



Epidemiological Study and Clinical Characterization of COVID-19 Cases in Xuzhou, China

Zhan-Zhong Liu¹, Chun-Ying Wang¹, Jian-Ye Yang², Qing-Hua Liu^{3,4},
Xiao Zhang^{3*} and Liang Wang^{3,4*}

¹Xuzhou Infectious Diseases Hospital, Affiliated Hospital of Xuzhou Medical University, Xuzhou 2210000, China

²Hubei Key Laboratory of Agricultural Bioinformatics, College of Informatics, Huazhong Agricultural University, Wuhan 430070, China

³Department of Bioinformatics, School of Medical Informatics and Engineering, Xuzhou Medical University, Xuzhou 221000, China

⁴Jiangsu Key Laboratory of New Drug Research and Clinical Pharmacy, School of Pharmacy, Xuzhou Medical University, Xuzhou 221000, China

Zhan-Zhong Liu and Chun-Ying Wang contributed equally to this study.

ABSTRACT

In this paper, an epidemiological study was performed by focusing on all confirmed patients with COVID-19 in Xuzhou, a prefecture-level city, and a transportation hub with 10.44 million population in the east region of China. The median age of the patients is 42-year-old and 45.57% are male; 25 cases (31.65%) are imported. 23 cases (29.11%) were confirmed between January 26 to 31, 2020 while 56 cases (70.89%) were from February 1 to 16, 2020. Among the ten administrative divisions of Xuzhou city, Suining county (n=31) and Pizhou City (n=15) have the most cases while Tongshan district has none. A representative familial cluster with 6 cases was analyzed in detail in order to get a better understanding of the transmission routes of the virus. Furthermore, we performed a retrospective, single-centre study of 41 COVID-19 patients at Xuzhou Infectious Diseases Hospital in terms of clinical findings, which provided an insightful understanding of the disease.

Article Information

Received 12 January 2021

Revised 25 December 2021

Accepted 26 January 2022

Available online 14 March 2022
(early access)

Published 22 April 2022

Authors' Contribution

Conceptualization, LW and XZ; Methodology, ZZZ and CYW; Software, LW; Validation, JYY; Formal analysis, ZZZ and CYW; Investigation, ZZZ and CYW; Resources, ZZZ and CYW; Data curation, JYY and QHL; Writing-original draft preparation, LW and XZ; Writing-review and editing, LW, XZ, ZZZ and CYW; Visualization, JYY; Supervision, LW; Project administration, LW and XZ; Funding acquisition, CYW and ZZZ. All authors have read and agreed to the published version of the manuscript.

Key words

SARS-CoV-2, COVID-19, Epidemiology, Clinical characterization, Familial cluster

INTRODUCTION

The outbreak of 2019 novel coronavirus disease (COVID-19) officially named by WHO (Heymann and Shindo, 2020) has been traced back to Huanan (Southern China) seafood wholesale market in Wuhan, China (Huang *et al.*, 2020). In addition, the novel coronavirus has been entitled by WHO as severe acute respiratory syndrome-related coronavirus 2, or SARS-CoV-2 because it is confirmed as a variant of the SARS-CoV (Enserink, 2020). So far, SARS-CoV-2 has caused a severe impact

on global public health and economies, which makes it necessary to get a deep understanding of its epidemiology. The urgently locked down in Wuhan, a megacity with 11 million people in the epicentre of the outbreak on Jan 23, 2020, greatly delayed the growth of the infection and limited the size of the epidemic (Tian *et al.*, 2020). However, the virus still spread rapidly both domestically and overseas, which may be partially due to Wuhan as the provincial capital city and the largest highway, railway and air transportation hub in central China, as well as the annual spring festival travel rush starting from Jan 10, 2020, during which there are typically 3 billion travel movements across China.

Unbiased whole genome sequencing of samples from patients with pneumonia, via a combination of Illumina and Nanopore platforms, revealed that SARS-CoV-2 is similar with some beta-coronavirus detected in bats and forms a clade within the subgenus Sarbecovirus, Orthocoronavirinae subfamily (Zhu *et al.*, 2020). Further sequencing analysis decoded another ten complete SARS-CoV-2 genome, revealing that the virus is about 88%

* Corresponding authors: changshui@hotmail.com; leon-wang@xzhmu.edu.cn
0030-9923/2022/0004-1747 \$ 9.00/0



Copyright 2022 by the authors. Licensee Zoological Society of Pakistan.

This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

similar to bat-SL-CoVZC45 and bat-SL-CoVZXC21, two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses while more distantly related with SARS-CoV and MERS-CoV (Lu *et al.*, 2020). Thus, it was indicated that the original host of SARS-CoV-2 could be bats. Normally, intermediate host is likely to be involved in the cross-species transmission of novel human viruses, which is the case for 2003 SARS-CoV outbreak (Chan and Chan, 2013). A new study focusing on the recombination of spike glycoprotein in SARS-CoV-2 indicated that intermediate host for SARS-CoV-2 could be snake (Ji *et al.*, 2020) while another metagenomics study suggested that pangolin facilitates the cross-species transmission, both of which, however, caused concerns and criticism due to lack of solid scientific evidence (Yranoski, 2020). In addition, during the viral transmissions among and interactions with hosts, multiple variants of SARS-CoV-2 have been identified. Except for the origin, transmission, and evolution of the novel coronavirus, some studies also pay close attention to the infection mechanisms of the virus and it is currently proposed that binding of the virus to the angiotensin-converting enzyme 2 (ACE2) receptor in humans leads to infection (Lu *et al.*, 2020).

R_0 , a parameter for describing the contagiousness or transmissibility of an infectious agent (Delamater *et al.*, 2019), was estimated by using exponential growth model method (Zhao *et al.*, 2020). However, the estimations might be biased due to insufficient data and the ongoing nature of the outbreak (Frieden and Lee, 2020). Based on current research findings, SARS-CoV-2 is highly contagious with estimated basic reproduction number R_0 ranging from 2.24 to 3.58 (Zhao *et al.*, 2020), which is generally similar with SARS-CoV (Jiang *et al.*, 2020). As for the death toll of COVID-19, previous epidemiological analysis showed that case-fatality rate of SARS-CoV-2 (2%) is much lower than SARS-CoV (9.6%) (Jiang *et al.*, 2020). However, there are still many uncertainties and the real number is unclear due to the ongoing nature of the pandemic. As far as we know, case-fatality rate varies and it is rather high in some countries such as Italy and Spain for now (Lazzerini and Putoto, 2020).

Although the research on its transmission, toxicity and immune mechanism has been relatively in-depth, the virus is still mutating and the pandemic is not over so far. Thus, research on the initial transmission and tracking of epidemics in the region based on epidemiological study remains of vital significance. Most of the epidemiological studies on COVID-19 focus on cases in megacities (Huang *et al.*, 2020; Zhu *et al.*, 2020; Jiang *et al.*, 2020; Chan *et al.*, 2020) while less about other areas such as prefecture-level cities. Xuzhou, is a major prefecture-level city with around 10.44 million registered population and 8.8 million

resident population; its GDP in 2018 reaches 680 billion yuan and ranks 33 out of 100 major cities in China. As one of the high-speed railway hub, Xuzhou forms a one-hour living circle with 4 provincial capitals: Nanjing, Zhengzhou, Jinan and Hefei. It is also noteworthy that there are multiple trains between Xuzhou and Wuhan each day within a three-hour driving distance. Thus, it would be meaningful to explore the outbreak of COVID-19 in Xuzhou. Since the outbreak, a total of 79 COVID-19 cases were reported in Xuzhou, together with 2097 close contacts. No new cases have been added since Feb 16, 2020.

In this study, we performed a descriptive study of all confirmed cases in Xuzhou and provided an epidemiological overview of the disease in the prefecture-level city. A representative familial cluster was reported in detail in order to better understand how the virus is transmitted. In addition, clinical findings of 41 confirmed COVID-19 cases admitted to a single hospital were also present. Through this study, a better understanding of the COVID-19 disease in Xuzhou was achieved, which might facilitate epidemic prevention of COVID-19 in local areas in future.

MATERIALS AND METHODS

Epidemiological study

A total of 79 cases confirmed from Jan 26 to Feb. 16, 2020 at Xuzhou, no new cases were reported except for two discharged patients re-appearing as SARS-CoV-2 positive. It is noteworthy that one patient was a high-speed passenger that was reported symptoms when the train stopped at Xuzhou station, then urgently taken to a designated hospital; thus, is not included in the geographic study. Patients confirmed as local cases were those without known travel history out of Xuzhou while other patients were considered as imported cases.

Case data were collected from both Xuzhou Statistical Bureau and Xuzhou Centre for Disease Control and Prevention (CDC), the intra-urban population migration data from Wuhan to other cities (Top 100) was obtained from Baidu Migration Map (<https://qianxi.baidu.com/>). Clinical characterization, laboratory diagnosis, chest CT scanning and medical treatments of all COVID-19 patients were sourced from Xuzhou Infectious Diseases Hospital.

Pathogen detection, laboratory tests, and chest CT

Laboratory confirmation of SARS-CoV-2 was stipulated via nucleic acid test (real-time fluorescent RT-PCR). Laboratory diagnoses including routine blood test (RBT), blood biochemistry, and infection test were performed for the clustered cases. Imaging features of pneumoniae (Chest CT) were used as clinical diagnosis and confirmation. A series of CT images were recorded to

show how the ground glass patches in lungs change during hospitalization, which were described in detail for the 41 COVID-19 patients in [Supplementary Table SI](#).

Medical treatments and discharge standards

Medical treatment during hospitalization follows the COVID-19 treatment plan of Complementary and Natural Healthcare Council (CNHC), which includes: antiviral medicines lopinavir/ritonavir (400 mg/100 mg bid po), oseltamivir, arbidol, and interferon alfa-2b (5 MIU, aerosolized inhalation); antibacterial drugs moxifloxacin hydrochloride (400 mg, ivgtt, qd), biapenem (300 mg, ivgtt, q8h), and/or linezolid (600 mg, ivgtt, q12h). Immunoglobulin (20g/day) was given to a couple of patients. Drugs prescribed for glucocorticoid therapy include methylprednisolone (20~60 mg bid ivgtt), ketotifen fumarate (1 mg, qd, qn) and/or budesonide inhalation (1 mg, qd). Traditional Chinese medicine (TCM) Xuebijing injection was also used when necessary. Other medicines such as magnesium isoglycyrrhizinate, thymalfasin, adenosylmethionine succinate, and ambroxol were also used infrequently. All patients received oxygen therapy. Specific treatments for the 41 patients are described in detail in [Supplementary Table SII](#).

Patients were discharged home by following the COVID-19 treatment plan of China National Health Commission. In particular, patients were discharged when their body temperatures returned to normal for more than 3 consecutive days with improved respiratory symptoms, and pulmonary imaging shows significant absorption of inflammation. Meanwhile, nuclei acid detection for the pathogen SARS-CoV-2 needs to be negative for two consecutive tests at least one day apart.

Statistical analysis

All statistical analyses such as cumulative growth curve, average, mean, and histogram were performed in R package and Excel. P-values were calculated by using two-tailed unequal variance Student's t-test. R and Excel were used for all data visualization and transmission route illustration.

RESULTS

Epidemiological study

Geographic analysis

Geographic analysis of the 79 confirmed COVID-19 patients reveals that these cases are not evenly distributed among the 10 administrative divisions in Xuzhou ([Supplementary Fig. S1a](#)). Suining County was the area most affected by the outbreak, having 31 confirmed cases, among which only two cases were imported (#23 and #52). Further survey revealed that the high number was due to

nosocomial infection of nurses and doctors. Pizhou City has 15 patients, the second highest among all divisions, among which 9 cases were imported. Both Pei County and Jiawang District have 7 cases, with 4 and 2 imported cases, respectively. They are then followed by Yunlong District and Quanshan District with 5 cases each. Both of them have 2 imported cases. In addition, Gulou District has 3 cases with 1 imported case while all 3 cases in Feng County were locally transmitted. As for Xinyi City, it has 2 confirmed cases, both cases were imported, while Tongshan District has none with no clear reason. The resident population for each administrative division in terms of the number of all confirmed cases and the number of imported cases were also compared in [Supplementary Fig. S1b](#). In addition, all the 9 clustered cases were present in [Supplementary Fig. S1c](#), which included asymptomatic and human-to-human transmissions in familial and hospital settings via close contacts ([Li et al., 2020](#)).

Demographic analysis

Demographic analysis in terms of age and gender of all the patients were performed. In addition, whether the cases were imported or infected locally due to close contact with confirmed case(s) were also analyzed. According to the result in [Figure 1](#), the ages of the infected people range from 13 to 80 years old with most cases (n=22) at the age of 40-50, with the median age at 42. As for the gender, there are as many males (total 36, accounting for 45.57%) as females (total 43, 54.43%) in the confirmed cases. In terms of the infection types, 25 cases (31.65%) were imported while 54 cases (68.35%) were locally transmitted.

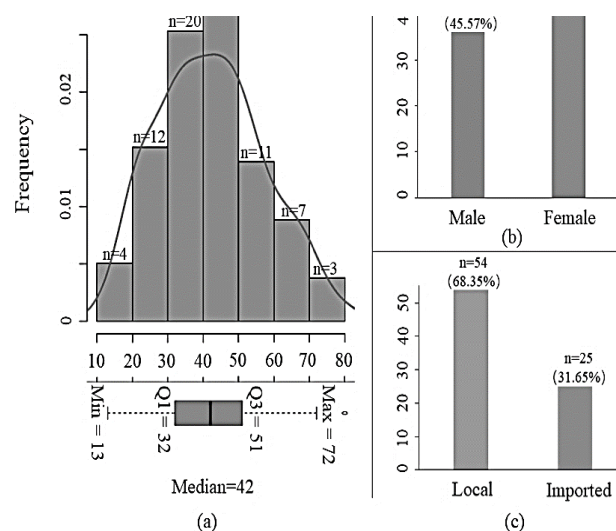


Fig. 1. Demographic analysis of 79 confirmed COVID19 cases in Xuzhou in terms of age, gender, and transmission routes. (a) age distribution, (b) sex ratio, (c) number of local and imported cases.

Cumulative growth

The number of daily new cases (from Jan. 26 to Feb. 16, 2020) and the discharged patients (from Feb. 5 to March 12, 2020) were analyzed (Fig. 2). The general trend of daily confirmed cases showed an approximately linear relationship with time (no. of cases= $3.91 \times \text{time}$) and the R-squared value (R^2) is equal to 0.9862 (Fig. 2a), indicating that 3.91 new cases emerge every day theoretically. R^2 is a statistical measure that represents the proportion of the variance for a dependent variable that is explained by an independent variable in this linear regression model. Here, it means that time and no. of cases are highly correlated in a linear mode. On the other hand, linear, polynomial, and logarithmic regressions show no specific patterns for the changing dynamics among daily-added new cases due to very small R^2 values. As for the relationship between time and discharged patients, linear regression showed no apparent correlation ($R^2=0.3295$). The first 3 were discharged on Feb. 5, 2020, on Feb. 17 reached the greatest, 14 patients were discharge home.

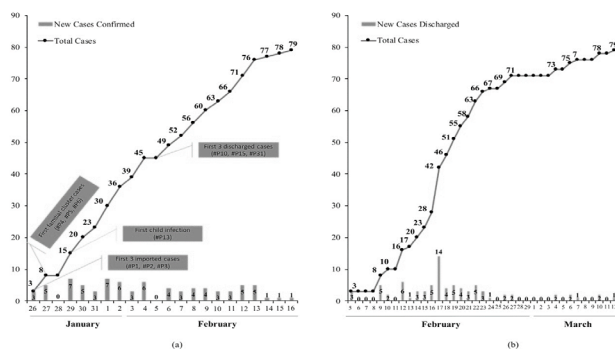


Fig. 2. Cumulative growth curve of new COVID19 cases and discharged patients in Xuzhou, China. (a) Daily new cases and cumulative sum curve. Continuously increasing trend of confirmed cases was observed. The first 3 cases (#P1, #P2, #P3) reported on Jan 26 were all imported and had Wuhan travel history. (b) Daily discharged cases and cumulative sum curve. On Feb 5, first 3 recovered patients (#P10, #P15, #P31) were discharged from hospital. All the patients were finally discharged and recovered from the disease.

Transportation analysis

A set of national transportation data from Jan 10 to Jan 24, 2020 were collected, revealing that the number of confirmed cases in a city is positively correlated with the percentage of input population from Wuhan city in a linear relationship ($R^2=0.9332$) (Fig. 3a), rather than from Hubei province ($R^2=0.4825$) (Fig. 3b). The top 3 cities with most confirmed cases had the highest percentage of input population from Wuhan. In addition, around 0.5 million

people left Wuhan before the lockdown on Jan 23, 2020 (Chen *et al.*, 2020), among which 0.15% of population that left Wuhan had entered into Xuzhou, meaning that theoretically there were around 7500 people from Wuhan entered into Xuzhou. Thus, even all imported 25 patients having Wuhan travel history, the actual infection rate could be very low at 0.33%.

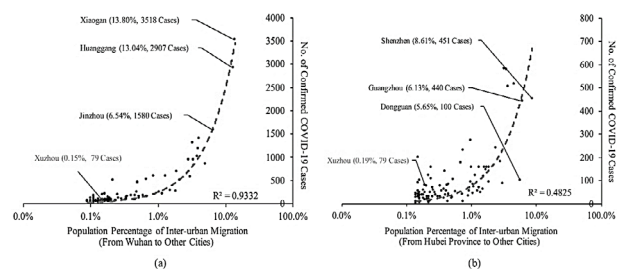


Fig. 3. Interurban population migration from (a) Wuhan city or (b) Hubei province to other cities in China from January 10 to the lockdown on January 24, 2020.

Familial cluster analysis

Among the 79 confirmed cases, we identified 11 clusters with clear case contact history (Supplementary Fig. S1c). To get a better look at how the virus transmits among cases, we studied in detail a representative familial cluster in Pizhou City, Xuzhou (Supplementary Fig. SII). A family of three (#P8: Father, #P45: Mother, #P13: Child) drove from Wuhan back to Pizhou on Jan. 20, 2020. They had a family gathering with #P11 (Mother of #P8), #P12 (Father of #P8), and #P14 (Sister of #P8) on Jan. 21. #P8 felt uncomfortable on Jan. 22, took medical treatment at local clinics on Jan. 23, and was isolated on Jan 24 due to lung infection. #P8 was finally confirmed positive through nucleic acid test of SARS-CoV-2 on Jan. 27. As a close contact of #P8, #P45 was isolated on Jan 26 and tested positive on Feb 04. As for #P11, #P12, #P13, and #P14, they were all tested positive on Jan 29.

Clinical findings

As the data provided and clinical findings were still lacking, we performed a single-centre analysis by focusing on patients admitted to Xuzhou Infectious Diseases Hospital only. As for 41 confirmed cases, average age is 42.16 ± 15.08 while male ($n=24$) and female ($n=17$) ratio is 1.41:1 (Supplementary Table SI), the average length of stay at hospital is 19 (7.0-39.0) days. Based on severity, these cases were classified into four categories: mild ($n=1$), moderate ($n=35$), severe ($n=4$), and critical ($n=1$). Before hospitalization, major clinical symptoms of the patients included cough (70.73%), fever (70.73%), throat congestion (70.73%), chest tightness (51.22%), sputum

(46.34%), and fatigue (39.02%) while minor symptoms were sore throat (21.95%), diarrhea (26.83%), headache (14.63%), shiver (19.51%), nausea and vomiting (7.32%), myalgia/arthritis (7.32%), and haemoptysis (2.44%). As for those with fever, peak body temperature ranges from 37.4 to 40 °C with the average at 38.4 °C. The pulse oxygen on admission ranges from 96 to 99% above the normal threshold of 94%. No cases were reported to have symptoms like tonsil enlargement, lymphadenopathy, and rash. In addition, no patients had hepatitis B. Underlying diseases in patients were also investigated, which showed that 7.32% of patients had diabetes, 17.07% hypertension, 4.88% coronary heart disease and 7.32% cerebrovascular disease; one patient was also diagnosed with hyperthyroidism (2.44%).

Laboratory tests

The 41 cases in terms of routine blood test (6 parameters), blood biochemistry test (16 parameters), and infection test (1 parameter) were retrospectively investigated, and the differential changes of each parameter at two time points with at least 7 days apart (earliest test date T1 and latest test date T2) were compared, 13 parameters of tests with significant changes were identified (Supplementary Table SII). Among which, those increased after medical treatment includes lymphocytes, platelet count, alanine aminotransferase, total cholesterol, triglycerides, potassium, chloride, and calcium while those decreased after medical treatments are lactate dehydrogenase, creatine kinase, total protein, creatinine, and C-reactive protein. Among these parameters, 4 of them were out of normal range, which were lymphocytes, creatinine, triglycerides, and C-reactive protein. In particular, lymphocytes count was lower than normal range at early infection probably due to the functional exhaustion of antiviral lymphocytes, which is consistent with early infection of SARS-CoV-2 (Zheng *et al.*, 2020) and then increased to normal range later after medical treatment, indicating improved immunity. It has been reported that elevated creatinine level is correlated with COVID-19 death due to kidney damage (Zhou *et al.*, 2020). In this study, creatinine changed from high level within normal range into lower out of range value, which might also indicate improved conditions of hospitalized patients. As for triglycerides, their level increased out of normal range after medical treatment, which might be linked with potential heart injury (Guo *et al.*, 2020). In addition, during early infection, C-reactive protein increased to abnormally high level (median=9.4 mg/L), which indicated high inflammation in the body. After treatment, the value returned to normal range with a median of 0.7 mg/L. Hence improved conditions. In sum, these laboratory test results

provided an overview of how patients responded toward medical treatment. For illustrative comparisons of the 13 significantly changed parameters, please refer to Figure 4.

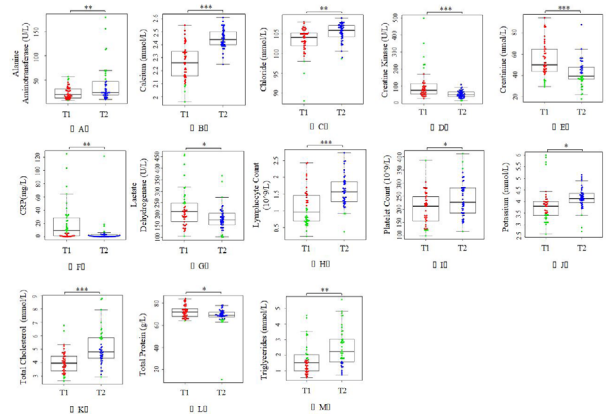


Fig. 4. Comparison of 13 parameters of laboratory tests in 41 COVID19 patients that were significantly changed after medical treatments for more than 7 days.

Notes: T1: first test. T2: second test. (A) Alanine Aminotransferase (normal range=950 U/L). (B) Calcium (mmol/L). (C) Chloride (mmol/L). (D) Creatine kinase (U/L). (E) Creatinine (umol/L). (F) CRP (mg/L). (G) Lactate dehydrogenase (U/L). (H) Lymphocytes ($10^9/L$). (I) Platelet count ($10^9/L$). (J) Potassium (mmol/L). (K) Total cholesterol (mmol/L). (L) Total protein (g/L). (M) Triglycerides (mmol/L). T1: Red dots. T2: Blue dots. Out of normal range: Green dots. Statistical significance was found in comparison via two tailed unequal variance Student's *t* test (*P* value: *, <0.05, **, <0.01, ***, <0.001).

Chest CT scanning

Of the 41 patients, 40 (97.56%) showed abnormal chest CT images, consisting 31 (75.61%) of bilateral pneumonia and 9 (21.95%) of unilateral pneumonia (Supplementary Table SI). Only 1 case (2.44%) had no abnormal density shadow, according to the clinical reports. During hospitalization, conditions of lung infection in some patients kept changing better. 34 out of 41 patients showed reduced inflammation and absorbed lesions. However, in some patients the situations of lung infection fluctuated or kept worsening.

Medical treatments

All patients were treated empirically by following the COVID-19 Treatment Plan of CNHC, received oxygen therapy and inhaled nebulized interferon, 32 patients took antibiotics to prevent secondary bacterial infection while 27 patients used HIV drugs lopinavir/ritonavir (Supplementary Table SII). In addition, 23 patients received arbidol treatment while 4 patients took oseltamivir. Both

oseltamivir and arbidol were antiviral drugs specifically for treating influenza. 22 patients were also given injection treatment of Xuebijing, which was used to as antagonism of endotoxin and suitable for systemic inflammatory response syndrome induced by infection. Moreover, 9 patients were given hormone therapy, though the treatment could lead to significant side effects based on the SARS treatment experience (Russell *et al.*, 2020). Several other medicines were also prescribed for treating patients during hospitalization. However, due to limited data access, we did not have detailed medication plan. The cure rate for COVID-19 patients was 100%, all were discharged home when fulfilling the discharge standards, the average length of stay at hospital was 19 days.

DISCUSSION

An epidemiological analysis of 1099 cases from 552 hospitals in 31 provinces/provincial municipalities until January 29th, 2020 in China showed an overview of the infected population as median age 47 years, ratio of male and female cases 1.39, and mortality rate of 1.36% (Guan *et al.*, 2020a). In addition, the median incubation period ranges from 0 to 24 days with a median of 3 days (Guan *et al.*, 2020b). A more comprehensive study of 44,672 confirmed cases by China CDC revealed that case-fatality rate was 2.9% while the male-to-female ratio was 0.99:1 in Wuhan, 1.04:1 in Hubei, and 1.06:1 in China overall (The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020). In this study, a similar epidemiological findings was conclude. In addition, an unevenly geographic distribution of the COVID-19 cases in 10 administrative regions in Xuzhou were identified, the reasons included nosocomial infection in Suining and high number of imported cases in Pizhou. Clustered cases have also been reported in China and overseas (Chan *et al.*, 2020; Phan *et al.*, 2020). In this study, 11 clustered among the 79 cases were identified and one representative familial cluster was reported in detail, which indicated the importance and necessity of the isolation/quarantine policy during the pandemic in order to control the number of the infected cases (Guan *et al.*, 2020b).

In terms of clinical findings, previous study confirmed that common symptoms at onset of illness due to SARS-CoV-2 infection include fever (40 [98%] of 41 patients), cough (31 [76%]), and fatigue (18 [44%]) while sputum (11 [28%] of 39), headache (3 [8%] of 38), haemoptysis (2 [5%] of 39), and diarrhoea (1 [3%] of 38) are less common. In our study, we found out that cough (70.73%), fever (70.73%), and throat congestion (70.73%) were the top 3 symptoms in 41 patients, which indicated that not all patients were guaranteed to have certain symptoms.

In addition, it was found that there were around 1.2% asymptomatic patients in a group of 44,672 confirmed cases (The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020). These results indicated that asymptomatic cases or cases with mild symptoms could pose a high risk to COVID-19. Through the analysis of the laboratory tests, we observed that 13 parameters were significantly changed after receiving medical treatments for more than 7 days. The changing patterns of some of the parameters such as WBC and CRP were consistent with previous reports, which reflected the intrinsic responses of immune systems (Wu *et al.*, 2020). In addition, these parameters could be used as biomarkers to assist the confirmation of the disease. However, due to the limited number of patients, these parameters need to be further verified by large samples and multi-centre data. As for chest CT scanning, it is of great significance for the diagnosis of COVID-19, which also facilitates the understanding of how the disease progresses during lung infection of SARS-CoV-2 (Wu *et al.*, 2020). As for medical therapy, we followed the COVID-19 Treatment Plan by CNHC. Nucleic acids tests of all the patients turned into negative for two consecutive times, which indicated the effectiveness of the empirical therapy. Currently, there is still no drugs for the disease (Wu *et al.*, 2020). However, several studies showed that hydroxychloroquine and Remdesivir could be promising potential treatment, although there are reported side effects and more clinical trials are required for further validation (Owens, 2020; Wang *et al.*, 2020). *In vitro* study has confirmed that hydroxychloroquine could inhibit SARS-CoV-2 (Liu *et al.*, 2020). A recent small-sized trial of the combination of hydroxychloroquine and azithromycin suggested that the treatment could reduce or eliminate the virus load in COVID-19 patients and FDA has authorized emergency use of this unapproved drugs (Liu *et al.*, 2020). However, the treatment is still very controversial and strict clinical trials are urgently needed to verify efficacy and safety of the drugs.

CONCLUSIONS

In this study, a comprehensive epidemiological study and clinical characterization of 79 COVID-19 cases in Xuzhou were performed, the geographic distributions, demographic features, inter-urban migration, clustered cases, and clinical findings of the confirmed cases were investigated. Clinical studies revealed that 13 laboratory test parameters changed significantly after more than 7-day hospitalization. Analysis of chest CT images provided insights into how lungs were influenced during the infection. Moreover, description of medical

therapy also provided empirical experience. This study aims to summarize the initial outbreak of Covid-19 in a prefecture level city, and provide experience for further epidemiological investigation.

ACKNOWLEDGMENT

This research was financially supported by 333 High-level Talent Project in Jiangsu Province (BRA2018277) and Xuzhou Science and Technology Plan Project (KC18165). We would like to thank the technical support from and helpful discussions with Prof. Michael J. Wise, Prof. Bing Gu, Dr. Jia-Wei Yan, Dr. Xiang-Yu Xi, and Ms. Ming-Qiu Wu. The authors would also like to thank the researchers who help us get better understanding of the SARS-CoV-2 virus and the medical doctors who work in the frontlines to save lives all over the world.

Ethics statement

This study was approved by the Ethics Committee of Xuzhou Infectious Diseases Hospital, an affiliated Hospital of Xuzhou Medical University (Approval No. XCYPJ-2020050501). All procedures were performed in accordance with the ethical standards of Ethics Committee at Xuzhou Infectious Diseases Hospital. Informed consent was obtained from all patients or if subjects are under 18, from a parent and/or legal guardian.

Supplementary material

The following documents are available as supplementary. [Supplementary Fig. S1](#): Schematic illustration of geographic distribution, case composition, and clusters of all COVID19 cases in Xuzhou, China. [Supplementary Fig. S2](#): Illustration of the contact history in a representative familial cluster with 6 cases at Pizhou City in Xuzhou. [Supplementary Table SI](#): Clinical description of chest CT images at different stages for 41 patients admitted into Xuzhou Infectious Diseases Hospital, Xuzhou, China. [Supplementary Table SII](#): Summary of medical treatment for 41 COVID-19 patients at Xuzhou Infectious Diseases Hospital.

The supplementary material can be access the online at: <https://dx.doi.org/10.17582/journal.pjz/20210112090155>

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

- Chan, J.F.W., Yuan, S., Kok, K.H., To, K.K.W., Chu, H., Yang, J., Xing, F., Liu, J., Yip, C.C.Y., Poon, R.W.S., Tsoi, H.W., Lo, S. K.F., Chan, K.-H., Poon, V.K.M., Chan, W.M., Ip, J.D., Cai, J.P., Cheng, V.C.C., Chen, H., Hui, C.K.M. and Yuen, K.Y., 2020. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: A study of a family cluster. *Lancet*, **395**: 514523. [https://doi.org/10.1016/S0140-6736\(20\)30154-9](https://doi.org/10.1016/S0140-6736(20)30154-9)
- Chan, P.K. and Chan, M.C., 2013. Tracing the SARS-coronavirus. *J. Thorac. Dis.*, **5**: S118-121.
- Chen, S., Yang, J., Yang, W., Wang, C. and Bärnighausen, T., 2020. COVID19 control in China during mass population movements at New Year. *Lancet*, **395**: 764766. [https://doi.org/10.1016/S0140-6736\(20\)30421-9](https://doi.org/10.1016/S0140-6736(20)30421-9)
- Delamater, P.L., Street, E.J., Leslie, T.F., Yang, Y.T. and Jacobsen, K.H., 2019. Complexity of the basic reproduction number (R_0). *Emerg. Infect. Dis.*, **25**: 1-4. <https://doi.org/10.3201/eid2501.171901>
- Enserink, M., 2020. Update: A bit chaotic. Christening of new coronavirus and its disease name create confusion. Available online: <https://www.science-mag.org/news/2020/02/bitchaoticchristeningnew-coronavirusanditsdiseasenamecreateconfusion> (accessed on 15 April 2020). <https://doi.org/10.1126/science.abb2806>
- Frieden, T.R. and Lee, C.T., 2020. Identifying and interrupting superspreading events implications for control of severe acute respiratory syndrome coronavirus 2. *Emerg. Infect. Dis.*, **26**: 1059-1066. <https://doi.org/10.3201/eid2606.200495>
- Guan, W.J., Chen, R.C. and Zhong, N.S., 2020a. Strategies for the prevention and management of coronavirus disease 2019. *Euro. Respirat. J.*, **55**: 2000597. <https://doi.org/10.1183/13993003.00597-2020>
- Guan, W.J., Ni, Z.Y., Hu, Y., Liang, W.H., Ou, C.Q., He, J.X., Liu, L., Shan, H., Lei, C.L., Hui, D.S.C., Du, B., Li, L.J., Zeng, G., Yuen, K.Y., Chen, R.C., Tang, C.L., Wang, T., Chen, P.Y., Xiang, J., Li, S.Y., Wang, J.L., Liang, Z.J., Peng, Y.X., Wei, L., Liu, Y., Hu, Y.H., Peng, P., Wang, J.M., Liu, J.Y., Chen, Z., Li, G., Zheng, Z.J., Qiu, S.Q., Luo, J., Ye, C.J., Zhu, S.Y. and Zhong, N.S., 2020b. Clinical characteristics of coronavirus disease 2019 in China. *N. Engl. J. Med.*, **382**: 17081720. <https://doi.org/10.1056/NEJMoa2002032>
- Guo, T., Fan, Y., Chen, M., Wu, X., Zhang, L., He, T., Wang, H., Wan, J., Wang, X. and Lu, Z., 2020. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID19). *JAMA Cardiol.*, **5**: 811-818. <https://doi.org/10.1001/jamacardio.2020.1017>

- Heymann, D.L. and Shindo, N., 2020. COVID19: what is next for public health? *Lancet*, **395**: 542-545. [https://doi.org/10.1016/S0140-6736\(20\)30374-3](https://doi.org/10.1016/S0140-6736(20)30374-3)
- Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie X., Yin, W., Li, H., Liu, M., Xiao, Y., Gao, H., Guo, L., Xie, J., Wang, G., Jiang, R., Gao, Z., Jin, Q., Wang, J. and Cao, B., 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*, **395**: 497-506. [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5)
- Ji, W., Wang, W., Zhao, X., Zai, J. and Li, X., 2020. Homologous recombination within the spike glycoprotein of the newly identified coronavirus may boost cross-species transmission from snake to human. *J. med. Virol.*, **94**: 433-440.
- Jiang, S., Xia, S., Ying, T. and Lu, L., 2020. A novel coronavirus (2019-nCoV) causing pneumonia associated respiratory syndrome. *Cell. mol. Immunol.*, **17**: 554. <https://doi.org/10.1038/s41423-020-0372-4>
- Lazzerini, M. and Putoto, G., 2020. COVID19 in Italy: momentous decisions and many uncertainties. *Lancet Glob. Hlth.*, **8**: e641-e642. [https://doi.org/10.1016/S2214-109X\(20\)30110-8](https://doi.org/10.1016/S2214-109X(20)30110-8)
- Li, C., Ji, F., Wang, L., Wang, L., Hao, J., Dai, M., Liu, Y., Pan, X., Fu, J., Li, L., Yang, G., Yang, J., Yan, X. and Gu, B., 2020. Asymptomatic and human to human transmission of SARS-CoV-2 in a 2-Family Cluster, Xuzhou, China. *Emerg. Infect. Dis.*, **26**: 1626-1628. <https://doi.org/10.3201/eid2607.200718>
- Liu, J., Cao, R., Xu, M., Wang, X., Zhang, H., Hu, H., Li, Y., Hu, Z., Zhong, W. and Wang, M., 2020. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV2 infection *in vitro*. *Cell Disc.*, **6**: 16. <https://doi.org/10.1038/s41421-020-0156-0>
- Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., Wang, W., Song, H., Huang, B., Zhu, N., Bi, Y., Ma, X., Zhan, F., Wang, L., Hu, T., Zhou, H., Hu, Z., Zhou, W., Zhao, L., Chen, J., Meng, Y., Wang, J., Lin, Y., Yuan, J., Xie, Z., Ma, J., Liu, W.J., Wang, D., Xu, W., Holmes, E.C., Gao, G.F., Wu, G., Chen, W., Shi, W. and Tan, W., 2020. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*, **395**: 565-574. [https://doi.org/10.1016/S0140-6736\(20\)30251-8](https://doi.org/10.1016/S0140-6736(20)30251-8)
- Owens, B., 2020. Excitement around hydroxychloroquine for treating COVID19 causes challenges for rheumatology. *Lancet Rheumatol.*, **2**: e257. [https://doi.org/10.1016/S2665-9913\(20\)30089-8](https://doi.org/10.1016/S2665-9913(20)30089-8)
- Phan, L.T., Nguyen, T.V., Luong, Q.C., Nguyen, T.V., Nguyen, H.T., Le, H.Q., Nguyen, T.T., Cao, T.M. and Pham, Q.D., 2020. Importation and human to human transmission of a novel coronavirus in vietnam. *N. Engl. J. Med.*, **382**: 872-874. <https://doi.org/10.1056/NEJMc2001272>
- Russell, C.D., Millar, J.E. and Baillie, J.K., 2020. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet*, **395**: 473-475. [https://doi.org/10.1016/S0140-6736\(20\)30317-2](https://doi.org/10.1016/S0140-6736(20)30317-2)
- The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team, 2020. Vital surveillances: The epidemiological characteristics of an outbreak of 2019 Novel Coronavirus Diseases (COVID19) China, 2020. *China CDC Weekly*, **2**: 113-122. <https://doi.org/10.46234/ccdcw2020.032>
- Tian, H., Liu, Y., Li, Y., Wu, C.H., Chen, B., Kraemer, M.U.G., Li, B., Cai, J., Xu, B., Yang, Q., Wang, B., Yang, P., Cui, Y.J., Zheng, P., Wang, Q.Y., Bjornstad, O.N., Yang, R.F., Grenfell, B., Pybus, O.G. and Dye, C., 2020. An investigation of transmission control measures during the first 50 days of the COVID19 epidemic in China. *Science*, **368**: 638-642. <https://doi.org/10.1126/science.abb6105>
- Wang, M., Cao, R., Zhang, L., Yang, X., Liu, J., Xu, M., Shi, Z., Hu, Z., Zhong, W. and Xiao, G., 2020. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) *in vitro*. *Cell Res.*, **30**: 269-271. <https://doi.org/10.1038/s41422-020-0282-0>
- Wu, J., Liu, J., Zhao, X., Liu, C., Wang, W., Wang, D., Xu, W., Zhang, C., Yu, J., Jiang, B., Cao, H. and Li, L., 2020. Clinical characteristics of imported cases of COVID19 in Jiangsu Province: A multicenter descriptive study. *Clin. Infect. Dis.*, **71**: 706-712. <https://doi.org/10.1093/cid/ciaa199>
- Yranoski, D., 2020. Did pangolins spread the China coronavirus to people? Available online: <https://www.nature.com/articles/d41586-020-00364-2> (accessed on 15, April, 2020).
- Zhao, S., Lin, Q., Ran, J., Musa, S.S., Yang, G., Wang, W., Lou, Y., Gao, D., Yang, L., He, D. and Wang M.H., 2020. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data driven analysis in the early phase of the outbreak. *Int. J. Infect. Dis.*, **92**: 214-217. <https://doi.org/10.1016/j.ijid.2020.01.050>

- Zheng, M., Gao, Y., Wang, G., Song, G., Liu, S., Sun, D., Xu, Y. and Tian, Z., 2020. Functional exhaustion of antiviral lymphocytes in COVID19 patients. *Cell. Mol. Immunol.*, **17**: 533-535. <https://doi.org/10.1038/s41423-020-0402-2>
- Zhou, F., Yu, T., Du, R., Fan, G., Liu, Y., Liu, Z., Xiang, J., Wang, Y., Song, B., Gu, X., Guan, L., Wei, Y., Li, H., Wu, X., Xu, J., Tu, S., Zhang, Y., Chen, H. and Cao, B., 2020. Clinical course and risk factors for mortality of adult inpatients with COVID19 in Wuhan, China: A retrospective cohort study. *Lancet*, **395**: 1054-1062. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)
- Zhu, N., Zhang, D., Wang, W., Li, X., Yang, B., Song, J., Zhao, X., Huang, B., Shi, W., Lu, R., Niu, P., Zhan, F., Ma, X., Wang, D., Xu, W., Wu, G., Gao, G.F. and Tan, W., 2020. A novel coronavirus from patients with pneumonia in China, 2019. *N. Engl. J. Med.*, **382**: 727-733. <https://doi.org/10.1056/NEJMoa2001017>