Clinical Features and Outcomes in Imported and Non-Imported Patients With COVID-19: A Retrospective, Multi-centre, Descriptive Study

Jing Wang
Department of Respiratory Medicine, the Second Clinical hospital of Chongqing Medical University
https://orcid.org/0000-0001-8405-5444

Guodan Yuan
Chongqing Public healthy Center

Shaoyun Chen
Chongqing Wanzhou District People's Hospital

Jianrong Li
Chongqing Wanzhou District People's Hospital

Xiaqian Zhu
Shengjing Hospital of China Medical University

Junwei Shi
the Second Clinical Hospital of Chongqing Medical Hospital

Lingfang Xu
the Second Clinical Hospital of Chongqing Medical University

Wanchun Gao
Qinjiang Central Hospital of Chongqing

Liyong Xu
Qianjiang Central Hospital of Chongqing

Yuyan Song
Chongqing Public Health Medical Center

Depeng Jiang (depengjiang@163.com)

Research

Keywords: SARS-Cov-2, imported, non-imported, asymptomatic infections, lymphocytopenia

DOI: https://doi.org/10.21203/rs.3.rs-60942/v1

License: © This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License
Abstract

Background: Global outbreak of novel coronavirus 2019 (COVID-19) continues to constitute a public health emergency of international concern. However, few studies have directly compared the differences of clinical features and outcomes between imported and non-imported COVID-19 patients. We aimed to directly compare the differences of clinical features and outcomes between imported and non-imported COVID-19 patients.

Methods: We enrolled 275 patients (53 imported and 222 non-imported cases) with laboratory-confirmed COVID-19 from four designated hospitals in Chongqing, China. Epidemiological, demographic, clinical, laboratory, treatment, and outcome data were collected and analyzed. Independent samples t-test, Mann-Whitney U test, Wilcoxon test, $\chi^2$ test, or Fisher’s exact test were adopted to compare the difference between imported and non-imported groups where appropriate.

Results: The imported group had a higher proportion of asymptomatic patients (18.9% vs. 3.8%, $p=0.016$), lower lymphocyte count ($1.1\times10^9$/L vs. $1.5\times10^9$/L, $p=0.018$), higher neutrophil-to-lymphocyte ratio (NLR) (2.6 vs. 2.3, $p=0.0237$), higher proportion of CD4$^+$ T cells reduction (70% vs. 44.6%, $p=0.043$), longer duration of viral shedding (20 days vs. 18 days, $p=0.0416$) than the non-imported group. The symptomatic non-imported group had a lower lymphocyte count ($1.3\times10^9$/L vs. $1.6\times10^9$/L, $p=0.003$), lower CD4$^+$ and CD8$^+$ T cells, longer viral shedding (20 days vs. 13 days, $p<0.001$) and hospital stay (17 days vs. 14 days, $p=0.015$) than the asymptomatic non-imported group. Furthermore, when compared with imported group, asymptomatic non-imported group showed higher lymphocyte count ($1.6\times10^9$/L vs. $1.1\times10^9$/L, $p<0.001$) and CD4$^+$ T cells (567 vs. 375, $p=0.029$), while the symptomatic non-imported group showed no difference in lymphocyte count, CD4$^+$ or CD8$^+$ T cells ($p\geq0.0894$).

Conclusion: Our results indicated that when compared with imported patients, damage to the immune system by SARS-Cov-2 in non-imported patients was milder, and this might be mainly due to its higher asymptomatic proportion.

Clinical trial registration: ChiCTR2000033980. Registered 19 June 2020 - Retrospectively registered, http://www.chictr.org.cn.

Introduction

The ongoing pandemic of novel coronavirus 2019 (COVID-19) has led to more than 6,064,439 cases and 370,248 deaths globally by the end of May, 2020. According to data from China National Health Commission (NHC) daily report[1], the mortality rates of COVID-19 in Wuhan and non-Wuhan areas are quite different. Wuhan, the capital of Hubei Province, China, where the first Chinese COVID-19 patient has been reported, has a substantially higher mortality rate (2.9%) than that in the rest of China (0.4%) as of February 11, 2020[2]. Despite that a high mortality rate in Wuhan was attributed in part to the lack of medical resource available at the time of immediate need, it has been reported that patients with COVID-
19 in non-Wuhan areas exhibited mild or moderate symptoms, as compared with cases in Wuhan[3-5]. Thus, it is speculated that the discrepancy in mortality rate between Wuhan and non-Wuhan areas may also be due to disease differences at these areas. Currently, epidemiological and clinical characteristics of patients with COVID-19 have been reported [5-8]{N, 2020 #6;C, 2020 #7}{N, 2020 #6;C, 2020 #7}. However, few studies have been conducted to directly compare the differences in COVID-19 patients between Wuhan and non-Wuhan areas.

Since the available medical resources and treatment options vary greatly in different areas, it is of great significance to investigate the clinical characteristics and outcomes between imported and non-imported cases in a designated city. As the largest municipality adjacent to Hubei, Chongqing has been predicted to be the next outbreak city because of its close interaction with Wuhan. According to the mathematical model deduction published on the Lancet, as many as 150,000 new cases would be confirmed every day in Chongqing at the height of the epidemic [9]. It has estimated that about five million people had already left Wuhan before the city's lock down, and Chongqing ranked at the second top destination city [10]. Therefore, Chongqing is a good model to investigate the clinical characteristics and outcomes in imported and non-imported COVID-19 cases, which could provide important information to further understand the disease and provide important information to improve the prevention and control strategies for this disease.

A total of 275 patients with laboratory-confirmed COVID-19 were enrolled in this study from four designated hospitals. According to epidemiological characteristics, they were classified into imported cases and non-imported cases. The clinical, laboratory and radiological characteristics, as well as the treatment and clinical outcomes were compared between the two groups.

Methods

Study design and participants

Our multi-center retrospective study included 275 laboratory-confirmed COVID-19 patients admitted and treated in four designated hospitals (Chongqing Public Health Medical Center, Chongqing Wanzhou District People's Hospital, the Second Clinical Hospital of Chongqing Medical University and Qianjiang Central Hospital of Chongqing) in Chongqing, China. Based on the Chinese clinical guidance for COVID-19 pneumonia diagnosis and treatment (7th edition)[11], a confirmed case of COVID-19 was defined as positive for SARS-Cov-2 nucleic acid by real-time fluorescent RT-PCR for respiratory or blood specimens. We obtained the medical records and compiled data from January 15 to March 1. The data cutoff for the study was March 1, 2020. This study is approved by Ethics Committees of the four hospitals mentioned above and written informed consent was obtained from each enrolled patient.

Grouping

It has been reported that the incubation period of the SARS-CoV-2 could be as long as 27 days[12]. The included patients were divided into the imported group (with a history of travel or residence in Wuhan city
within 30 days before the onset of the disease) and the non-imported group (with no history of travel or residence in other cities 30 days before the onset of the disease). A total of 275 patients were included in our study, including 53 imported patients and 222 non-imported patients.

Data collection

The collected information including epidemiological, demographic, clinical, laboratory, treatment, and outcome data extracted from electronic medical records. All the clinical information and data during their hospitalization were followed up till Mar 1, 2020. During the process of data collection, we communicated with the attending physicians and other nursing staff directly if there was requirement of verification or loss of data. All the data were examined by two physicians (Zhu Xiaoqian and Yuan Guodan). As described previously, 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 individuals with confirmed or suspected COVID-19[5]. Viral shedding duration was defined as the time from illness onset to the first day of continuous negative tests with intervals of at least 24 hours[13]. The illness severity of COVID-19 was defined according to the Chinese clinical guidance for COVID-19 pneumonia diagnosis and treatment (7th edition)[11].

Statistical analysis

All statistical analyses were performed with SPSS 22.0 software program and p values < 0.05 were considered significantly. Continuous variables were presented as mean (SD) if they were normally distributed or median (IQR) if they are not, and categorical variables were presented as count (%). We used the independent samples t-test, Mann-Whitney U test, Wilcoxon test, χ² test, or Fisher’s exact test to compare the difference between imported and non-imported groups where appropriate.

Results

Epidemiological clinical features

The demographic and clinical characteristics of the patients are shown in Table 1. 275 patients with laboratory-confirmed COVID-19 were enrolled in this study, including 53 (19.3%) imported cases and 222 (80.7%) non-imported cases. Among them, 133 were male and 142 were female, with age ranging from 10 to 86 years and an average age of 47.4 years. The proportion of males patients in the imported group was higher than that in the non-imported group (62.3% vs. 44.6%, p = 0.015). The age distribution in the imported and non-imported groups were similar (47.2±14.4 vs. 47.5±16.8, p=0.101). In total, 62 of the 275 patients (22.6%) had at least one coexisting illness (e.g., hypertension or coronary heart disease). Except that non-imported group had a higher proportion of coronary heart disease of 14.4% (32/222) than that in the imported group (1.9%, 1/53, p=0.011), there was no significant difference between these two groups.
In terms of clinical classification, 13 (24.5%) patients were severe type including 6 (11.3%) critically ill cases in the imported group. In the non-imported group, 50 (22.5%) patients were severe type including 22 (9.9%) critically ill cases, according to the Chinese clinical guidance for COVID-19 pneumonia diagnosis and treatment (7th edition)[11]. No statistical difference was observed in the proportion of severe or critical illness between the two groups (p=0.523). The median incubation period was eight days in the non-imported group and six days in the imported group, both were longer than four days reported previously[14, 15]. Although the incubation period of the non-imported group was slightly longer than that of the imported group, there was no statistical difference between the two groups (p=0.334). The median time from symptoms onset to hospital admission are 4 days in both imported and non-imported groups.

The most common symptoms at illness onset in the imported group were cough and fever (both were 58.5%), fatigue and sore throat (both were 20.8%), diarrhea (13.2%) and headache (11.3%). The most common symptoms in the non-imported group were cough (54.1%), fever (36%), and fatigue (12.7%). When the two groups were compared, the proportion of asymptomatic patients in the non-imported group was significantly higher than that in the imported group (18.9% vs. 3.8%, p=0.016), and the proportions of symptoms of fever, sore throat, hemoptysis and diarrhea were all lower than those in the imported group (p≤0.048).

**Radiologic features**

Table 2 shows the radiologic and laboratory findings. Of 218 computer tomography (CT) scans that were performed at the time of admission, 78.9% revealed abnormal results including ground-glass opacity, local patchy shadowing, bilateral patchy shadowing and interstitial abnormalities. The most common patterns on chest CT in both imported and non-imported cases were bilateral patchy shadowing and local patchy shadowing. The abnormal patterns of two or more types were 33.3% in the imported group and 37.4% in the non-imported group. In general, there was no statistical difference in the proportion of the imported group and the non-imported group for each image performance (p≥0.175).

As to asymptomatic patients, 33.3% had no abnormal chest CT images. The most common patterns on chest CT were ground-glass opacity (20%) and local patchy shadowing (15.6%). The proportion of bilateral patchy shadowing and interstitial change was 6.7% and 4.4%, respectively. 22.2% of the patients had two or more of the above abnormal images on chest CT. When compared with the symptomatic patients, the ground-glass opacity was more common in asymptomatic patients (20% vs. 5.2%, p=0.004), while the proportions of bilateral patchy shadowing (6.7% vs. 22.5%) and multiple manifestations (22.2% vs. 39.9%) were lower (p≤0.02).

**Laboratory findings**

Lymphocytopenia was presented in 59.6% of the enrolled patients, and the proportion of lymphocytopenia in the imported group and the non-imported group was 69.8% and 57.2%, respectively. The difference was not statistically significant (p=0.093). However, the absolute value of lymphocyte count in the imported group was significantly lower than that in the non-imported group (1.1×10^9/L [IQR
0.9-1.6] vs. 1.5×10⁹ /L [IQR 1.0-1.8], p=0.018). 35.6% of the patients had increased C-reactive protein (CRP). The proportion of increased C-reactive protein in the imported group was 49.1%, which is higher than that (32.4%) in the non-imported group (p=0.02). The neutrophil-to-lymphocyte ratio (NLR) of the imported group was 2.6 [IQR 2.0-3.6], which is higher than that of the non-imported group (2.3 [IQR 1.5-3.6]) (p=0.0237). In total, 65.5% of the patients had elevated levels of activated partial thromboplastin time (APTT). 34.2% had elevated erythrocyte sedimentation rate (ESR), 24% had elevated Lactate dehydrogenase (LDH), and 23.3% had elevated procalcitonin (PCT). Less common were elevated levels of D-dimer, alanine aminotransferase (ALT), aspartate aminotransferase (AST), prothrombin time (PT) and creatine kinase (CK). There was no statistical difference between the two groups in all of these indicators (p≥0.065).

Furthermore, we investigated the CD4⁺ and CD8⁺ T cells between imported and non-imported groups. We found that the proportion of CD4⁺ T cells reduction in the imported group was higher than that in the non-imported group (70% vs. 44.6%, p=0.043), while the count of CD4⁺ T cells was not different between the imported and the non-imported group (375/μL [IQR 274-509.5] vs. 509 /μL [IQR 281-612], p=0.15), although the imported group indeed had a lower median value. The difference in proportion of CD8⁺ T reduction or the count of CD8⁺ T cells between the imported and non-imported groups was not statistically significantly different (p≥0.275).

As to asymptomatic and symptomatic patients, higher lymphocyte count as well as CD4⁺ T and CD8⁺ T lymphocyte was found in asymptomatic patients compared with symptomatic patients (p≤0.029).

Moreover, when compared with imported group, asymptomatic group showed higher lymphocyte count (1.6×10⁹/L vs. 1.1×10⁹/L, p<0.001) and CD4⁺ T cells(567 vs.375, p=0.029), while the symptomatic group showed no difference in lymphocyte count, CD4⁺ or CD8⁺ T cells (p ≥ 0.0894).

**Treatment and clinical outcomes**

All patients received antiviral therapy for 3-12 days, including oseltamivir, opivina and ritonavir tablets, arbidol or interferon alpha inhalation. 31.2% patients received antibiotic treatment. The duration of antibiotic treatment was 3-15 days (median 6 days [IQR 4–9]). 20.7% patients were also treated with systemic glucocorticoids. 20.4% patients received non-invasive ventilator mechanical ventilation for 3-20 days (median 8 days [IQR 6–18]). 3 (1.1%) patients used an invasive ventilator to assist ventilation for 3-20 days (median 17 [12–19]). Overall, there was no significant difference between the imported group and the non-imported group in all of these indicators.

As of March 1, 2020, all of the 53 patients in the imported group were discharged from the hospital, while 188 of the 222 patients in the non-imported group were discharged, and no patients had died. The median duration of hospitalization was 17 days (IQR 11.8-24.3) in the imported cases and 15 days (IQR 12-20) in the non-imported cases. There was no statistical difference in the two groups. Median duration
of viral shedding was 20 days (IQR 13.8-27) in the imported cases, which was longer than that of 18 days in the non-imported cases (IQR 12-23) \( (p = 0.0416) \).

Furthermore, the median duration of viral shedding in symptomatic patients was 20 days, which was longer than that of 13 days \( (p<0.001) \) in the asymptomatic patients, and the median duration of hospital stay in the symptomatic patients was longer than that in the asymptomatic patients (17 days vs. 14 days \( p=0.015 \)).

**Discussion**

It was found in our retrospective study that, compared with the imported cases, the non-imported cases displayed higher lymphocyte count, lower proportion of CD4\(^+\) T cells reduction, lower NLR value, shorter duration of viral shedding, but more atypical symptoms and a much higher asymptomatic proportion. As to asymptomatic non-imported patients, they had higher lymphocyte count including both CD4\(^+\) T and CD8\(^+\) T lymphocyte, shorter duration of viral shedding and length of hospital stay when compared with symptomatic non-imported group. Further subgroup analysis suggested that counts of lymphocyte and CD4\(^+\) T cell from non-imported asymptomatic group were higher than those in the imported patients, but there were no difference between non-imported symptomatic and imported patients.

Lymphocytopenia is a dominant feature of patients with COVID-19\(\) and the decrease of lymphocyte count was found to be more apparent in severe group compared with non-severe group\(\)\(\)\[16\]\. It has been suggested currently that the severity of lymphocytopenia reflects the severity of SARS-CoV-2 infection, serving as a key indicator for disease progression and outcome \(\)\[17\]\. However, there was no significant difference between the imported and non-imported groups in the proportion of severe type or critically ill type in our study. We speculated that this might be due to the relatively better general condition in imported cases, while the critically ill or frail patients were trapped in Wuhan due to their intolerance of long-distance travel. It is consistent with the fact that the proportion of severe cases in our imported group was much smaller than that previously reported in Wuhan area\(\)\[7\], which is consistent with previous reports\(\)\[3, 18\]\.

Lymphocytes and their subsets play a decisive role in maintaining immune homeostasis and inflammatory response throughout the body \(\)\[17\]\, which was highly involved in the pathological process of COVID-19\[19\]\. It has been reported that the immune responses induced by SARS-CoV-2 infection are two phase: immune defense-based protective phase and the second inflammation-driven damaging phase. Once a protective immune response was damaged, virus propagation and extensive tissues destruction occurred and a wide range of symptoms developed. Previous results have shown that SARS-Cov-2 mainly damaged T lymphocytes, especially CD4\(^+\) T lymphocytes \(\)\[19, 20\]\. Our findings of higher lymphocyte count and lower proportion of CD4\(^+\) T cells reduction in the non-imported group suggested that damage to the immune system in non-imported patients was milder. It may explain, at least in part, the observation in our study that the non-imported group has lower NLR and shorter duration of viral shedding than those in the imported group. Furthermore, higher lymphocyte count including both CD4\(^+\) T
and CD8⁺ T lymphocyte was found in asymptomatic non-imported COVID-19 patients indicated a stronger immune defense in these patients, which might contribute to the shorter duration of viral shedding and the shorter length of hospital stay.

The neutrophil-to-lymphocyte ratio (NLR), a well-known marker of systemic inflammation and infection, has been studied as a prognostic indicator for patients suffering from various diseases. It has been indicated that high NLR was associated with high levels of inflammation [21]. Systemic inflammation is associated with the development and progression of COVID-19. Higher NLR value has been demonstrated in severe COVID-19 cases when compared with the non-severe cases[19]. NLR has been indicated as an independent prognostic biomarker affecting disease progression in COVID-19 [19]. Thus, the higher NLR value in the imported group indicated a more serious inflammatory response.

Our study found that the median duration of viral shedding was shorter in the imported group. Viral load, virulence, immune response, therapeutic regimen are the main factors that affect the duration of viral shedding [22-26]. However, so far, there is no report of any clinically approved antiviral drugs that are effective against COVID-19[27-29]. In addition, our results displayed no significant difference in treatment strategy or the interval from symptoms to admission between the imported and non-imported groups. Previous research has shown that the lower the lymphocyte count is, the higher the viral load is [30]. A recent study has found that the SARS-CoV-2 RNA load in COVID-19 patients of nasopharyngeal was negatively correlated with lymphocyte count[31]. Therefore, we speculated that the duration of viral shedding varied between the imported and the non-imported groups was mainly due to difference in lymphocyte count in these groups.

The asymptomatic proportion was 18.9% in the non-imported group, which was significantly higher than that in the imported group (3.8%). Furthermore, only 36% of the patients in the non-imported group had fever, significantly lower than the 58.5% in the imported group. Meanwhile, the incidences of sore throat, haemoptysis and diarrhea in the non-imported group were also lower than that in the imported group, which suggested that atypical symptoms were more common in the non-imported group. Thus, symptom-based screening alone would fail to detect a high proportion of infectious cases. Also, 33.3% of asymptomatic patients had no abnormal chest CT findings. Thus, active contact tracing, strict health monitoring coupled with nucleic acid testing as well as serological test when necessary should be highlighted to identify asymptomatic infections.

It is noted that this study has some limitations. First, due to the retrospective study design, not all laboratory tests were done in all patients, including cytokine. Some difference in clinical features might be underestimated. Second, interpretation of our findings might be limited by the sample size. Despite these limitations, this study is, to our knowledge, the largest case series to date of direct comparison between imported and non-imported patients as well as symptomatic and asymptomatic patients. It is an extended and a more in-depth investigation of the previous report.

**Conclusion**
When compared with imported patients, damage to the immune system by SARS-Cov-2 in non-imported patients was milder, and this might be mainly due to its higher asymptomatic proportion.

**Abbreviations**

COVID-19: coronavirus 2019

NHC: National Health Commission

RT-PCR: Reverse transcription polymerase chain reaction

CT: computer tomography

CRP: C-reactive protein

NLR: neutrophil-to-lymphocyte ratio

APTT: activated partial thromboplastin time

ESR: erythrocyte sedimentation rate

LDH: Lactate dehydrogenase

PCT: procalcitonin

ALT: alanine aminotransferase

AST: aspartate aminotransferase

PT: prothrombin time

CK: creatine kinase

SpO2: Pulse Oxygen Saturation.

**Declarations**

**Ethics approval and consent to participate**

Ethics committee approval was obtained for the Second Clinical Hospital of Chongqing Medical University (reference number: 2020(83)), and all subjects provided written informed consent.

**Consent for publication**

Not applicable.
Availability of data and materials

The datasets used and/or analyzed during this current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Founding

This work was supported by Emergency Research Projects for COVID-19 of Chongqing Medical University (No. COMUNCP0309), Natural Science Foundation of Chongqing Science and technology bureau (No. cstc2018jcyjAX0115), National Natural Science Foundation of Chongqing (No. cstc2019jcyj-msxmX0849), the Joint Fund of Science and Health Medicine of Chongqing (No. 2019QNXM004).

Author contributions:

Depeng Jiang designed the research and wrote the manuscript, Jing Wang wrote the manuscript and analyzed partial data, Guodan Yuan collected data and wrote the manuscript, Shaoyun Chen, Jianrong Li, Xiaqian Zhu, Junwei Shi, Lingfang Xu, Wanchun Gao, Liyong Xu, Yuyan Song collected data. All authors approved the final version for submission.

Acknowledgments

We thank the participating centers of Chongqing Public Health Medical Center, Chongqing Wanzhou District People's Hospital, Qianjiang Central Hospital of Chongqing, and the Second Clinical Hospital of Chongqing Medical University and thank Huajie Lv in Southwest Hospital, Army Medical University for statistical analysis of this article.

References

1. Novel coronavirus in china
2. Epidemiology Working Group for Noip Epidemic Response CCfDC, Prevention: [The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. Zhonghua Liu Xing Bing Xue Za Zhi 2020, 41:145-151.
3. Wu J, Liu J, Zhao X, Liu C, Wang W, Wang D, Xu W, Zhang C, Yu J, Jiang B, et al: Clinical Characteristics of Imported Cases of COVID-19 in Jiangsu Province: A Multicenter Descriptive Study. Clin Infect Dis 2020.
4. Zhao XY, Xu XX, Yin HS, Hu QM, Xiong T, Tang YY, Yang AY, Yu BP, Huang ZP: Clinical characteristics of patients with 2019 coronavirus disease in a non-Wuhan area of Hubei Province, China: a retrospective study. BMC Infect Dis 2020, 20:311.
5. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, et al: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020, **395**:497-506.

6. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, et al: Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020, **395**:507-513.

7. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, et al: Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020, **395**:1054-1062.

8. Hu Z, Song C, Xu C, Jin G, Chen Y, Xu X, Ma H, Chen W, Lin Y, Zheng Y, et al: Clinical characteristics of 24 asymptomatic infections with COVID-19 screened among close contacts in Nanjing, China. *Sci China Life Sci* 2020.

9. Wu JT, Leung K, Leung GM: Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. *Lancet* 2020, **395**:689-697.

10. Chen ZL, Zhang Q, Lu Y, Guo ZM, Zhang X, Zhang WJ, Guo C, Liao CH, Li QL, Han XH, Lu JH: Distribution of the COVID-19 epidemic and correlation with population emigration from Wuhan, China. *Chin Med J (Engl)* 2020, **133**:1044-1050.

11. China NHCoT/PsRo: Diagnosis and treatment protocols of pneumonia caused by a novel coronavirus (trial version 7). [http://www.nhc.gov.cn/yzygj/s7652m/202003/a31191442e29474b98bfed5579d5af95.shtml](http://www.nhc.gov.cn/yzygj/s7652m/202003/a31191442e29474b98bfed5579d5af95.shtml).

12. Reuters. Coronavirus incubation could be as long as 27 days, Chinese provincial government says.

13. Fielding JE, Kelly HA, Mercer GN, Glass K: Systematic review of influenza A(H1N1)pdm09 virus shedding: duration is affected by severity, but not age. *Influenza Other Respir Viruses* 2014, **8**:142-150.

14. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, Liu L, Shan H, Lei CL, Hui DSC, et al: Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 2020, **382**:1708-1720.

15. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 2020, **368**:m792.

16. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Deng Y, Weng Z, Yang L: Lymphopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A systemic review and meta-analysis. *Int J Infect Dis* 2020, **96**:131-135.

17. Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, Wang Q, Miao H: Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther* 2020, **5**:33.

18. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, Ma CL, Li SB, Wang HY, Zhang S, Gao HN, et al: Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 2020, **368**:m606.

19. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, Xie C, Ma K, Shang K, Wang W, Tian DS: Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *Clin Infect Dis* 2020.
20. Zheng M, Gao Y, Wang G, Song G, Liu S, Sun D, Xu Y, Tian Z: Functional exhaustion of antiviral lymphocytes in COVID-19 patients. *Cell Mol Immunol* 2020, 17:533-535.

21. Li W, Ai X, Ni Y, Ye Z, Liang Z: The Association Between the Neutrophil-to-Lymphocyte Ratio and Mortality in Patients With Acute Respiratory Distress Syndrome: A Retrospective Cohort Study. *Shock* 2019, 51:161-167.

22. Lee N, Chan PK, Hui DS, Rainer TH, Wong E, Choi KW, Lui GC, Wong BC, Wong RY, Lam WY, et al: Viral loads and duration of viral shedding in adult patients hospitalized with influenza. *J Infect Dis* 2009, 200:492-500.

23. Gustavsson L, Skovbjerg S, Lindh M, Westin J, Andersson LM: Low serum levels of CCL5 are associated with longer duration of viral shedding in norovirus infection. *J Clin Virol* 2015, 69:133-137.

24. Ling LM, Chow AL, Lye DC, Tan AS, Krishnan P, Cui L, Win NN, Chan M, Lim PL, Lee CC, Leo YS: Effects of early oseltamivir therapy on viral shedding in 2009 pandemic influenza A (H1N1) virus infection. *Clin Infect Dis* 2010, 50:963-969.

25. Khoury J, Szwarcwort M, Kra-Oz Z, Saffuri M, Seh K, Yahalomi T, Braun E, Azzam ZS, Paul M, Neuberger A: Duration of viral shedding and factors associated with prolonged shedding among inpatients with influenza treated with oseltamivir: a prospective cohort study. *Eur J Clin Microbiol Infect Dis* 2018, 37:319-323.

26. Leung YH, Lim WL, Wong MH, Chuang SK: Delayed oseltamivir treatment is associated with longer viral shedding of pandemic (H1N1) 2009 virus. *Epidemiol Infect* 2012, 140:814-817.

27. Chakraborty I, Maity P: COVID-19 outbreak: Migration, effects on society, global environment and prevention. *Sci Total Environ* 2020, 728:138882.

28. Tang W, Cao Z, Han M, Wang Z, Chen J, Sun W, Wu Y, Xiao W, Liu S, Chen E, et al: Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ* 2020, 369:m1849.

29. Srinivas P, Sacha G, Koval C: Antivirals for COVID-19. *Cleve Clin J Med* 2020.

30. Wang WK, Chen SY, Liu JJ, Kao CL, Chen HL, Chiang BL, Wang JT, Sheng WH, Hsueh PR, Yang CF, et al: Temporal relationship of viral load, ribavirin, interleukin (IL)-6, IL-8, and clinical progression in patients with severe acute respiratory syndrome. *Clin Infect Dis* 2004, 39:1071-1075.

31. Liu Y, Liao W, Wan L, Xiang T, Zhang W: Correlation Between Relative Nasopharyngeal Virus RNA Load and Lymphocyte Count Disease Severity in Patients with COVID-19. *Viral Immunol* 2020.

Tables

Table 1. Demographics and clinical characteristics of patients with COVID-19
| Characteristics          | All patients (n=275) | Imported cases (n=53) | Non-imported cases (n=222) | P value |
|--------------------------|----------------------|-----------------------|----------------------------|---------|
| Disease severity status  |                      |                       |                            | 0.943   |
| General                  | 212(77.1%)           | 40(75.5%)             | 172(77.5%)                 |         |
| Severe                   | 35(12.7%)            | 7(13.2%)              | 28(12.6%)                  |         |
| Critical                 | 28(10.2%)            | 6(11.3%)              | 22(9.9%)                   |         |
| Age, years               | 47.4±16.6            | 47.2±14.4             | 47.5±16.8                  | 0.101   |
| Sex                      |                      |                       |                            | 0.015   |
| Female                   | 142(51.6%)           | 20(37.7%)             | 123(55.4%)                 |         |
| Male                     | 133(48.4%)           | 33(62.3%)             | 99(44.6%)                  |         |
| Smoking                  | 48(17.5%)            | 12(22.6%)             | 36(16.2%)                  | 0.268   |
| Coexisting disorder      |                      |                       |                            |         |
| Any                      | 62(22.6%)            | 13(24.5%)             | 49(22.1%)                  | 0.114   |
| Hypertension             | 26(9.5%)             | 5(9.4%)               | 21(9.5%)                   | 0.964   |
| Diabetes                 | 8(2.9%)              | 2(3.8%)               | 6(2.7%)                    | 0.694   |
| Coronary heart disease   | 33(12%)              | 1(1.9%)               | 32(14.4%)                  | 0.011   |
| Respiratory system disease| 4(1.5%)             | 1(1.9%)               | 3(1.4%)                    | 0.412   |
| Otherd                   | 33(12.0%)            | 8(15.1%)              | 25(11.3%)                  | 0.314   |
| Symptoms                 |                      |                       |                            |         |
| Symptomless              | 45(16.4%)            | 3(5.7%)               | 42(18.9%)                  | 0.016   |
| Fever                    | 111(40.4%)           | 31(58.5%)             | 80(36%)                    | 0.004   |
| Cough                    | 151(54.9%)           | 31(58.5%)             | 120(54.1%)                 | 0.246   |
| Myalgia                  | 17(6.2%)             | 4(7.6%)               | 13(5.9%)                   | 0.388   |
| Headache                 | 23(8.4%)             | 6(11.3%)              | 17(7.7%)                   | 0.234   |
| Sore throat              | 25(9.1%)             | 11(20.8%)             | 14(6.3%)                   | 0.001   |
| Fatigue                  | 39(14.2%)            | 11(20.8%)             | 28(12.6%)                  | 0.075   |
| Rhinorrhoea              | 13(4.7%)             | 3(5.7%)               | 10(4.5%)                   | 0.002   |
| Chest pain               | 3(1.1%)              | 0                     | 3(1.4%)                    | 0.546   |
| Haemoptysis              | 2(0.7%)              | 2(3.8%)               | 0                          | 0.034   |
|                          | Group A        | Group B        | Group C        | p-value |
|--------------------------|----------------|----------------|----------------|---------|
| Dyspnoea                 | 14 (5.1%)      | 2 (3.8%)       | 12 (5.4%)      | 0.402   |
| Nausea or vomiting       | 11 (4%)        | 1 (1.9%)       | 10 (4.5%)      | 0.360   |
| Diarrhoea                | 20 (7.3%)      | 7 (13.2%)      | 13 (5.9%)      | 0.048   |
| SpO_2 (%) on admission   | 97±2.1         | 97.5±2.5       | 96.8±1.9       | 0.914   |
| Time from illness onset to hospital admission (days) | 4 (1-7) | 4 (2-6.8) | 4 (1-7) | 0.198 |
| Incubation period (days) | 7 (4-12)       | 6 (3.3-9.8)    | 8 (4-13)       | 0.334   |

Data are expressed as mean(SD), median (IQR), n (%). p values were calculated by independent samples t-test, Mann-Whitney U test, $\chi^2$ test, or Fisher's exact test, as appropriate. SpO2: Pulse Oxygen Saturation.

**Table 2. Radiographic and laboratory findings of patients with COVID-19**
| Variable                        | All patients (n=218) | Imported case (n=34) | Non-imported cases (n=184) | P value |
|--------------------------------|----------------------|----------------------|-----------------------------|---------|
| **CT findings**                |                      |                      |                             |         |
| Ground-glass opacity           | 18(8.3%)             | 1(2.9%)              | 17(9.2%)                    | 0.32    |
| Local patchy shadowing         | 25(11.5%)            | 6(17.7%)             | 19(10.3%)                   | 0.241   |
| Bilateral patchy shadowing     | 42(19.3%)            | 9(26.5%)             | 33(17.9%)                   | 0.244   |
| Interstitial abnormalities     | 7(3.2%)              | 2(5.9%)              | 5(2.7%)                     | 0.3     |
| No abnormal density shadow     | 46(21.1%)            | 4(11.8%)             | 42(22.8%)                   | 0.175   |
| Multiple manifestations        | 80(36.7%)            | 12(35.3%)            | 68(37.0%)                   | 0.647   |
| **Laboratory findings**        |                      |                      |                             |         |
| WBC count (x10^9/L)            | 5.1(4.1-6.3)         | 4.7(4.1-6.2)         | 5.1(4.1-6.3)                | 0.28    |
| Neutrophil count (x10^9/L)     | 3.3(2.4-4.2)         | 3.2(2.7-4.0)         | 3.3(2.4-4.2)                | 0.161   |
| Lymphocytes(x10^9/L)           | 1.5(1.0-1.8)         | 1.1(0.9-1.6)         | 1.5(1.0-1.8)                | 0.018   |
| <1.5x10^9/L                    | 164(59.6%)           | 37(69.8%)            | 127(57.2%)                  | 0.093   |
| NLR                            | 2.3(1.6-3.6)         | 2.6(2.0-3.6)         | 2.3(1.5-3.6)                | 0.0237  |
| Platelet count(x10^9/L)        | 180(137-227)         | 175(141-212)         | 181(136.5-229.5)            | 0.986   |
| CRP (mg/L)                     | 11.3(3.1-26.6)       | 12.4(3.9-34.6)       | 9.2(2.6-22.2)               | 0.879   |
| >10 mg/L                       | 98 (35.6%)           | 26(49.1%)            | 72(32.4%)                   | 0.02    |
| Procalcitonin (ng/mL)          | 0.04(0.03-0.07)      | 0.05(0.04-0.08)      | 0.04(0.03-0.07)             | 0.512   |
| >0.05 ng/mL                    | 64(23.3%)            | 17(32.1%)            | 47(21.2%)                   | 0.065   |
| ESR                            | 28(12-43)            | 32(20.5-48.5)        | 30.5(12-50.8)               | 0.463   |
| >20mm/h                        | 94(34.2%)            | 20(37.7%)            | 74(33.3%)                   | 0.372   |
| D-dimer (mg/L)                 | 0.23(0.13-0.43)      | 0.17(0.12-0.35)      | 0.23(0.13-0.4)              | 0.101   |
| >0.55 ng/mL                    | 45(16.4%)            | 9(17%)               | 36(16.2%)                   | 0.912   |
| LDH (U/L)                      | 188(163.5-250.5)     | 198(175-253)         | 187.5(163.8-243)            | 0.399   |
| >250U/L                        | 66(24%)              | 14(26.4%)            | 52(23.4%)                   | 0.403   |
| ALT ( U/L)                     | 19.5(14-30.3)        | 22(13-23.9)          | 19(14-31)                   | 0.852   |
| Parameter          | Value 1 (IQR)       | Value 2 (IQR)       | Value 3 (IQR)       | p value    |
|--------------------|--------------------|--------------------|--------------------|------------|
| >50U/L             | 35(12.7%)          | 4(7.5%)            | 31(14%)            | 0.256      |
| AST (U/L)          | 22(18-30.3)        | 22(18-30)          | 23(18-31)          | 0.699      |
| > 40U/L            | 25(9.1%)           | 2(3.8%)            | 23(10.4%)          | 0.184      |
| CK                 | 68(47-118)         | 64(46-112)         | 67(48.3-104)       | 0.831      |
| >200 U/L           | 19(6.9%)           | 5(9.4%)            | 14(6.3%)           | 0.367      |
| CKMB               | 9.5(6.9-12)        | 10.6(8.3-13.0)     | 9.1(6.4-11.9)      | 0.712      |
| >25 U/L            | 11(4%)             | 3(5.7%)            | 8(3.6%)            | 0.695      |
| Albumin            | 42(39.4-44.6)      | 42.5(39.3-45.1)    | 41.8(39.4-44.5)    | 0.609      |
| Scr (μmol/L)       | 66.5(57.4-79.6)    | 74(59.7-83.4)      | 65.8(57.1-78)      | 0.864      |
| >106μmol/L         | 14(5.1%)           | 4(7.6%)            | 10(4.5%)           | 0.232      |
| BUN (mmol/L)       | 3.8(3.0-4.7)       | 3.9(3.2-5.0)       | 3.7(3.0-4.7)       | 0.227      |
| >8.3 mmol/L        | 6(2.2%)            | 3(5.7%)            | 3(1.4%)            | 0.247      |
| Glucose (mmol/L)   | 6.1(5.3-7.1)       | 6.1(5.5-6.8)       | 6.0(5.2-7.1)       | 0.827      |
| > 6.1 mmol/L       | 80(29.1%)          | 16(30.2%)          | 64(28.8%)          | 0.912      |
| <3.9 mmol/L        | 1(0.4%)            | 0                  | 1(0.5%)            | 0.957      |
| PT (s)             | 11.7(11-12.4)      | 12(10.9-12.4)      | 11.7(11.1-12.35)   | 0.986      |
| > 14 s             | 21(7.6%)           | 3(5.7%)            | 18(8.1%)           | 0.774      |
| APTT (s)           | 37.8(31.2-41.6)    | 36.5(29.4-42.3)    | 38.1(32.6-41.8)    | 0.265      |
| > 40 s             | 180(65.5%)         | 31(58.5%)          | 149(67.1%)         | 0.262      |
| CD4+/uL            | 424(277-604)       | 375(274-510)       | 509(281-612)       | 0.15       |
| CD4+ T-lymphocytopenia | 118(47.8%)     | 28(62.2%)          | 90(44.6%)          | 0.047      |
| CD8+/uL            | 301(186-449)       | 304(221-449)       | 300(183-449)       | 0.694      |
| CD8+ T-lymphocytopenia | 78(32.1%)      | 12(27.9%)          | 66(33%)            | 0.592      |

Data are expressed as median (IQR), n (%). p values were calculated by Mann-Whitney U test, χ² test, or Fisher's exact test, as appropriate. CT, computer tomography; WBC, white blood cells counts; NLR, neutrophil-to-lymphocyte ratio; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, Lactate dehydrogenase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, Creatine kinase; CKMB, creatine kinase-MB Scr, Serum creatinine; BUN, Blood urea nitrogen; PT, Prothrombin time; APTT: Activated partial thromboplastin time.
Table 3. Treatments and clinical outcomes patients with COVID-19

| Treatment                        | All patients (n=275) | Imported cases (n=53) | Non-imported cases (n=222) | P value |
|----------------------------------|----------------------|-----------------------|---------------------------|---------|
| Antibiotic treatment             | 86(31.2%)            | 15(28.3%)             | 68(32.0%)                 | 0.868   |
| Antiviral therapy                | 275(100%)            | 53(100%)              | 222(100%)                 |         |
| Systemic glucocorticoids         | 57(20.7%)            | 12(22.6%)             | 45(20.3%)                 | 0.708   |
| Traditional Chinese medicine     | 258(93.8%)           | 48(69.8%)             | 164(73.9%)                | 0.33    |
| Oxygen support                   | 176(64%)             | 32(60.4%)             | 144(64.9%)                | 0.323   |
| Mechanical ventilation           |                      |                       |                           |         |
| Noninvasive or high-flow nasal cannula | 56(20.4%)   | 12(22.6%)             | 44(19.8%)                 | 0.362   |
| Invasive                         | 3(1.1%)              | 0                     | 3(1.4%)                   | 0.25    |
| **Outcomes**                     |                      |                       |                           |         |
| Duration of viral shedding       | 18(12-24)            | 20(13.8-27)           | 18(12-23)                 | 0.0416  |
| Length of hospital stay          | 16(12-21)            | 17(11.8-24.3)         | 15(12-20)                 | 0.177   |
| Clinical outcome                 |                      |                       |                           |         |
| Remained in hospital             | 34                   | 0                     | 34                        |         |
| Discharged                       | 241                  | 53                    | 188                       |         |

Data are expressed as median (IQR), n (%). p values were calculated by Mann-Whitney U test, $\chi^2$ test, or Fisher's exact test, as appropriate.

Table 4. Comparison of radiographic, laboratory findings and clinical outcome between asymptomatic and symptomatic COVID-19 patients
### CT findings

| CT finding                      | Symptomatic patients (n=143) | Asymptomatic patients (n=42) | p value |
|--------------------------------|-----------------------------|-----------------------------|---------|
| Ground-glass opacity           | 8(5.6%)                     | 9(21.4%)                    | 0.004   |
| Local patchy shadowing         | 14(9.8%)                    | 5(11.9%)                    | 0.44    |
| Bilateral patchy shadowing     | 30(21%)                     | 3(7.1%)                     | 0.027   |
| Interstitial abnormalities     | 3(2.1%)                     | 2(4.8%)                     | 0.318   |
| No abnormal density           | 29(20.3%)                   | 14(33.3%)                   | 0.063   |
| Multiple manifestations        | 59(41.3%)                   | 9(21.4%)                    | 0.014   |

### Laboratory findings

| Laboratory finding             | Symptomatic patients (n=180) | Asymptomatic patients (n=42) | p value |
|--------------------------------|-----------------------------|-----------------------------|---------|
| Lymphocytes(×10^9/L)           | 1.3(1.0-1.4)                | 1.6(1.2-2.2)                | 0.003   |
| CD^4+ T cells (/uL)            | 414(267.5-572.5)            | 567(369.8-750.8)            | 0.003   |
| CD^8+ T cells (/uL)            | 279(178.3-420.5)            | 370(254-537.3)              | 0.029   |
| NLR                            | 2.3(1.5-3.9)                | 2.0(1.6-2.7)                | 0.093   |

### Clinical outcomes

| Clinical outcome               | n=180                       | n=42                        | p value |
|--------------------------------|-----------------------------|-----------------------------|---------|
| Duration of viral shedding     | 20 (13-24)                  | 13(9-17.8)                  | < 0.001 |
| Length of hospital stay        | 17(12-22.5)                 | 14(11-19)                   | 0.015   |

Data are expressed as median (IQR), n (%). p values were calculated by Mann-Whitney U test, χ² test, or Fisher's exact test, as appropriate. CT, computer tomography; NLR, neutrophil-to-lymphocyte ratio.