggestion. We have discussed the limitation of use of throat swab samples in the revised manuscript (see Page 13, line 261-267).

Changes in the text: “In addition, we did not test the sputum, and possible pathogens in sputum were not available in our study. Although previous studies have demonstrated the sensitivity and specificity of oropharyngeal swabs is relatively high (30), the detected pathogens may not be the causes of pneumonia (31). Thus, the correlation between RSV and severe CAP cannot be confidently said, as our study did not analyze other pathogens such as bacteria that cause pneumonia.”

Comment 4 Comparison of RSV detection rate differences in different genders should be based on different gender composition ratios in the study samples.

Reply 4: Thank you for your suggestion. We have modified our text as advised (see Page 8, line 160-161).

Changes in the text: “The detection rate of RSV in male children (1,024/6,266, 16.4%) was significantly higher than that in female children (483/3,611, 13.4%) ($P < 0.001$).”

In addition, a Table 1 which demonstrated the baseline characteristics and medical information of all children in our study was added in the revised manuscript.

Comment 5 There are errors in the images, such as missing ordinate names, etc.

Reply 5: We apologize for making this confusion. We have provided ordinate names and SD in figures 2-4, and revised the corresponding main text and figure legends.

Reviewer B re-review comments:

Comment 1 What is the purpose or scientific hypothesis of the study? To prevent and treat RSV as the authors mentioned? But what the suggestions based on the findings?

Reply 1: Thank you for your important question. This study aimed to investigate the epidemiological characteristics of RSV infection in hospitalized children with CAP in Guangzhou and provide reference for policy makers and doctors in the prevention and treatment of RSV infection. We have modified our text as advised (see Page 13-14, line 270-278).

Changes in the text: "In this study, the data on RSV infection in hospitalized children with CAP in Guangzhou from 2010 to 2019 were analyzed in many respects. The current study suggested that January to March were the key months for prevention and control of CAP caused by RSV in Guangzhou, and children less than 0.5 years old were the key population for prevention and control of CAP caused by RSV. Policy makers should make timely adjustments to prevention measures and medical resources based on these epidemiological characteristics. Our study also found that RSV-positive CAP children with co-infection were more likely to develop severe pneumonia, which suggested the importance of early treatment and close attention in these patients."

Comment 2 How did the study select these subjects from a large number of cases over a 10-year specimen collection period?

Reply 2: Thank you for your question. Our project comes from a sub-project of the National Natural Science Foundation of China (81970003). Because RSV is the most common viral pathogen in children with CAP, we conduct this epidemiological research of hospitalized children in Guangzhou to provide reference for the prevention and treatment of RSV-related CAP. From 2010 to 2020, all < 14 years old children with CAP can receive free RSV test, and the information of demographics, clinical characteristics and laboratory tests were recorded. In our study, we extracted research objects from this database according to the inclusion and exclusion criteria which have been detailed described in our manuscript (see Page 6, line 111-118).

Changes in the text: Please see the inclusion and exclusion criteria.

Comment 3 How to verify the reliability of the Multiplex real-time RT-PCR?

Reply 3: Thank you for your important question. In our study, all procedures are

strictly in accordance with the manufacturer's protocol which has been verified in previous studies[1,2]. In addition, to ensure sequence accuracy, PCR amplification and sequencing were conducted at least twice (see Page 7, line 139-141).

References:

[1] Liu WK, Chen DH, Liu Q, er al. Detection of human bocavirus from children and adults with acute respiratory tract illness in Guangzhou, southern China. BMC Infect Dis. 2011 Dec 14;11:345.

[2] Liu WK, Liu Q, Chen DH, et al. Epidemiology and clinical presentation of the four human parainfluenza virus types. BMC Infect Dis. 2013 Jan 23;13:28.

Changes in the text: "To ensure sequence accuracy, PCR amplification and sequencing were conducted at least twice. The detailed testing procedure has been provided in previous reports (7,8)."

Comment 4 For the different detection rates of different genders, the authors' analysis might be inadequate without population-based study.

Reply 4: Thank you for your suggestion. Per the editor's comment, we have modified our text as advised (see Page 10, line 206-208).

Changes in the text: "Similar to the results in our study, Radhakrishnan et al. found that there were more males than females (63.8% vs. 44.2%) children who were hospitalized for RSV infection in a population-based study of children in Ontario, Canada."