

Detailed comments from the meeting:

1. Thank you for sending us your interesting case series at this early stage in the outbreak of 2019nCoV. We would like to proceed with fast track publication and ask that you revise your manuscript as quickly as possible.

**Response:** We would like to thank the committees and the reviewers for the thoughtful and detailed review and consideration of our manuscript. The comments and suggestions made by the editor and reviewers have helped us to improve the manuscript significantly. Below please find the point-by-point response to the comments. All the changes have been highlighted in the revised manuscript.

2. We think your study is best characterized as a case series rather than an observational study. Please alter the title accordingly.

**Response:** We appreciate this suggestion, and have changed the title to “Clinical findings of a group of patients with 2019 novel coronavirus outside of Wuhan: a retrospective case series study.” Please refer to the revised manuscript.

3. Please give more attention to describing how you assessed the timing of exposure and onset of symptoms as this will influence the reliability of the estimates of incubation period.

**Response:** we understand the importance of assessing the timing of exposure and onset of symptoms. We have provided additional information in methods also as the following: *“We collected information on the dates of illness onset, visits to clinical facilities, and hospitalization. Epidemiologic data were collected through brief interviews with each patient. The investigator interviewed each patient to collect exposure histories during the two weeks before the illness onset, including the dates and times of close contact with a confirmed case or suspected cases from Wuhan, Hubei Province. The incubation period was defined as the time from exposure to the onset of illness, which was estimated among patients who can provided exact date of close contact with a confirmed case or suspected case in Wuhan.”*

4. Please describe the criteria for inclusion into your study. We understand that these are cases admitted to hospital but was there an increased vigilance and tendency to

admit suspected cases to an institution in order to monitor this new disease? If that is the case then it may explain the milder spectrum of disease compared to the initial cases before more active surveillance.

**Response:** we have provided more information regarding how the patients were screened and finally enrolled in our study. *“Since the outbreak of the 2019-nCoV, strict precautions have been implemented in Zhejiang, including setting up fever clinic receiving all suspected cases with fever and dry cough, especial those with travel history to Wuhan or history of exposure to infected person within 2 weeks before the onset of illness since January, 2020. The case definitions of confirmed human infection with the 2019-nCoV are according to WHO interim guidance <sup>1</sup>. Only patients with laboratory-confirmed infection were enrolled in this study.”*

5. We understand that this infection may be relatively prolonged and therefore it may be a little early to comment on the absence of deaths. Similarly until everyone has been discharged it is not possible to comment on the length of stay. Please alter your conclusions accordingly.

**Response:** we agree with you that it is a little ambitious to discuss the absence of deaths at the early stage. We have deleted the section in our discussion.

6. We note the geographical separation of your hospital from the original source of the outbreak. Can you comment on why so many cases have been seen in your area rather than other cities and regions in China?

**Response:** Zhejiang is one of coastal province where private enterprises is flourishing. Therefore, millions of individual temporally migrate to other area of China to do business, and return to Zhejiang in the spring festival vacation starting at 10 January, 2020. Up to date, Zhejiang province reported the largest number of confirmed 2019-nCov cases except for Hubei province, the original source of the outbreak.

7. Without information on the denominator (number of people exposed) it is not possible to comment with much certainty about the transmissibility of the infection. Please reconsider some of your statements about this.

**Response:** we have revised some statements in our manuscript including deleted the sentence of *“2019-nCoV was easily transmitted from human to human”*, and revised

the last rows of first paragraph in discussion as “*According to our data, none of the infection cases in Zhejiang had been exposed to the Huanan seafood marker, and there are a large part of family clusters in Zhejiang infected cases, which might suggest a possible human to human transmission. This finding is also consistent with Professor Yuan's article. However, the exact transmission route urges further detailed investigations.*”

8. We agree with the reviewers that more clinical information describing the cases would be very helpful. At the moment your summaries are very high level and "epidemiological". Please include as much of the information suggested by the reviewers as possible.

**Response:** we appreciate the reviewers’ suggestions. We have modified our manuscript accordingly. Please also refer to our response to the reviewer in the following.

9. Since you are reporting a case series we do not think it necessary to apply statistical tests to any descriptions or comparisons made.

**Response:** We appreciate this suggestion and have amended the manuscript accordingly.

10. Please revise your paper to respond to all of the comments by the reviewers. Their reports are available at the end of this letter, below.

**Response:** we appreciate the hard work of each reviewer and editor. We found all the suggestions and questions very helpful. We have responded point-by-point to the feedback in the letter below, as well as in the revised manuscript in the marked changes.

Comments from Reviewers

Reviewer: 1

Recommendation:

Comments:

Li et al. described patients with laboratory-confirmed infection 2019-nCoV in Zhejiang province. None of these patients have exposure to Huanan Seafood Market but all have exposure to infected patients. Furthermore, these patients either have long-term residence in Wuhan or short-term trip to Wuhan. This paper provided more information about the clinical features of 2019-nCoV infected patients. However, several important limitations should be addressed for this paper. 1) Human transmission was inferred from the study by lack of exposure to the Huanan Seafood Market from all patients, but lack of exposure history to the Market is not sufficient for proving person-to-person transmission, especially under the condition that all the patients have been to Wuhan and that the source for 2019-nCoV was still not clear. 2) The authors did not provide clear definition of second-generation and how all these patients enrolled in the study were identified as second-generation. 3) The definition of incubation period was not clearly provided. The authors mentioned in Result section patients who had short term trip to Wuhan were included to calculate the incubation period, but the numbers provided in the table were for all patients enrolled in the study. 4) Tables were not informative as no important comparison was made (also no p values). Other points are addressed as follows:

**Response:** we really appreciate your review service in such short time. We will response your comments by point by point. 1) Indeed, it is too arbitrary to conclude the human-to-human transmission in context of our data. Therefore, we downplay the conclusion on transmission and pay more attention to clinical features. 2) We admitted that it is inappropriate to regards all patients in our study as second-generation cases because we did not collect detailed transmission data or genetic data to ascertain the generations of transmission. We revised the whole manuscript to underscore our sample is a group of patients outside of Hubei Province. 3) The incubation period was defined as the time from exposure to the onset of illness, which was estimated among patients who can provide exact date of close contact with a confirmed case or suspected case in Wuhan. We also modified the table to indicate how many patients have the date to allow the incubation estimate. 4) Since our study is case series study, and the sample size is very limited. The editor suggests that there is no need for statistical comparison.

#### Major

1. Abstract, Line 64: How was the time point for infection exposure identified for patients who either have long-term residence in Wuhan or short-term trip to Wuhan? This should be clarified.

**Response:** the time point of the infection exposure was only determined among patients who can provided exact date of close contact with a confirmed case or suspected case in Wuhan. Please refer to the first paragraph of methods.

2. Methods: The word “course” was ambiguous. Does this mean length of hospitalization or the time since illness onset? Please clarify.

**Response:** we are sorry for this ambiguity. It is the time since illness of onset. We have changed it accordingly.

3. Methods: The authors included 62 cases in this study, but mentioned “a large number of patients showed up” so they just collected “most but not all” patients. Is there a justification for choosing these 62 cases? Are they the earliest cases? Or please indicate a time period for collecting cases.

**Response:** this is an ongoing epidemic, and every day many new cases are identified and admitted. We have determined a cutoff period from January 10 2020 to January 26 2020 to include the lab confirmed cases. Please refer to the first paragraph in methods section.

4. Methods-Statistical analysis: In the research conducted by Huang et al, the median time from onset of symptoms to ICU admission was 10.5 days. This number was calculated among those with ICU admission. However, among 62 patients enrolled in this study, only one patient was admitted to ICU. Nearly all of the patients are still in hospitalization when the authors submitted the paper. This means patients will gradually move from duration time <10d to duration time >10d. The duration of hospitalization cannot reflect the disease severity and is not a good classification variable at this specific time point.

**Response:** In previous studies on SARS, H7N9, and MERS, admission to ICU was used as proxy for disease severity. In Huang ET all’s study we know the median time between illness onsets to admission to ICU was 10 days. As you indicated that some of patients with time since the illness onset may not sufficient long to allow us to assess disease severity. However, we do have some patients with time since the illness onset longer than 10 days, and they were separated to estimate the disease severity. Among those patients with the time since the illness onset longer than 10 days, only 1 was admitted to ICU.

5. Methods-Statistical analysis: It is not reasonable to make comparisons between all the patients enrolled in the study and patients with course longer than 10 days, as

the latter ones were part of patients included in the study. The authors should make comparisons between those with and without course longer than 10 days.

**Response:** Since our study is case series study, we are not going to make statistical comparison. However, we still stick to your suggestion and will present the characteristics separately for those with and without course longer than 10 days in our tables.

6. Methods-Statistical analysis: The authors only gave brief description of different characteristics. Statistical analysis should be performed with statistics calculated and p values listed in each table.

**Response:** Since our study is case series study, we are not going to make statistical comparison.

7. Results-Lines 155-156: Why only patients who had short term trip to Wuhan were included to calculate the incubation period? How was the time point for infection exposure identified? In lines 171-172, the incubation period was calculated for all the 62 patients. These were inconsistent through the article.

**Response:** The incubation period was defined as the time from exposure to the onset of illness, which was estimated among patients who can provided exact date of close contact with a confirmed case or have short-time period visit to Wuhan. We also modified the table to indicate how many patients have the date to allow the incubation estimate.

8. Discussion: “According to our data, none of the infection cases in Zhejiang had ever been exposed to the Huanan seafood market, all the patients were infected by human transmission.” This sentence should be revised. Without exposure to Huanan Seafood Market is not the sufficient conditions of human to human transmission as the source of infection is still not clear.

**Response:** we have revised some statements in our manuscript including deleted the sentence of “2019-nCoV was easily transmitted from human to human”, and revised the last rows of first paragraph in discussion as “*According to our data, none of the infection cases in Zhejiang had been exposed to the Huanan seafood market, and there are a large part of family clusters in Zhejiang infected cases, which might suggest a possible human to human transmission. This finding is also consistent with Professor Yuan's article. However, the exact transmission route urges further detailed investigations.*”

9. Discussion: Chen et al. published their data on 99 cases of 2019-nCoV patients on Jan 30, 2020 in the Lancet. Clinical characteristics from these patients should also be discussed, apart from the 41 patients in Huang et al.'s cohort.

**Response:** we have added some discussion.

10. Conclusion: Line 254 "The 2019-nCoV could be easily transmitted from human to human." This sentence should be revised. A study focusing on clinical features of admitted patients shall not reveal the transmission status. Please refer to the epidemiological study published by Li et al on January 30th in New England Journal Medicine.

**Response:** we have revised some statements in our manuscript including deleted the sentence of "2019-nCoV was easily transmitted from human to human." We have paid more attention on clinical features.

11. Table 1-3: No comparison was made with only the descriptive values listed. These tables are not informative.

**Response:** Since our study is case series study, we are not going to make statistical inference.

12. Table 4: Information listed in the table can be found in Table 1-3. Descriptive comparison between results from this study and that from Dr. Cao should be addressed only in discussion section but not in a separate table.

**Response:** We have deleted Table 4 and addressed in discussion section

13. Moderate linguistic (English) corrections are desirable. Present version has some punctuation, grammatical and typological sentence framing issues which should be taken care of by the authors.

**Response:** we have sent our manuscript to editing and we hope the revised manuscript is improved.

Minor

1. Line 50: Grammar mistake: "covered", "are located in", "parts".

**Response:** We have changed the sentence to "The study covered seven hospitals which are located in the different parts of Zhejiang Province".

2. Line 52: please be specific about the date.

**Response:** The specific period was from January 10th 2020 to January 26th 2020, and the whole sentence was changed to “From January 10th 2020 to January 26th 2020, we collected data of 62 hospitalized patients with laboratory-confirmed 2019-nCoV in designated hospitals of Zhejiang Province”.

3. Line 63: “Few” patients, not “rare”. Do you mean shortness of breath at illness onset, or during hospital treatment? Same for line 176 and 182.

**Response:** We have changed “Rare” to “Few”. The “few” referred to the shortness of breath at illness onset. Because most of the patients were still in hospitalization, the data during hospital treatment are not complete.

4. Line 67: “secondary infection” should be replaced with “second-generation”?

**Response:** We realize that it is inappropriate to regards all patients in our study as second-generation cases because we did not collect detailed transmission data or genetic date to ascertain the generations of transmission. We revised the whole manuscript to underscore our sample is a group of patients outside of Hubei Province.

5. Line 79: “most” is better than “nearly all”, because only 66% had been exposed to the market in this cohort.

**Response:** We appreciated the suggestion and changed “nearly all” to “most”.

6. Line 86: This number has already surpassed the sum for SARS-Cove and MERS-Cove, please update. Same for line 202.

**Response:** We updated the data up till the date of 8th Feb, 2020. Line 86 has changed to “Up to 8 February, 2020, there were a total of 37589 confirmed cases all over the world, including 302 oversea cases from 24 countries”.

Line 202 has changed to “As of January 278 February, 2020, more than 30,000 laboratory-confirmed 2019-nCoV infections were reported in China”

7. Line 88-89: “the clinical investigation of patients was still limited in the literature”. Please clarify what is “limited in the literature”. Do you mean “number of published studies is limited”?

**Response:** We mean that the clinical observation and investigation of 2019-nCOV patients was still insufficient. We have changed this sentence to “Despite the increasing number of confirmed cases, the clinical investigation of patients was still insufficient.”

8. Line 97-98: Should be reference #9. Please specify what are defined as imported case?



**Response:** “Imported” here were not appropriate to conclude all the patients enrolled in our cohort, so we have deleted the related words.

9. Line 100: What are “these people”? Please specify.

**Response:** “These people” referred to the enrolled patients. We have changed it to “the enrolled patients”.

10. Line 109: What is the definition for suspected case? Does travel or contact history count as a mandatory criterion for suspected case? Should be “especially” (line 110).

**Response:** travel or contact history are not mandatory criterion for suspected case. We described how to receive the suspected patients in the methods.

11. Line 125: For laboratory confirmation, what samples did you use for RT-PCR? Nasopharyngeal swabs or BALF?

**Response:** We used sputum and throat-swabs to perform the RT-PCR. We have added them in the methods.

12. Line 128: Please specify what is “and so on”? Any tests for other common respiratory pathogens?

**Response:** We performed other respiratory viruses including influenza A virus (H1N1, H3N2, and H7N9), influenza B virus, respiratory syncytial virus, parainfluenza virus and adenovirus at admission. We have added in the methods.

13. Line 128: Most patients, without the “of”.

**Response:** We have deleted the “of”.

14. Line 129: What is “Loping veletonavir”? I assume it is “Lopinavir/Ritonavir”.

**Response:** We sorry about the mistake, we have corrected it .

15. Line 132: Please provide dosage for corticosteroid therapy and IVIG.

**Response:** The dosage of corticosteroid is 40-80mg/day, and the dosage of IVIG is 15-20g/day.

16. Line 134: What is the unit of CRP?

**Response:** The unit of CRP is mg/L, and we have added it in the methods.

17. Line 136: Please clarify the definition of “2019-nCoV clearance”.

**Response:** 2019-nCoV clearance refers to results of two real-time RT-PCR of 2019-nCoV RNA were negative with 24 hours apart.

18. Line 156, Line 166: Please avoid the word “select”.

**Response:** We have changed “select” to “analyzed”.

19. Line 164: Is 1.6% the percentage for COPD or diabetes? Same for line 168.

**Response:** Both COPD and diabetes were 1.6%, we have corrected the sentences.

20. Line 165, Line 169: What is the meaning of “associated with” familial clusters? Did the authors mean relatives of the 21 patients were also reported to be infected by 2019-nCoV? Were the relatives included in this cohort?

**Response:** We mean that at least one of these 21 patients’ relatives was reported to be infected by 2019-nCoV and the patient had a contact history to the infected relative within 2 weeks. All the relatives were included in this cohort.

21. Line 177: “... course over 10 days. We found” should be revised to ““... course over 10 days, we found””.

**Response:** We have revised this sentence.

22. Line 185: “The D-dimer level was higher (median D-dimer level 0.2 mg/L [IQR 0.2-0.5]).” Higher than what? No comparison was made.

**Response:** We are sorry to make the mistake. The “higher” should be replaced with “normal”.

23. Line 193: “patient transferred” should be revised to “patient was transferred”.

**Response:** We have revised this sentence.

24. Line 194: By antiviral, is it lopinavir or oseltamivir?

**Response:** We described the antiviral therapy in detail in Table 3.

25. Line 197: “One patient has”. Singular form.

**Response:** We have revised this sentence.

26. Line 206: Suggest adding “early” before “2019-nCoV cases in Wuhan”. Chen et al. has reported clinical features for another 99 cases in Wuhan (the Lancet) who had similar features.

**Response:** We are appreciated with the suggestion and have added “early” before “2019-nCoV cases in Wuhan”.

27. Line 211-212: Please clarify “air prevention”. Do you mean “airborne transmission precaution”?

**Response:** We have deleted this sentence, because we can’t draw any conclusion about the transmission mode of 2019-nCOV in this study.

28. Line 217 “developed to”→”developed”

**Response:** We have revised the sentence.

29. Line 218 “admitted”→”were admitted”

**Response:** We have revised the sentence.

30. Line 219: “Fewer” patients.

**Response:** We have revised the sentence.

31. Line 230: Please clarify “not much”. Addressing the difference in antiviral therapy, patients in Huang et al. paper did not use lopinavir and many were given empirical oseltamivir.

**Response:** we are sorry for this ambiguity. Here we just wanted to state that all of the patients in both cohort accepted antiviral treatment, but we noticed that they were offered different drugs and therapies. We have changed this sentence as” Patients in two cohorts all received antiviral treatment, but the certain drugs used were different. Lopinavir/ritonavir was reported to have the potential to treat SARS infection,<sup>15</sup> and we supposed it might benefit on 2019-nCOV treatment.”

32. Line 236 “Given that most infections in Zhejiang were secondary-generation infections, .....” This sentence contradicted with the Line 207-209, where you stated all patients were infected by human transmission. Please clarify.

**Response:** We noticed that it is inappropriate to regards all patients in our study as second-generation cases because we did not collect detailed transmission data or genetic date to ascertain the generations of transmission. We revised the whole manuscript to underscore our sample is a group of patients outside of Hubei Province.

Reviewer: 2

Recommendation:

Comments:

This is a very important manuscript as it deals with the outbreak in Zhejiang which is the second largest outbreak of the novel coronavirus outside of Wuhan. Although no deaths have been reported from Zhejiang, the size of the outbreak is huge with close to 600 reported cases to date. Also the measures taken by the province are drastic with the total shutdown of Wenzhou. As such the manuscript is timely but there are several issues which need to be addressed. They include

Major

1) The rationale for using a 10 day cutoff to divide the cohort is not clear. In the Huang et al reference cited to justify this, the median time to dyspnea was 8 days and the median time to ARDS was 9 days, ICU admission 10.5 days. It would make more sense to look at the cohort as a whole and provide some data on the duration of illness for the whole cohort.

**Response:** In previous studies on SARS, H7N9, and MERS, admission to ICU was used as proxy for disease severity. In Huang et al.'s study, we know the median time between illness onset to admission to ICU was 10 days, so we divided the cohort using 10 days cutoff aiming to estimate the disease severity. In our cohort, only one patient was administrated in ICU, and most patients didn't develop dyspnea, ARDS or need transfer to ICU.

2) The way the results are presented also does not make sense. Patients in the tables are essentially counted twice – first in the whole cohort and then in the “10 day cohort” Given the fact that patients were essentially kept in hospital until they were presumably PCR negative for the coronavirus, what the two groups appear to represent are those who presented earlier in the epidemic in Zhejiang vs those who presented later in the epidemic. This should be emphasized and perhaps the whole cohort analysed together.

**Response:** Thank you for your suggestion. We will stick to your suggestion and will present the characteristics separately for those with and without course longer than 10 days in our tables.

3) It is not clear from recently published reports (references 1,9 and 10) that “most of the patients had been to the local seafood market as stated in lines 72 and 73. Also the viral genomes are not closely related to snake genomes!

**Response:** We are appreciated about the concern, and we have deleted the related sentence.

4) The figure in line 76 is misleading as the total number of cases of SARS and MERS appear to be added up although the references only refer to MERS. It would be clearer to separate MERS from SARS and report cases and deaths from both.

**Response:** We deleted the data of reported cases and deaths, and quoted some other references to compare SARS and MERS with 2019-nCoV on the gene characterisation and epidemiology.

5) The statement in line 82 that the virus is mainly transmitted from animals to humans is also not supported by any data. Although the virus is related to a bat virus, to date, there has been no animal shown to be infected with this virus. Perhaps the authors could say instead “The virus is believed to have been transmitted from animals”

**Response:** We appreciated the suggestions and have revised the sentence.

6) The case definition needs to be provided. There is a citation to reference 1 which does not have a clinical case definition but has only two cases described without a case definition.

**Response:** We diagnosed the 2019-nCoV patients according to the WHO guideline. We have revised the reference in the methods.

7) While the drug “Lopinavir-ritonavir” may be available in China as a variant of lopinavir-ritonavir, some reference needs to be provided to help understand its pharmacology (line 129) similarly for inhaled interferon 1B

**Response:** Lopinavir/ritonavir was reported to have the potential to treat SARS infection<sup>1</sup>, and we supposed it might benefit on 2019-nCoV treatment. IFN-I bind to a cell surface receptor complex known as the IFN- $\alpha/\beta$  receptor (IFNAR), which is widely expressed on almost all kinds of immunocytes and epithelial tissue<sup>2</sup>, so it might also benefit on treating 2019-nCoV. We listed the detailed antiviral therapies in Table 3.

1. Chu CM, Cheng VC, Hung IF, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax* 2004;59(3):252-6. doi: 10.1136/thorax.2003.012658 [published Online First: 2004/02/27]

2. Cunningham CR, Champhekar A, Tullius MV, et al. Type I and Type II Interferon Coordinately Regulate Suppressive Dendritic Cell Fate and Function during Viral Persistence. *PLoS Pathog* 2016;12(1):e1005356. doi: 10.1371/journal.ppat.1005356 [published Online First: 2016/01/26]

8) Details also should be provided for steroids, “gamma globulin” and probiotics used in the patients. Perhaps an additional table could be used to list out the different treatment modalities used and the outcomes in simple terms such as number of days on oxygen therapy

**Response:** The kind and dose of steroids, gamma globulin and antiviral drugs were listed in the methods. We just list the classes of antibiotics because the dose of antibiotics vary with the situation of patients. A mix of probiotics were provided to the patients so that it was hard to calculate the dose.

9) It is not clear what is the difference between “long term residents” of Wuhan and “short term visitors” if all the study subjects lived in Zhejiang. Presumably all of the individuals studied had left Wuhan for Zhejiang at some point in time and the duration that they stayed in Wuhan might be considered a variable in estimating their exposure to infected patients in Wuhan perhaps. That is unless the “long term residents” were people who fled Wuhan to avoid the lockdown and thus were more likely to be incubating the virus. This does not seem to be the case as the presumption is that all the infections were acquired in Wuhan and the incubation period is calculated from the time the short term visitors left the city.

**Response:** We have provided additional information about estimating exposure in methods as the following: “The incubation period was defined as the time from exposure to the onset of illness, which was estimated among patients who could provide the exact date of close contact with a confirmed case or suspected case in Wuhan. We also investigated the familial clusters, meaning that there were index cases who travelled to Wuhan and then infected others in their families.”

10) Line 165 includes the intriguing figure of one third of the cases associated with family clusters. More information is needed on this – did whole families travel to Wuhan and get infected or were there index cases who travelled who infected others in their families?

**Response:** Actually, not all family clusters travelled to Wuhan and get infected. Some were infected by their relatives returning from Wuhan. We have added this in the methods section as “We also investigated the familial clusters, meaning that there were index cases who travelled to Wuhan and then infected others in their families.”

11) There are contradictions in the numbers of individuals in the family clusters – line 165 says that overall, it was more than one third 21/62 but of those who had been infected earlier – i.e. hospitalised for more than 10 days, it was “less than one third” but reported as 21/33 (line 169). This may be a typo but it is interesting if indeed the first cohort were more likely to be travellers while the more recently infected were locally acquired in Zhejiang from family members. This needs to be clarified.

**Response:** We are sorry that we made a mistake on this data. Line 165 has been revised as More than one one-third of these patients had underlying diseases (13 [39.4%]), including liver disease (4 [12.1%]), hypertension (4 [12.1%]), chronic obstructive pulmonary disease (1 [3%]), diabetes (1 [3%]), and cardiovascular disease (1 [1.6%]). 21 (33.9%) patients were found to be associated with familial clusters.”

12) Line 184 describes leukopenia as a feature of the patients but it was apparently seen in only a third so it may not be the case

**Response:** We are sorry that we didn’t describe the features accurately. The sentence is changed to “the blood counts of 19 (30.6%) patients showed leucopenia (white blood cell count less than  $4 \times 10^9/L$ ) and 26 (41.9%) patients showed lymphopenia 185 (lymphocyte count  $<1.0 \times 10^9/L$ ; table 2).”

13) Line 188 states that all patients had abnormal chest x-rays or CT scans. Then line 192 states that one patient did not have pneumonia. It is not clear what were the findings in the patient without pneumonia

**Response:** We are sorry that we made a mistake here. We have changed the sentence in Line 188 to “Abnormalities in chest CT images or X ray were detected among nearly all patients except one patient.”

14) Line 196 has the most intriguing statement that based on criteria of 3 days of stability and clearance of virus, only one of 62 patients was able to be discharged. This should be clarified – did these patients with apparently mild disease continue shedding virus? Or were they still unstable? This should be clarified

**Response:** Our fitness for discharge is based on abatement of fever for at least 3 days, with improvement of chest radiographic evidence and viral clearance in respiratory samples from lower respiratory tract. At the moment of submission, only one patient had met the criteria. We have added this criteria in the results.

15) The main conclusions are not clearly supported by the data. The mildness of the infection cannot be confirmed without more data. With the family clusters, it is not clear if these are just secondary infections or are they tertiary infections. Person to person transmission has been established since the beginning of the infection as there is still no evidence of an animal source.

**Response:** We have revised some statements in our manuscript including deleted the sentence of “2019-nCoV was easily transmitted from human to human”, and revised the last rows of first paragraph. As it is inappropriate to regards all patients in our study as second-generation cases, we also revised the whole manuscript to underscore our sample is a group of patients outside of Hubei Province.

Minor

1) The grammar needs some work – for example in the objectives, patients are not imported. The disease is imported with patients who move. Terms such as “Rare of patients developed shortness of breath” should be re-written as “It was rare for patients to develop shortness of breath”

**Response:** We revised all the sentences mentioned above and the language was edited by a native English specialist.

2) The case report form should be provided in the supplementary material and ideally this should conform to standard case reporting

**Response:** We provided the standard in the supplementary material.

Reviewer: 3

Recommendation:

Comments:

This is a retrospective observational study describing clinical findings in patients infected with the 2019-nCoV in the Zhejiang province, which reports the greater toll



in China after the Hubei province. Available data in the literature on clinical course of patients infected by the 2019-nCoV are still scarce, and gathering clinical findings is of high interest.

In general, the manuscript would benefit from thorough language editing.

The study has been approved by local ethics committee, and the authors clearly specify that informed consent has been waived because of the urgent need to collect data on a new pathogen.

Some shortcomings needs to be addressed.

Major concerns:

Zhejiang is the province where most of the cases are reported after Hubei, where 829 confirmed patients were reported as of Feb 3, 2020. The authors present here important clinical data. However, only 33 of the patients they describe have a follow-up of more than 10 days after onset of disease, and the length of the disease is not specified. As the author stated, Huang et al. reported in the Lancet that the novel 2019 pneumonia is a long disease, and that complications (and ICU admissions) appear in median 10 days after onset of symptoms. Most of the patients described here are still hospitalized at the time of the writing, and their final outcome is still unknown. The authors state that in their cohort, patients present with milder disease than what has been described from Wuhan, based on the fact that only one on 33 patient with symptoms lasting more than 10 days presented with dyspnea. However, all but one of the described patients presented with imaging confirmed pneumonia, and no data is available on pulse oximetry or on the need for supplemental oxygen. It would be of great interest to have data presenting the whole course of disease and the outcome of the patients, in order to be able to conclude that the disease is less severe that what has been observed in Wuhan.

**Response:** We understand the reviewer's concern. It is indeed that the disease progression is long and our sample only consists of a small number of patients (33) with over 10 days after onset of symptoms. The conclusion based on this small sample size is limited. We have pointed this in our limitation section. However, we still want to point out that our study is the first study that report clinical features outside of Wuhan, the source site of outbreak. This information is important given the widespread of the disease across China or even the world. In addition, this small sample size is still comparable with the initial 41 cases reported by Huang, et al.

The authors should specify which clinical material was used to confirm the diagnosis, and what were the results of the RT-PCR tests in the different specimen tested, if available.

**Response:** We used sputum and throat-swabs to perform the RT-PCR. We have added them in the methods.

The authors report temperature and respiratory rate of the patients. Are there any data on pulse oximetry or blood pressure available? This is important since the authors state that patients with a saturation below 93% in ambient air have been treated with investigational therapeutics, and since this is a marker of the severity of a lung disease.

Among administered treatment, could the authors specify how many patients benefited from supplementary oxygen therapy?

**Response:** We agreed that pulse oximetry and BP are important index to analyze the disease severity. However, most patients received supplementary oxygen therapy once the 2019-nCoV infection was confirmed, so the pulse oximetry cannot reflect the patients' condition. We thought FiO<sub>2</sub> and oxygenation index would be better index than pulse oximetry, and have added FiO<sub>2</sub>, oxygenation index and mean arterial pressure in Table 1.

Minor concerns:

The authors state in the design of the study that data come from multiple centers. Could the authors specify (line 111) how many “designated hospitals” participated to the study, and which type of center it involves (tertiary, secondary, primary).

**Response:** We enrolled 7 designated hospitals into our study, which are all tertiary hospitals. The detailed case numbers of different hospitals were listed in the supplementary material.

Introduction:

- Line 73: the fact that snakes are intermediate hosts of this novel coronavirus is highly criticized in the scientific community. There is no current proof that coronaviruses can infect species other than mammal and Aves, and I would suggest to remove the word “snake” to avoid any further misunderstanding.

**Response:** We agreed and have removed the sentence.

- Lines 73 to 76: The statement that 2019-nCoV is “very similar” to SARS-CoV and MERS-CoV should be revised: all of those viruses are within the same genus of the subfamily Orthocoronavirinae in the family Coronaviridae. 2019-nCoV is like

SARS-CoV, a member of the subgenus Sarbecovirus (Beta-CoV lineage B), with which it shares more than 79% of its sequence, but is more distant to MERS-CoV, which belongs to the Merbecovirus subgenus (only 50% homology with nCoV). A reference on SARS should be added. Total cases of MERS and SARS shouldn't be added, since they display different case fatality rates.

**Response:** We appreciated the constructive suggestion and have revised the sentence and reference accordingly.

Methods:

- Could the authors share their standardized case-report form as supplementary material?

**Response:** We have added it in the supplementary materials.

- Line 125: "... real-time RT-PCR..." please correct.

**Response:** We have corrected the sentence.

- Line 128 "and so on": please specify which test has been performed.

**Response:** We have listed the laboratory tests in detail.

- Line 129: "lopina veltonavir" please use the international nonproprietary name

**Response:** Here we referred to Lopinavir/Ritonavir.

- Lines 132-133: please specify the dose and the molecule used for each treatment

**Response:** We have added the dose and molecule used for treatment.

- Please specify which antibiotic has been administered

**Response:** quinolones and Second generation  $\beta$ -lactams were administered if the fever lasted longer than 7 days or CRP  $\geq$  30.

- Line 135-136: only confirmed patients can clear the virus. The sentence should be rephrased for more clarity.

**Response:** The sentence was changed to "Suspected patients were ineligible for hospital discharge or discontinuation of isolation until 2019-nCoV clearance was granted (results of two real-time RT-PCR of 2019-nCoV RNA were negative > 24 hours apart)"

- Not being an epidemiologist, I won't extend on the statistical analysis.

**Response:** We have revised the statistical analysis according to other reviewers' advices.

Results:

- Characteristics of the patients: could the authors specify the age of the two younger patients? Are there any children below 5 years-old?

**Response:** The two younger patients were aged 10 and 11, and we have added in the result. There was no children below 5 years-old.

- Line 155-156: the method of calculation of the incubation period should be described in the methods section

**Response:** We have provided additional information in methods as the following: "The incubation period was defined as the time from exposure to the onset of illness, which was estimated among patients who could provide the exact date of close contact with a confirmed case or suspected case in Wuhan. We also investigated the familial clusters, meaning that there were index cases who travelled to Wuhan and then infected others in their families."

- When presenting the data in the table, clinical data such as temperature and respiratory rate should be displayed next to each other for more clarity, then followed by symptoms.

**Response:** We have adjusted the item of respiratory rate next to the temperature.

- Could the authors specify if patients presented with upper respiratory symptoms?

**Response:** We have listed specific upper respiratory symptoms, which are Cough, Expectoration and Hemoptysis. We found that there is a mistake with the data of hemoptysis in all patients group in Table 1, and we have corrected it.

- Could the authors specify the normal laboratory values range in table 2?

**Response:** We have added the normal laboratory values in Table 2.

- lines 185-186: "the D-dimer level were higher": this sentence should be rephrased for more clarity.

**Response:** We are sorry to make the mistake that "higher" should be replaced with "normal".

Discussion:

- Could the authors specify what they mean by "air prevention"?

**Response:** We have deleted this sentence, because we can't draw any conclusion about the transmission mode of 2019-nCoV in this study.

- The authors should discuss the fact that antiviral therapy, gamma globulins and steroids were administered within an uncontrolled study, and that no conclusion can be drawn on their effect.

**Response:** We agree that antiviral therapy, gamma globulins and steroids haven't been proven to benefit on the treatment of 2019-nCoV and have mentioned in the discussion that "Whether the use of antiviral drugs, antibiotics and steroids affects the prognosis of patients remains unknown."

In a nutshell, gathering clinical data during an outbreak of a new pathogen is of high importance. The manuscript should benefit from a revision before publication. If data are available at the time of the revision and if the authors chose to review their paper, the paper could be updated with new available data on the outcome of the patients in their cohort.

**Response:** we have updated the data to the date of February 8, 2020.