An outbreak of severe neonatal pneumonia caused by human respiratory syncytial virus BA9 in a postpartum care centre in Shenyang, China

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Dr. Yan Zhang
National Institute for Viral Disease Control and Prevention, China CDC
Beijing
China

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Reviewer comments:

Reviewer #1 (Comments for the Author):
You should focus on the genotype that you found in your samples and not conclude that the cause of outbreak are the nurses.

Reviewer #2 (Comments for the Author):
The authors studied molecular epidemiological analyses regarding an outbreak of pneumonia in neonate due to RSV-B, genotype BA9. Overall, the draft manuscript was well described, although subjects were relatively small numbers. I think that some major and
minor concerns should be improved.

1. The authors made a phylogenetic tree using NJ method. I think that this was made by ML method by MEGA.
2. Please provide the approval number of ethics committee.
3. Please provide analyzed nucleotide numbers of these sequences.
4. Please provide relevant discussion for amino acid substitutions in HRV2 in your strains comparing with other previous reports.

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Thank you for submitting your paper to Microbiology Spectrum.
An outbreak of severe neonatal pneumonia caused by human respiratory syncytial virus BA9 in a postpartum care centre in Shenyang, China

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Keywords: Human respiratory syncytial virus (HRSV); outbreak; neonatal pneumonia; BA9 genotype; postpartum care centre

Running title: Outbreak of severe neonatal pneumonia caused by HRSV genotype BA9
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Abstract

Human respiratory syncytial virus (HRSV) is a major pathogen of lower respiratory tract infections in children (< 5 years) and older individuals, with outbreaks mainly reported among infants in hospital paediatric departments and intensive care units (ICUs). An outbreak of severe neonatal pneumonia occurred in a postpartum centre in Shenyang city, China, from January to February, 2021. In total, 34 respiratory samples were collected from 21 neonates and 13 nursing staff. The samples were screened for 27 pathogens using a TaqMan low density array, and 20 samples tested positive for HRSV, including 16 neonates and 4 nursing staff samples. Among the 16 hospitalized neonates, seven were admitted to an ICU and nine to general wards. Four of the nursing staff had asymptomatic infections. To investigate the characteristics and source of the HRSV, the second hypervariable region (HVR2) of the G gene of HRSV was sequenced from six neonates and two nursing staff. Phylogenetic analyses revealed that eight of the sequences were identical, clustering with the HRSV B subtype, close to the BA9 genotype reference sequences, designated BA9-SY/CHN/2021. Subsequent genetic analysis showed that BA9-SY/CHN/2021 belonged to lineage 7 of the BA9 genotype and possessed five amino acid mutations compared with the BA9 reference strain (GenBank: AB603467). In conclusion, this outbreak of severe neonatal pneumonia was caused by HRSV genotype BA9, likely transmitted from the nursing staff. Our findings highlight the critical need for strict hygiene and disease control measures.
at such centres, to prevent outbreaks of severe infectious respiratory diseases.

**Importance**

Human respiratory syncytial virus (HRSV) is one of the leading causes of acute lower respiratory infections (ALRI) worldwide, which is highly contagious and can cause outbreaks in hospitals, military veteran centers, postpartum care centre among infants, the elderly, and immunocompromised population. This is the first reported an outbreak of neonatal severe clustered pneumonia caused by HRSVB BA9 at a postpartum care centre in China, which leads to severe clinical symptoms of ALRI such as cough, respiratory failure and even heart failure in neonates. Based on the molecular epidemiological investigation, environmental monitoring of the postpartum care centre, and working patterns of the nursing staff, it is speculated that the outbreak may have been caused by transmission of HRSV asymptomatic nurses to neonates.

**Keywords:** Human respiratory syncytial virus (HRSV); outbreak; neonatal pneumonia; BA9 genotype; postpartum care centre

**Introduction**

Human respiratory syncytial virus (HRSV) is one of the most common pathogens of acute lower respiratory infections (ALRI) in young children under 5
years of age, usually requiring hospitalization and mainly causing pneumonia and bronchiolitis, and in even death severe cases (1, 2). The main manifestations of ALRI caused by HRSV are a stuffy nose, runny nose and fever, cough, shortness of breath, and respiratory failure(2). Its serious disease burden has aroused great public concern. In 2015, an estimated 33.1 million children infected with HRSV-related ALRI were reported worldwide, of which 3.2 million children were hospitalized(3).

HRSV is a negative-sense, single-stranded RNA virus of the genus Orthopneumovirus, and the family Pneumoviridae (4). According to antigenic and genetic differences, HRSV is divided into the HRSVA and HRSVB subtypes (5). Based on the second hypervariable region (HVR2) located in the C-terminal domain of the G gene, subtypes HRSVA and HRSVB can be further classified into 15 genotypes and 30 genotypes, respectively (6-9). In recent years, the BA9 genotype with a 60-bp repeat insertion in the G protein HVR2 region has gradually become the predominant genotype globally(10).

Outbreaks of HRSV infection usually occur in general paediatric wards and neonatal intensive care units (ICU) but have occasionally been reported in postpartum care centre settings(1, 11-14). In recent years in China, an increasing number of postpartum women seek professional care in postpartum care centre in the first few months after discharge from maternity hospitals, so that neonates may be exposed to some potential risk factors for respiratory disease infection in the
This study describes an outbreak of neonatal pneumonia in a postpartum care centre in Shenyang city, Liaoning province, China, during January and February 2021. Clinical samples were collected from neonates and nursing staff to identify the etiological agent and determine its origin. Screening of the samples indicated that the outbreak was caused by HRSV. HVR2 fragments of the G gene of Shenyang (SY) strains of HRSV were obtained to clarify the genetic characteristics of the virus and the source of the virus infection.

Materials and Methods

Ethics statement

This study was approved by the second session of the Ethics Review Committee of the National Institute for Viral Disease Control and Prevention of the Center for Disease Control and Prevention (CDC) in China. Written informed consent for the use of clinical specimens was obtained from all patients involved in this study or their guardians. This study did not involve human experimentation; the only human material used in this study was nasopharyngeal swab and throat swab specimens collected from suspected ALRI cases during an outbreak in Shenyang city of Liaoning province, China, from January to February, 2021.

Specimen collection
During the outbreak period, nasopharyngeal swab and throat swab were collected from all neonates and nursing staff at the postpartum care centre. All specimens were collected by epidemiology staff of Shenyang CDC and were transported in sterile containers with a cold package (controlled low temperature of 4°C) to the Institute for Viral Disease Control and Prevention for further analysis.

**RT-PCR and sequencing**

The viral nucleic acid was directly extracted from the clinical specimens using the TianLong nucleic acid extraction kit (Tianlong Biotechnology, Xian, China) according to the manufacturer’s instructions. The samples were screened for human respiratory pathogens, including 16 viruses and 11 bacteria using multiplex real-time RT-PCR with the TaqMan low density array (TLDA) kit (Thermo Fisher Scientific Inc., Waltham, USA). The subtypes of HRSV were further identified by in-house real-time RT-PCR. The second hypervariable region (HVR2) (637–968 nt) of the G gene of HRSVB subtype was amplified using a one-step reverse transcription-PCR kit (TaKaRa Biotechnology, Dalian, China) and the primer pair GPB/F1 (15). The reaction conditions, as well as the purification and sequencing protocols were as described previously(15, 16).

**Phylogenetic analysis**

Sequences were edited with Sequencher 5.0 (GeneCodes, Ann Arbor, MI,
USA). Multiple sequence alignments and pairwise distance were determined using the MEGA program (Version 5.0; Sudhir Kumar, Arizona State University). Phylogenetic trees were generated in MEGA using the neighbour-joining (NJ) method and the maximum composite likelihood nucleotide substitution model. Maximum likelihood (ML) phylogenetic trees were also generated. The reliability of phylogenetic inference was estimated using the bootstrap method with 1000 replicates. Bootstrap values ≥70% are shown.

Nucleotide sequence accession numbers
All sequences obtained in this study were submitted to the GenBank database under the accession numbers OM892937-OM892944.

Results
Epidemiological investigation
From January 17 to February 3, 2021, an outbreak of neonatal pneumonia was reported in a postpartum care centre in Shenyang city, China. In total, 16 out of 21 neonates from Shenyang postpartum care centre were hospitalized for clinical treatment because of symptoms of ALRI. Among the 16 hospitalized ALRI cases, seven neonates including premature twins were diagnosed with pneumonia and admitted to the ICU, and nine neonates belonged to mild respiratory infection cases. The average age of these 16 neonates was 23 days after birth (range: 12–28
days). In addition, 4 of 13 nursing staffs working in the postpartum care centre during the outbreak belonged to lab-confirmed respiratory infection cases and the average age of cases was 39 years (range: 24-47 years). No additional cases were reported after February 3, 2021.

The index case of this outbreak (case No.1) occurred in the postpartum care centre on January 17, 2021 with symptoms such as respiratory failure, and was subsequently admitted to hospital after 3 days onset. Then, Case No. 2 in the same postpartum care centre developed severe clinical symptoms 7 days after the onset of case No.1, including a cough, shortness of breath, respiratory failure and anemia. Cases No. 2 and 3 were twins that were born prematurely, and case No. 3 presented the similar symptoms with case No.2 except for heart failure. Afterwards, case No. 4, 5, 6 and 7 from the same centre presented the same symptoms as the above cases, while all the subsequent cases had relatively mild symptoms, mainly manifested as coughing and nasal congestion (Table 1). Seven of the neonates (case No.1 to No. 7) were transferred to the ICU because of heart failure and respiratory failure, and all received intubation treatment. All neonatal cases recovered after treatment in hospital.

**Etiological identification**

To identify the cause of this outbreak, pharynx swabs or nasopharyngeal aspirates were collected from 21 neonates, while throat swabs were collected from
13 nursing staff. All of the samples were screened for 16 viruses, namely: adenovirus; human bocavirus; parainfluenza virus; respiratory syncytial virus; influenza virus; varicella zoster virus; Epstein–Barr virus; cytomegalovirus; human herpesvirus 6; human metapneumovirus; measles virus; coronavirus 229E, HKU1, NL63, OC43; mumps virus; enterovirus; rhinovirus; and human parecho virus; and 11 bacteria, namely: *Bordetella; Bordetella holmesii; Bordetella pertussis; Chlamydophila pneumoniae; Haemophilus influenzae; Klebsiella pneumoniae; Legionella pneumophila; Moraxella catarrhalis; Mycoplasma pneumoniae; Staphylococcus aureus and Streptococcus pneumoniae*. Twenty of the 34 samples tested positive only for HRSV, and negative results were obtained for all other viruses and bacteria. The 20 HRSV-positive samples were from 16 hospitalized neonates and four nursing staff with asymptomatic infections. The other five asymptomatic neonates and nine nursing staff were negative for all 27 pathogens.

**Characterization of HRSV associated with this outbreak**

The HVR2 fragment of G gene of HRSV was successfully amplified from six neonates and two nursing staff. Genetic analysis revealed that these eight sequences were 100% identical. Phylogenetic trees were constructed with the eight sequences from this study and HRSV B reference sequences downloaded from the GenBank database. These eight Shenyang (SY) sequences were clustered into the same branch as the BA9 genotype references sequences. The sequences of the
viruses identified in this study were most closely related (98% homology) to viruses detected in the Netherlands and Spain during 2018 and 2019 (Figure 1a). The same results were obtained by performing a BLAST search of the SY sequences against the GenBank database.

Next, 83 representative BA9 HVR2 sequences originating from 26 countries during 2005 and 2019 were retrieved from the GenBank database. Phylogenetic analysis was performed on the SY sequences and the 83 representative BA9 HVR2 sequences. The results showed that SY virus BA9-SY/CHN/2021 clustered with lineage 7 of the BA9 genotype, which comprised viruses circulating in many countries during 2017–2019 (Figure 1b, Table supplement).

Compared with the BA9 reference strain NG-102-06 (GenBank: AB603467), there were five amino acid mutations (A271V, T276A, I281T, T290I and T312I) in the HVR2 region of SY strain. The SY strain possessed a mutation in a stop codon (from TAA to CAA) compared with the BA9 reference strain, resulting in a seven amino acid extension to the G protein (Q-R-L-Q-S-Y-A).

Discussion

From January to February 2021, an outbreak of neonatal pneumonia caused by a new lineage of the BA9 genotype of HRSV was reported in a postpartum care centre in Shenyang, China. The outbreak resulted in the hospitalization of 16 neonates and of the nine severe cases, seven presented with respiratory failure,
including a pair of premature twins who also presented with heart failure. Based on our epidemiological investigation, the transmission source for this outbreak may have been the nursing staff who took care of the neonates.

The most common transmission routes of HRSV are via the respiratory tract and direct contact, and the virus is able to survive on surfaces such as countertops and cribs for hours (17). The HRSV incubation period ranges from 3 to 8 days (18). Although the index case was identified among neonates, the nursing staff with asymptomatic HRSV infections were considered as the possible source of this outbreak, which could be supported by the following evidence. First, all of these neonates were transferred from different maternity hospitals after birth and the onset of disease in the index infant was 21 days after moving to the postpartum care centre, which is much longer than the HRSV infection incubation period. Therefore, it is likely that the index case was infected at the postpartum care centre rather than the maternity hospital. Second, each neonate was cared for in a separate room, but shared the same nursing staff. The nursing staff did not routinely wear masks, and took care of different neonates without hand sanitation or changing gowns. The viruses may therefore have been carried by the nursing staff and transmitted from one neonate to another. Third, an investigation of the postpartum care centre after the HRSV outbreak found that it is a relatively independent building, covering an area of 800 m², with 28 rooms across three floors. Each room contains a bathroom and a baby cot. There were no sterilization records for any
objects or rooms, the stored sanitizer had expired and the rooms were poorly ventilated. In addition, the centre had no procedure in place for routine monitoring of the health status of staff members. There was deemed a potential risk of indoor cross-infection. Our nucleotide sequence analysis revealed that viral sequences obtained from neonates and nursing staff were 100% identical. This indicated that the HRSV associated with the pneumonia outbreak in neonates was originally transmitted from nursing staff who had asymptomatic infections. It does not rule out the transmission from the visiting family members, but unfortunately that no samples have been collected and cannot be confirmed.

Genotype BA9 was first reported in 2006 and has since become the predominant genotype worldwide(19). According to a previous publication, the sequences of BA9 genotype strains circulating worldwide from 2015–2019 could be grouped into seven lineages, of which the 2017–2019 viruses belonged to lineage 7 (20). Phylogenetic analysis in this study included the BA9 viruses circulating worldwide from 2005–2019, and found that the virus associated with the investigated outbreak clustered on the same branch as lineage 7 of the BA9 genotype. We detected a mutation in a stop codon of SY virus that resulted in a seven amino acid extension to the G protein. This was consistent with a previous report from The Observational United States Targeted Surveillance of Monoclonal Antibody Resistance and Testing of HRSV (OUTSMART-RSV) study, which analyzed viruses circulating in the USA during 2016 and 2017(21). The function of
these seven extended amino acids in the G protein remains to be determined, and this extended G protein has not previously been linked to outbreaks of severe cases. However, future research and surveillance to monitor the effect of this genetic modification on viral epidemiology, transmission and disease severity is warranted.

In conclusion, this outbreak of neonatal pneumonia was caused by the 2017–2019 lineage of HRSV genotype BA9 and is believed to have been transmitted from the nursing staff who cared for the neonates. Our findings highlight the importance of strict hygiene and disease control measures, including wearing/changing masks, hand washing, and changing gowns between neonates, to prevent potential outbreaks of severe respiratory infectious diseases in such clinical settings. To the best of our knowledge, this is the first report to describe a severe neonatal pneumonia outbreak caused by HRSV of the BA9 genotype in a postpartum care centre in China.

**Funding**

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**Conflict of interest**

The authors declare that no competing interests exist.
Contributors

BW and JJS carried out most of data analysis and drafted the manuscript. YZ designed and coordinated the study and revised the manuscript. JHS, NYM, LJY, CY, QY, BL and XZB performed the sequencing and sequence analysis. All authors read and approved the final manuscript.

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### Table 1. Characteristics of nine severe cases of human respiratory syncytial virus infection hospitalized in Shenyang Children's Hospital

| Case No. | Age | Gender (M/F) | Data of disease onset | Pneumonia on CT scan | diagnose | Nasal | Cough* | Fever* | WBC/L | Respiratory failure | Heart failure | Hospitalized | ICU |
|----------|-----|--------------|----------------------|----------------------|-----------|-------|--------|--------|-------|-------------------|--------------|-------------|-----|
| 1        | 27d | M            | Jan 17               | yes                  | ALRI      | no    | 4d     | no     | 11.4×10⁹/L | yes               | no            | yes         | yes |
| 2        | 26d | F            | Jan 23               | yes                  | ALRI      | no    | 10d    | no     | 9.7×10⁹/L | yes               | no            | yes         | yes |
| 3        | 26d | F            | Jan 26               | yes                  | ALRI      | no    | 7d     | no     | 9.7×10⁹/L | yes               | yes           | yes         | yes |
| 4        | 17d | M            | Jan 28               | yes                  | ALRI      | 4d    | 3d     | no     | 7.7×10⁹/L | yes               | no            | yes         | yes |
| 5        | 28d | M            | Jan 29               | yes                  | ALRI      | 2d    | 2h     | no     | 9.9×10⁹/L | yes               | no            | yes         | yes |
| 6        | 22d | M            | Jan 30               | yes                  | ALRI      | 3d    | 3d     | no     | 9.2×10⁹/L | yes               | no            | yes         | yes |
| 7        | 12d | M            | Feb 1                | yes                  | ALRI      | no    | 2d     | no     | 9.2×10⁹/L | yes               | no            | yes         | yes |
| 8        | 27d | M            | Jan 30               | yes                  | ALRI      | 1d    | 4d     | 1d     | 12.93×10⁹/L | no                | no            | yes         | no |
| 9        | 23d | M            | Feb 3                | yes                  | ALRI      | 2d    | 2d     | no     | 6.3×10⁹/L | no                | no            | yes         | no |

*The number of days

M, male; F, female; HRSV, human respiratory syncytial virus; WBC, white blood cells.
Figure 1. Neighbor-joining phylogenetic tree of the entire coding region nucleotide sequence of HVR2 of the G gene of HRSV subgroup B isolated from the postpartum care centre. Red circles represent sequences from neonates; red triangles represent sequences from nursing staff. (b) Phylogenetic analysis of the sequences of BA9-SY/CHN/2021 isolates from the outbreak in Shenyang (shown in red) and 83 genotypes of BA9 strains (2005–2019) retrieved from the GenBank database. Blue triangles indicate representative strains from China.
Following are the point-by-point responses to reviewers

Reviewer #1 (Comments for the Author):
You should focus on the genotype that you found in your samples and not conclude that the cause of outbreak are the nurses.

Response:
Thank you very much for your valuable comments, we really appreciated the time that you spent in reviewing our manuscript. We agreed with you and have already revised the manuscript as you suggested.

Minor comments:
Line 57, I think that a new name should not be given to the BA9 strain found.
Response:
Thank you very much for your comments. Sorry for the confusing name. We used the name of “SY strain” to refer the viruses identified in this study (line 58).

Line 97, You should eliminate bibliography 9 because it talks about the second hypervariable region of the G gene and citation 9 corresponds to a study of the F gene.
Response:
Thank you very much for your suggestion. As suggested, we deleted the bibliography 9.

Line 111-113, Because it refers to a particular strain, Shenyang (SY)?
Response:
Sorry for the confusing name. Shenyang (SY) strains refers to “SY strain”. To avoid the confusion, we used the name of “SY strain” to refer the viruses identified in this study, in the whole manuscript.
Line 141, You must describe the methodology because it has not been previously published or is not cited.

Response:

Thank you very much for your comments. As suggested, we referred the reference of the real-time RT-PCR methodology in the revised manuscript (line 141).

Line 264-267, Due to the fact that it was not possible to obtain a sample from the relatives, it cannot be concluded that the outbreak was caused by the nurses.

Response:

Thank you very much for your comments. We agree with you. So we revised the conclusion in the manuscript: It is inferred that this outbreak of neonatal pneumonia might be spread by nursing staffs with asymptomatic infections, but could not rule out the visiting relatives who might bring the HRSV virus to the postpartum care centre. Unfortunately, the samples were not available from the visiting relatives so that no evidence to support this speculation. Please see the modification in the line of 264-267.

Reviewer #2 (Comments for the Author):

The authors studied molecular epidemiological analyses regarding an outbreak of pneumonia in neonate due to RSV-B, genotype BA9.

Overall, the draft manuscript was well described, although subjects were relatively small numbers. I think that some major and minor concerns should be improved.

Response:

We really appreciated your positive comments on our manuscript, thank you very much for your expertise and your valuable comments.
1. The authors made a phylogenetic tree using NJ method. I think that this was made by ML method by MEGA.

Response:

After double check, we found the phylogenetic tree analysis showed in this manuscript was made by NJ method of MEGA, rather than ML method.

2. Please provide the approval number of ethics committee.

Response:

Thank you very much for your comments. As suggested, we provided the approval number of the ethics committee is IVDC 2018 No. 012 (line 119-120).

3. Please provide analyzed nucleotide numbers of these sequences.

Response:

Thank you very much for your comments. As suggested, we provided analyzed nucleotide numbers (324 nucleotide) of eight sequences in the manuscript. Please see the line 206 in the revised manuscript as below: The HVR2 fragment of G gene of HRSV (324 nucleotide) was successfully obtained from six neonates and two nursing staff respectively.

4. Please provide relevant discussion for amino acid substitutions in HRV2 in your strains comparing with other previous reports.

Response:

Thank you very much for your comments. Compared with the previous reports, we supplemented the relevant contents of amino acid mutation in HRV2 in the discussion as below: amino acid analysis of the SY strains identified in this study showed there were five mutations in the HVR2 of the G protein gene, including A271V, T276A, I281T, T290I and T312I. Previous studies have found the same amino acid mutation sites, and five simultaneous amino acid mutation sites were found in six identical sequences from patients hospitalized with community acquired pneumonia (CAP) patients from China during 2018. However, whether these five amino acid mutations
found in the viruses associated with severe neonatal pneumonia could be beneficial for the virus replication and transmission remains to be further studied (line 274-282).
June 3, 2022

Dr. Yan Zhang
National Institute for Viral Disease Control and Prevention, China CDC
Beijing
China

Re: Spectrum00974-22R1 (An outbreak of severe neonatal pneumonia caused by human respiratory syncytial virus BA9 in a postpartum care centre in Shenyang, China)

Dear Dr. Yan Zhang:

Thank you for submitting your manuscript to Microbiology Spectrum. When submitting the revised version of your paper, please provide (1) point-by-point responses to the issues raised by the reviewers as file type "Response to Reviewers," not in your cover letter, and (2) a PDF file that indicates the changes from the original submission (by highlighting or underlining the changes) as file type "Marked Up Manuscript - For Review Only". Please use this link to submit your revised manuscript - we strongly recommend that you submit your paper within the next 60 days or reach out to me. Detailed instructions on submitting your revised paper are below.

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Sincerely,
Daniela Rajao
Editor, Microbiology Spectrum
Journals Department
American Society for Microbiology
1752 N St., NW
Washington, DC 20036
E-mail: spectrum@asmusa.org

Reviewer comments:

Reviewer #1 (Comments for the Author):

After reviewing the responses to my comments, I found that they were all taken into consideration and included in the text.

Reviewer #2 (Comments for the Author):

NJ is not well regarded among evolutionary biologists as its methods are too ad hoc. Moreover, this method is not suitable for rapid evolutionary gene including the G gene. The author should remake the phylogenetic tree using ML method.
Second, the authors used lineage in the phylogenetic tree. In general, the term lineage or clade usually can use large cluster having large genetic divergence (i.e., corresponded phylogenetic distance at more than around 0.2 or 0.3. The present strains probably had less than 0.1. Thus, the suitable term is cluster.

Staff Comments:

Preparing Revision Guidelines
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Thank you for submitting your paper to Microbiology Spectrum.
Following are the point-by-point responses to reviewers

Reviewer #1 (Comments for the Author):
After reviewing the responses to my comments, I found that they were all taken into consideration and included in the text.
Thank you for your review again.

Reviewer #2 (Comments for the Author):

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Response:
Thank you very much for your expertise and your valuable comments. The phylogenetic tree has been reconstructed using ML method. In addition, we changed “lineage” to “cluster” and modified it in the whole manuscript.
June 18, 2022

Dr. Yan Zhang
National Institute for Viral Disease Control and Prevention, China CDC
Beijing
China

Re: Spectrum00974-22R2 (An outbreak of severe neonatal pneumonia caused by human respiratory syncytial virus BA9 in a postpartum care centre in Shenyang, China)

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Thank you for submitting your paper to Spectrum.

Sincerely,

Daniela Rajao
Editor, Microbiology Spectrum

Journals Department
American Society for Microbiology
1752 N St., NW
Washington, DC 20036
E-mail: spectrum@asmusa.org

Supplemental file 1: Accept