Reviewer’s report

Title: Human metapneumovirus prevalence and patterns of subgroup persistence identified through surveillance of pediatric pneumonia hospital admissions in coastal Kenya, 2007-2016

Version: 0 Date: 12 May 2019

Reviewer: Keisuke Yoshihara

Reviewer's report:

Dear Editor in Chief

"BMC infectious diseases"

Here I have attached the review comments of mine for the submitted article entitled as the following.

Manuscript Number: INFD-D-19-00547

Title: "Human metapneumovirus prevalence and patterns of genotype persistence identified through surveillance of pediatric pneumonia hospital admissions in coastal Kenya, 2007-2016"

Decision: Minor revision

Reviewer's summary

The authors summarized the situation of HMPV circulation and prevalence among hospitalized children with severe and very severe pneumonia cases during the period of 2007 through 2016 in coastal Kenya (Kilifi). As HMPV-related epidemiological surveillance data is still limited from entire Africa continent, the current results from authors add epidemiologically important values for the public health sector. Although, the overall number and prevalence of HMPV positive cases was quite low, they presented important data regarding the HMPV genotype shift over time as well as the clinical data comparison among different genotypes. The long-term coverage of multiple study year allowed us to observe the seasonal circulation trend of HMPV-related hospitalizations in the current study setting. This is particularly useful for maximizing the vaccination trial in the future. Furthermore, they investigated the evolutionary characteristics of each genotypes, in which they presented certain genotype may differ than others in terms of evolutionary characteristics. The association of HMPV evolutionary characteristics with clinical aspect as well as viral transmission capacity etc. needs to be further investigated in the future. Overall, they stated clinically and viral evolutionary valuable findings of Kenyan HMPV strains in the manuscript and summarized data in proper way; however, some part particularly in methods and results section may require editing prior to next submission. Otherwise, overall English in the current manuscript is understandable and no need further editing.
Comments (Minor and major):

Abstract

1. Line 34: The part you described about the prevalence of HMPV among all samples tested, you can just use 1 decimal place like other parts in the paper.

Materials and Methods

2. Line 92-93: for the inclusion criteria, it is mentioned that those children with either severe or very severe pneumonia were enrolled in the study. Did you also do HMPV screening test for those with ARI hospitalized children without pneumonia symptom? If so, it might be good to put those data in supplementary data as it might be an interest for some readers. It might be better if you could include the definition for hospitalization in this hospital setting as well.

3. Line 90-93: You stated that you collected throat swabs, nasal aspirates and washes, or sputum specimen. Is it consistent in terms of type of samples being collected from each study participant? For example, it may be technically difficult to collect nasal aspirate / wash or sputum from younger children compared to adult participants. Ideally, the type of samples collected should be nearly identical among all age groups.

4. Line 95-96: For the sample collection, it was described that nasal wash, NP, or NP/OP were collected from enrolled cases. in terms of the samples used for the HMPV screening step, was it consistent throughout the current study period?

5. Line 100-111: For the HMPV screening as well as nucleic acids extraction methods used in different study period, did you verify that detection sensitivity etc. do not statistically vary among different kit?

6. Line 162 and 246: I feel rather comfortable to use the term "genotype shift" over "genotype change" since "genotype change" may probably mean that a certain genotype (that already exists) change to another genotype, which is wrong in this context.

7. Line 163-164: could you justify the reason why use chi-squared test for the clinical severity comparison among different HMPV genotypes? As shown in the table 3, the value of some cells are less than 10; for example, (n=2) in A2c (very severe) and (n=10) in B2. In this case, the result of chi-square test may not reliable as the one from fisher's exact test.
Results

8. Line 172-173: it was described that clinical samples were successfully collected only from 74% of those study enrolled patients. It is considerably high and needs to be mentioned in discussion section. Also, it may be necessary to state that those samples-collected group and group without clinical sample are not significantly different in terms of characteristics if that is the case.

9. Figure 1: in figure legend, it might be informative if you could put which bootstrap value was used as cut-off. For example, those bootstrap value higher than 70 was considered to be significant etc. Same for other ML-based phylogenetic analysis.

10. Figure 4: I understand that cluster unique amino acid substitutions were presented in figure 5, it might be also informative to put some of those information at the branches of Figure 4 if this will not make the trees too complicated. In that way, it might be easier for readers to visually understand the uniqueness of each genetic cluster.

11. Line 217-220 & Line 232-235: have you tried to statistically compare the difference in evolutionary rates among different genotypes? If this is your interest, you can easily compare using such as Welch's test, in which it assume two groups in comparison have normal distribution, yet the standard deviation may differ between two. In case of comparison among more than two groups, it might be worth using Kruskal Wallis test for testing null-hypothesis.

Discussion

12. Line 279-284: You mentioned about the difference in evolutionary rates among genotypes, particularly in A2b and B1. Please elaborate the evolutionary implication etc. based on this results. Furthermore, the faster evolutionary rate in hMPV in comparison with RSV reported elsewhere? You may want to add some discussion of this result in discussion section.
Are the methods appropriate and well described?  
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?  
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?  
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?  
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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